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## RESEARCH ARTICLE

**Editorial**

# Improving Quality of Maternal Health Services Through Research and Improvement of Health System in Indonesia

***Dwiana Ocviyanti***

The Indonesian Maternal Mortality Ratio (MMR) in 2015 was estimated at 305 deaths per 100.000 live births.[1] For years, maternal health programs in Indonesia focused on increasing the number of skilled personnel and promoted facility-based births.[2] The government and also private sector effort in increasing the number of health care facilities and health care provider especially midwives, doctor and obstetrics and gynecology specialists seems successfully increase the coverage of maternal health care and services in Indonesia. The Basic Health Research (RISKESDAS) in 2018 showed that the coverage of antenatal care by a health care provider in Indonesia is already high (96.1%).[3] The coverage of deliveries attended by the health care provider is also high (93.1%).3 Data from the Ministry of Health shows that during 2010 until 2013 the coverage of antenatal care and deliveries attended by the health care provider is already high and keep increasing, but still, it doesn't reflect in the decreasing of maternal mortality rate. The chief cause of maternal death in Indonesia are still bleeding and hypertension which covers 30.3% and 27.1% of maternal death in 2013. Obstructed labour and abortion as the cause of maternal death in 2013 are already rare (nearly 0%), so also infection (7.3%), but the percentage of maternal death because of other diseases like heart disease, renal disease, tuberculosis and cancer is increasing, from 32.2% in 2010 to 40.8% in 2013.[4,5] Some researches had already been done in trying to find the lack of correlation between the coverage of maternal health care programs and services and the maternal mortality in Indonesia.[6-11] Antenatal care has an integral role in detecting medical problem and/or diseases in pregnant women so also early detection of preeclampsia. Early referral to higher-level health facilities will save the mother from having complications in late gestational age or during delivery that will result in maternal and neonatal morbidity and mortality. A safe place for delivery means not only the facilities is well equipped for an emergency situation during delivery, but also means that these facilities are in 'reachable'' distance from the referral hospital if the mother and/or the baby need emergency referral. An evidence summit intended to gather all relevant evidence related to the cause of maternal and newborn death had been done by the Ministry of Health in collaboration with the Indonesian Academy of Sciences in 2018. The evidence is synthesized and translated into recommendations as a basis for stakeholders to formulate new health policies and follow up to accelerate the reduction of maternal and newborn mortality rates.[11] Evidence-Informed Policy Making (EIPM) approach was used to achieve the goal. EIPM focused on six topics, namely quality of care, referral system, implementation of national health insurance, local governance contributions, utilization of evidence for decision making and equity of woman. Several methods were used to collect evidence such as systematic reviews, public policy evaluation, practical implementation, lesson learned, political judgment, simple reviews of trusted global literature, and expert consensus. The quality of the evidence determines the level of confidence in recommendations. Policy and further research recommendations were arranged according to topic areas. Evidence-Based Health Policy Approach is still a big challenge in Indonesia, so this evidence summit is expected to increase awareness and culture about the importance of using scientific evidence and stakeholder involvement in formulating public policies.

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**Research Article**

# Incidence of Positive Human Papillomavirus High Risk in Negative Cytology Result

## *Insidensi Kejadian Human Papillomavirus RisikoTinggi Positif pada Hasil Sitologi Negatif*

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## Abstract

**Objective :** To report the incidence of positive HPV high risk in negative cytology result.

**Methods :** We collected 83 women underwent liquid-based cytology (LBC) and HPV DNA examination at the same time. We were using Diag Cor GenoFlow Human Papillomavirus Array Test (GenoFlow), a novel HPV test based on PCR and "Flow-through" hybridization that can identify 33 HPV subtypes: 18 types of High risk HPV such as 16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 81 and 82.

**Results :** We grouped the subjects based on age below or equal to 30 years old (n=6) and above 30 years old (n=77). We found a significant difference in HPV DNA result within this group (P = 0.034), with 19.3% had HPV DNA type 16 and 18 in a group of age above 30 years old. Our study showed that 27 women (32.5%) underwent screening for cervical cancer having negative LBC result but showed positive HPV DNA positive.

**Conclusions :** We found a significant difference in HPV DNA test result among women above 30 years old. Co-testing of Pap and HPV DNA is needed, especially if HPV DNA type 16 and 18 were found among negative Pap results.

**Keywords :** Cervical cancer, HPV DNA, incidence, LBC, screening.

## *Abstrak*

***Tujuan :*** *Melaporkan insidensi dari HPV risiko tinggi yang positif pada hasil sitologi negatif.*

***Metode :*** *Kami mengumpulkan 83 perempuan yang menjalani liquid based cytology (LBV) dan pemeriksaan HPV DNA pada waktu yang bersamaan. Dengan menggunakan DiagCor GenoFlow Human Papilloma Virus Array Test (GenoFlow), yaitu sebuah uji HPV terbaru yang berbasis PCR dan "Flow-throug" hybridization dapat mengidentifikasi 33 subtipe HPV: 18 tipe HPV risiko tinggi seperti 16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 81 dan 82.*

***Hasil :*** *Kami mengelompokkan subjek berdasarkan usia di bawah atau setara 30 tahun dan di atas 30 tahun (n=77). Kami menemukan perbedaan signifikan dari hasil HPV DNA dalam kelompok ini (P=0,034), dengan 19.3% memiliki HPV DNA tipe 16 dan 18 dalam kelompok usia diatas 30 tahun. Penelitian ini menunjukkan 27 perempuan (32,5%) menjalani skrining kanker serviks memiliki hasil LBC yang negatif namun menunjukkan HPV DNA positif.*

***Kesimpulan :*** *Terdapat perbedaan signifikan dari uji HPV DNA pada wanita usia diatas 30 tahun. Pemeriksaan bersamaan antara Pap dan HPV DNA dibutuhkan terutama ketika HPV DNA tipe 16 dan 18 ditemukan pada hasil Pap negatif.*

***Kata kunci :*** *HPV DNA, insidensi, kanker serviks, LBC, skrining.*

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## INTRODUCTION

Indonesian population is estimated at around 93.15 million, where the majority of women with age above 15 years old, has an increased risk of cervical cancer. Cervical cancer is the second most affecting cancer in women in Indonesia, with the incidence of 20,928 per year since 2012. Based on the age category in Indonesia, cervical cancer also the second most frequent female cancer in women at the age of 14-55 years old. Approximately 4% of female in Indonesia is infected with Human Papilloma Virus (HPV) type 16/18 which cause 87% of cervical cancer.[1]

In the last 40 years in the United States, yearly screening with Pap smear will dramatically decrease the morbidity and mortality related to cervical cancer.[2] In Indonesia, the diagnostic methods such as Pap smear, Visual Inspection of acetic acid[3], and also HPV Deoxyribonucleic Acid (DNA) were also used with the screening number 24.4% until 2017, with the most common in the age 30 to 50 years old and five years screening period.1 Worldwide, two type of HPV (16 and 18) cause more than 70% of cervical cancer, 41-67% High-Grade Cervical Lesions (HSIL) and 16-32% Low-Grade Cervical Lesion (LSIL).

DiagCor GenoFlow Human Papillomavirus Array Test (Geno Flow) is a novel HPV test based on PCR and "Flow-through" hybridization that can identify 33 HPV subtypes[4], 18 types of High risk HPV such as16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58,59, 66,68, 73, 81 and 82 that count as the cause of the other 20% of cervical cancer[5,6] and the low risk HPV 15 type such as 6, 11, 26, 40, 42, 43, 44. 54, 55, 57, 61, 70, 71, 72, and 84.[6]

The newest guideline based on American Society for Colposcopy and Cervical Pathology ASCCP and American College of Obstetricians and Gynecologists ACOG recommended the DNA-HPV High-Risk examination as an additional routine examination in pap smear screening in women with the age of 30 or more. [2,7] NA-HPV has a potential role in the three main areas such as as the case triage inpatients with abnormal cytology LSIL or ASCUS, as monitoring for the post-therapy in patients with Cervical Intraepithelial Neoplasia8, and the last one as primary screening for the alternative or additional Pap smear.[7]

Food Drug Administration (FDA) in the United States agree in combination examination of DNA-HPV and cytology inpatients with the age of 30 or above. The age 30 or above was the critical ages for screening as the 30 years and below had the lower risk for invasive cervical cancer although has the high possibility to get the HPV infection temporarily.

Furthermore, the prevalence of HPV infection in women at the of 30 or above is lower than women with the younger age that causes increasing number in specificity in DNA-HPV examinaion.[9]

Although there is already an agreement in the screening age of 30, there is still an unclear issue whether there is still the same pattern in the age above 30 as long the women is still in screening methods. This is due to the score of pre-neoplastic incidence in this age group was low.[2] Based on the newest study, with Athena calculation that contributed as much as 35.000 women age 30 years and above, reported the decreasing number of high-risk DNA-HPV detection related with increasing age in all category with all degree of CIN that proves with pathological that shows the decreasing number dramatically in the HPV type 16 detection. The cohort study with high-risk DNA-HPV detection and cervical problem in perimenopause women (35 to 60 years old) shows the same results with decreasing correlation with the increasing age.[2]

The purpose of this paper is to assess the relationship between high-risk DNA HPV detection and normal cytology based on age category.

## METHODS

Every woman who came to Colposcopy clinic in the department of Obstetrics and Gynecology clinic in January to December 2016 to participate in the cohort prospective study to study the natural history of HPV infection along with the transition age in perimenopause women. Inclusion criteria in this study are female age 35 to 60 years, no cervical cancer, got information about the study and willing to participate in the study. The exclusion criteria of the study were pregnant women, intending to get pregnant, history of organ transplantation, and HIV positive.

After the subject sign the informed consent, the subject will complete the basic data and gynaecology examination the ethical committee of Faculty of Medicine Universitas Indonesia. The history of sociodemographic characteristic, reproduction history and menstruation, sexual history and the latest sexual activity, cigarette history were compiled in the anamnesis. The cervical screening and medical therapy history that include the result of HPV and Pap smear before, colposcopy, and therapy-related with the condition was also collected. All of the examinations were performed by the gynaecology consultant. The examination protocol of DNA HPV was done by speculum and cervical brush examination. With transport by the standard medium transport (clinical pathology), and got approval from the research ethics committee. We were using GenoFlow Human Papillomavirus Array Test for identifying HPV DNA subtype. The lowest detection limits of the GF assay for HPV16 and HPV18 were 25 copies and 20 copies, respectively, with a sensitivity of 80% and specificity of 23%.[10]

## Cervical Abnormality Detection and HPV Infection

The Pap smear classification was arranged to the severe level such as negative, ASCUS, LSIL, ASC-H, HSIL or cancer. At the cytology, classification is based on ASCUS or above ASCUS.

The extraction of the DNA-HPV detection and genotyping from the cervical specimen was by using GenoFlow Human Papillomavirus Array Test. For this analysis, HPV type 16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 81 and 82 are classified as high risk HPV. The other HPV besides that type was classified as negative even the result is positive.

## Statistical Analysis

Analysis of statistic using SPSS version 22 for analyzing the relationship between the variables. We analyze the relationship between LBC result and HPV DNA test, and as well as LBC result and HPV DNA type.

## RESULTS

We recruited 83 women who underwent LBC and HPV DNA examination. Our study showed that women having positive HPV DNA test were around 40 to 45 years of age, with the age of first sexual intercourse around 20 years old. Most of our HPV DNA positive population (56.5%) is having a one-time marriage, and work as housewives (28.9%) (Table 1).

**Table 1.** Demographic Data

| | HPV DNA Positive % | HPV DNA Negative % | *P- value* |
|---|---|---|---|
| Age (years) | 43 (95CI 40.38 – 45.62) | 45 (95CI 41.16 – 48.84) | >0.05 |
| Parity | 2 (95CI 1.67 – 2.49) | 2 (95CI 1.73 – 2.64) | >0.05 |
| Abortus | 0 (95CI .13 – .43) | 0 (95CI .07 – .66) | >0.05 |
| Living Child | 2 (95CI 1.58 – 2.30) | 2 (95CI 1.56 – 2.31) | >0.05 |
| Sexual Partner(s) | 46 (55.4) | 31 (37.3) | >0.05 |
| Single | | | |
| Multiple | 4 (4.8) | 2 (2.4) | |
| Duration of Mariage (years) | 20 (95CI 17.55 – 23.97) | 24 (95CI 18.01 – 25.87) | >0.05 |
| Age of First Sexual Contact | 20.5 (95CI 20.43 – 22.85) | 20 (95CI 19.89 – 23.5) | >0.05 |
| Cigarette Smoking | 11 (13.3) | 2 (2.4) | >0.05 |
| yes | | | |
| no | 39 (46.9) | 31 (37.4) | |
| Occupation | 24 (28.9) | 18 (21.7) | >0.05 |
| Housewife | | | |
| Private Sector | 21 (25.3) | 9 (10.8) | |
| Governmental Sector | 5 (10.0) | 6 (18.2) | |
| Contraception | 24 (28.9) | 14 (16.9) | >0.05 |
| None | | | |
| Sterilization | 2 (2.4) | 1 (1.2) | |
| IUD | 13 (15.7) | 12 (14.5) | |
| DMPA | 6 (7.2) | 4 (4.8) | |
| Condom | 0 (0) | 1 (1.2) | |
| OCP | 4 (4.8) | 1 (1.2) | |
| Implant | 1 (1.2) | 0 (0) | |

From our data, the eldest subject was 68 years old, and the youngest was 20 years old. We grouped the subjects by age below or equal to 30 years old (n=6) and above 30 years old (n=77). We found significant difference HPV DNA result within this grouping (P = 0.034), with 19.3% had HPV DNA type 16 and 18 in the group of age above 30 years old (Table 2).

**Table 2.** Relationship between Age below or Above 30 Years Old and HPV DNA Test

| Agey o | HPV DNA High Risk | | HPV DNA Low Risk/Negative | *P-value** |
|---|---|---|---|---|
| | HPV DNA Type 16 and/or 18 | Other HPV High-Risk Type | | |
| < 30 | 1 (1.2) | 0 (0) | 5 (6.0) | 0.034 |
| > 30 | 16 (19.3) | 33 (39.7) | 28 (33.7) | |
| Total | 17 (20.5) | 33 (39.7) | 33 (39.7) | |

*Chi-square test, relations between Age below or above 30 years old and HPV DNA result

Our study showed that 27 women (32.5%) underwent screening for cervical cancer having negative LBC result but showed positive HPV DNA positive. Only seven women (8.4%) that showed HSIL from LBC result, having HPV DNA test positive. There is no significant relation ($p<0.05$) between LBC result and HPV DNA result (Table 3).

**Table 3.** Relationship between LBC Result and HPV DNA Test

| | | HPV DNA Result | | Total | *P-value** |
|---|---|---|---|---|---|
| | | High Risk | Low Risk/Negative | | |
| LBC Result | HSIL | 7(8.4) | 2 (2.4) | 9 (10.8) | >0.05 |
| | LSIL | 2(2.4) | 1 (1.2) | 3 (3.6) | |
| | ASCH | 7 (8.4) | 8 (9.6) | 15 (18.1) | |
| | ASCUS | 7 (8.4) | 1 (1.2) | 8 (9.6) | |
| | Negative | 27 (32.5) | 21 (25.3) | 48 (57.8) | |
| | Total | 50 (60.2) | 33 (39.8) | 100 (100) | |

HPV DNA type that recorded positive in our study population mostly is HPV type 59 found in 19 women (22.8%), and yet 12 (14.5%) out of them showed negative LBC result. Only three women (3.6%) with HPV DNA of type 16 showed LBC result of HSIL (Table 4).

**Table 4.** Relationship between HPV DNA Type and LBC Result

| HPV DNA Type | LBC Result | | | | | | |
|---|---|---|---|---|---|---|---|
| | HSIL | LSIL | ASCH | ASCUS | Negative | Total | *P-value* |
| 16 | 3 (3.6) | 1 (1.2) | 1 (1.2) | 1 (1.2) | 8 (9.6) | 14 (16.8) | >0.05 |
| 18 | 1 (1.2) | 0 (0) | 1 (1.2) | 0 (0) | 3 (3.6) | 5 (6.0) | >0.05 |
| 58 | 2 (2.4) | 0 (0) | 0 (0) | 1 (1.2) | 0 (0) | 3 (3.6) | >0.05 |
| 59 | 1 (1.2) | 0 (0) | 3 (3.6) | 3 (3.6) | 12 (14.5) | 19 (22.8) | >0.05 |
| 52 | 1 (1.2) | 1 (1.2) | 3 (3.6) | 2 (2.4) | 11 (13.3) | 18 (21.6) | >0.05 |
| 35 | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (1.2) | 1 (1.2) | >0.05 |
| 56 | 0 (0) | 0 (0) | 3 (3.6) | 1 (1.2) | 3 (3.6) | 7 (8.4) | >0.05 |
| 66 | 0 (0) | 0 (0) | 4 (4.8) | 2 (2.4) | 10 (12.0) | 16 (19.2) | >0.05 |
| 68 | 1 (1.2) | 0 (0) | 4 (4.8) | 2 (2.4) | 9 (10.8) | 16 (19.2) | >0.05 |
| 51 | 1 (1.2) | 0 (0) | 1 (1.2) | 0 (0) | 2 (2.4) | 4 (4.8) | >0.05 |
| 45 | 0 (0) | 0 (0) | 2 (2.4) | 0 (0) | 2 (2.4) | 4 (4.8) | >0.05 |
| 81 | 0 (0) | 0 (0) | 0 (0) | 1 (1.2) | 0 (0) | 1 (1.2) | >0.05 |
| 53 | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (1.2) | 1 (1.2) | >0.05 |
| 33 | 1 (1.2) | 0 (0) | 1 (1.2) | 0 (0) | 1 (1.2) | 3 (3.6) | >0.05 |
| 39 | 1 (1.2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (1.2) | >0.05 |

## DISCUSSION

In our study, women that performed the screening is between the age of 20 – 68 years old, and the first sexual intercourse is 14 – 39 years old. Based on data in Indonesia, the median age of women that performed the sexual intercourse is 19-21.8years old; the cigarette prevalence is 3.8%, hormonal contraception is 49.4%, total fertility birth 2.6.[5]

From our study, we found significant differences in HPV DNA result among a group of age below 30 years old and above 30 years old. The guideline that is used nowadays that related to the cervical cancer screening is included all women with the age of 30 and above in one category. Based on this research, make an important question of homogeneity and HPV interpretation and Pap test at this age. Although the proportion of relative abnormality in low grade and high grade do not change with increasing age. It showed the loss of conformity between HR HPV detection and cytology abnormality with the increasing of age. Decreasing of HPV prevalency between all of the cytology level also found with the increasing age in the cohort study that contributed almost 1 million women with the age of 30 to 64 years.2For patients below 30 years old, especially in adolescents and young women, screening adolescents leads to the unnecessary evaluation and potentially to the treatment of pre-invasive cervical lesions that have a high probability of regressing spontaneously.[11]

Several studies show that HR HPV examination in a low degree of the lesion in women with older age shows beneficial to differentiate HPV infection that will grow into the precancer lesion. This is opposite to the study in the USA with RCT conclude that HR HPV screening has limited access to detect in low degree lesion. The approximate age in this study relatively young (27.9 years old) that makes it difficult to conclude in women above 30 years old, although from this study report 2x decreasing HR HPV prevalence in 18% of women LSIL above 30 years.[2]HR HPV type 16 and 18 need to have our attention since women with negative Pap and also had HPV-16 or HPV-18, colposcopy is recommended. ASC-US who also had HPV-16 or HPV-18 detected had approximately twice the risk of CIN 3+ as women with ASC-US and high-risk HPV types other than 16 or 18. Therefore, this population needs further colposcopy examination.

Although the presentation of HR HPV decrease in linear shape as related with age in the cytology abnormality, HPV prevalence with U shape and highest in the older age group. This pattern suggests that LR HPV dan HR HPV contributed to detection in patients with an older age group. Moreover, there is a strong relationship between the infection with low lever HPV and cervical abnormality in women with age above 45 years old that not seen in women with a younger age group. This condition is corresponding with observaional study before that mention the cervical transformation regression zone in older women and the high prevalence in LR HPV in vagina compare in cervical ephitelial.[2]

DNA HPV has better sensitivity. Therefore this could be an optional method in the HPV screening. A report in a cohort study with 324 women. Sensitivity and specivicity in cervical cytology, colposcopy, and DNA HPV is 66.66% and 93.54%, 86.84% and 86.32%, and 90% and 84.61%. With the false-negative as much as 33.3%, 8.95%, and 10%.[12] In a meta-analysis that compared the DNA HPV examination and cervical cytology with contribute 39050 participant with the asymptomatic clinic and 2% of pathological result NIS 1-2 from 11 studies, mentioned that the sensitivity and specificity of DNA HPV is 94% and 90%, with cervical cytology 70% and 95%. The false-negative in DNA HPV is 1/1000 women, and in cytology, the cervix is 6/1000 women.[13]The epidemiology data in Indonesia, the HPV type 16 and 18 prevalence in Indonesia is 4% in normal cytology and 87% in cervical cancer, and there is no data in HSIL and LSIL.[1]

The false negative in cervical cytology is caused by the 4 main problems, which are the error in the taking the sample with not taking the lesion part, tranfer error form the taking sample until the microsopic examination, error in the cell detection when the abnormal cell does not identify during the screening, the interpretation error when the abnormal cell detected but wrong interpretation. The minimal abnormal cell in the media could cause the false negative that frequently happen in the conventional Pap smear, with the highest error in the number of the abnormal cell< 30. The availability of micro

biopsy or Liquid-Based Cytology (LBC)group has a relatively smaller false negative, which is 6% if compared to conventional Pap smear (14%). Categorized the cause od the false negative in the cytology interpretation into; the high density of the micro biopsy and hyperchromatic material (27.3%), discariotic cell that broken, small or pale (37.8%), foreign material (8.4%), low level of contrast (7.4%), unexplainable (5.3%).[14]False negative is more frequent to be found in tumour type glandular than in squamosa (52% compare to 16%).[15]

The cervical cytology and DNA HPV has better accuracy. In a meta-analysis of two RCTs and six cross-sectional studies in women with NIS ≥2 mention that cytology examination only will show sensitivity (74.3%), specificity (95.1%) and false-negative(22.6%). On the other hand, in combination examination (cytology and DNA HPV) will give sensitivity (93.7%), specificity (85.8%) and false negative (8.3%).[16]A report in the cross-sectional study with 615 samples showed that DNA HPV positive in the negative cytology occurred in the HPV type based on the most frequent: 16,18, 51, 52, 6,56, 90, 39, 66, 33, dan 526.

This study reported routine examination in cervical cancer screening (cytology and DNA HPV) could give a different result. The HPV DNA test is having better sensitivity compare to citology. We found 32.5% of our study showed negative in cytology but having high-risk DNA result. A review reports that comparing HPV test and cervical smear with pooled sensitivity 94% and 70% respectively and specificity of 90% and 95% respectively.[13] Other studies reported this discrepancy occurred among their study population varies around 2.2% - 6.7%.2,6,[17]Several factors including a number of subject studies, preparation of patients, sampling, adequacy in samples and pathology reading, contribute to our result with the previous study as our HR HPV (+) with Pap (-) number considered higher. This may increase our awareness for screening of precancerous lesion of the cervix.

## CONCLUSION

From Pap examination, we found 32.5% negative cytology result with high-risk HPV DNA result. The highest findings of HPV DNA type in our study was type 59 (22.8%). We found a significant difference in HPV DNA test result among women above 30 years old. Co-testing of Pap and HPV DNA is needed, especially if HPV DNA type 16 and 18 was found among negative Pap results.

## CONFLICT of INTEREST

None to declare.

## FUNDING STATEMENT

The authors did not receive any finansial support for this study.

## Data Avaibility

The master data used to support the findings of this study are available from the corresponding author upon request.

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**Research Article**

# Choice of Delivery Places and Factors which Influence it in the Aceh Besar Regency

## *Pilihan Tempat Persalinan Ibu dan Faktor-Faktor yang Mempengaruhinya di Kabupaten Aceh Besar*

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## Abstract

**Objective :** To determine the relationship of maternal delivery and the factors that influence in Aceh Besar regency of Aceh Province.

**Methods :** We used a cross-sectional study design. Data were collected in all Community Health Centres in each sub-district in Aceh Besar regency of Aceh province. The total sample size of this study was 80 patient data, with details of 40 maternity patients in health facilities and 40 patients who were delivered to non-health facilities. Data were taken on factors that influence the choice of place of delivery, i.e. travel time from home to health facilities, age, parity, antenatal care, education, and income.

**Results :** The result of chi-square test showed significant relation time (p = 0.000), Education (p = 0.011), parity (p = 0.000), antenatal care (p = 0.025), age (p = 0.003), revenue (p = 0.022) with maternity delivery in Aceh Besar regency. From the result of multivariate analysis found that travel time is the most influential factor in choosing the birth place with (OR = 51.976).

**Conclusions :** The result of multivariate analysis showed that travel time was the most influential factor in choosing the delivery place with 51.976 times.

**Keywords :** health facilities, maternal mortality rate, safe delivery.

## *Abstrak*

***Tujuan :*** *Untuk mengetahui hubungan tempat persalinan ibu dan faktor-faktor yang mempengaruhi di Kabupaten Aceh Besar Provinsi Aceh.*

***Metode :*** *Penelitian ini menggunakan desain potong lintang. Data diambil di seluruh Puskesmas di setiap kecamatan di Kabupaten Aceh Besar Provinsi Aceh. Jumlah total sampel penelitian ini adalah 80 data pasien, dengan rincian 40 pasien yang bersalin di fasilitas kesehatan dan 40 pasien yang bersalin di non fasilitas kesehatan. Data yang diambil mengenai informasi faktor yang mempengaruhi pilihan tempat persalinan, yaitu waktu tempuh dari rumah ke fasilitas kesehatan, usia, paritas, ANC, pendidikan, danpendapatan.*

***Hasil :*** *Hasil uji chi-square menunjukkan terdapat hubungan secara signifikan waktu tempuh (p=0,000), pendidikan (p=0,011), paritas (p=0,000), ANC (p=0,025), usia (p=0,003), pendapatan (p=0,022) dengan pemilihan tempat persalinan ibu di Kabupaten Aceh Besar. Dari hasil analisis multivariate didapatkan waktu tempuh adalah faktor yang paling berpengaruh dalam memilih tempat persalinan dengan (OR=51,976).*

***Kesimpulan :*** *Berdasarkan hasil analisis regresilogistik, kelompok yang waktu tempuhnya dari rumah ke fasilitas kesehatan <30 menit 51,976 kali lebih besar kemungkinan memilih tempat persalinan difasilitas kesehatan.*

***Kata kunci :*** *angka kematian ibu, fasilitas kesehatan, persalinan aman.*

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## INTRODUCTION

Maternal Mortality Rate (MMR) in Indonesia based on Indonesia's demographic and health surveys is still very high at 359 maternal deaths per 100,000 live births for the period 2008-2012, whereas in the period 2004-2007 there were 228 maternal deaths per 100,000 live births.[1,2] Regency Aceh Besar Aceh Province is one of the contributing areas of MMR in Indonesia. Based on the health profile of Aceh province in 2012, MMR reached 192 per 100,000 live births.[3]

Causes of maternal death can occur directly and indirectly. In Indonesia, the causes of maternal mortality are postpartum hemorrhage, eclampsia or disturbances due to high blood pressure during pregnancy, long-standing complications of abortion, and infection. Bleeding that is usually unpredictable and occurs suddenly

is responsible for 28% of maternal deaths. Most cases of bleeding during the puerperium occur because of placental retention and uterine atony. This indicates a lack of proper management of the third stage of the birth process (prenatal, antenatal, and postnatal) and service of obstetric emergencies and timely neonatal care. Eclampsia is the second leading cause of maternal death, which is 24% of maternal deaths in Indonesia. Unsafe abortion. Responsible for 5% of maternal deaths in Indonesia.

One of the main factors contributing to high maternal mortality is the limited number of adequate delivery sites as well as delivering in non-health facilities. Globally 60 million mothers deliver in non-health facilities, especially at home, and 52 million birth mothers are not helped by professional health workers.[4] High rates of neonatal mortality are common in childbirth,[5] especially in preterm infants.[6] Efforts to reduce the risk of maternal and child health is of utmost importance by choosing a place of delivery at a health facility. Several studies have been conducted suggesting the relationship between travel time and choice of place of perspectives, as in Kenya the distance from home to health facility is the factor that most influences the choice of delivery.[7] Research in Nigeria states 31% of mothers who do not give birth in health facilities because they do not have adequate means of transportation.[8] Studies in the Philippines say a 1% reduction in travel time to public transport is likely to increase the choice of delivery sites in health facilities by about 1.2%,[9] and community must have a good assumption on health facilities to determine the choice of delivery.[10,11]

The help of nationally trained health workers increased from 46.13% in 1995 to 81.25% in 2011. Primary Health Care Survey Data 2010 showed a proportion of 82.20%. However, deliveries at health facilities are still low, at 55.40% (Primary Health Care Survey Data, 2010) .[12] Many unwanted outcomes from childbirth in non-health facilities, such as maternal deaths, mostly occur at the time of delivery, of which 9 out of 10 deaths mother occurs during delivery and around it (Ministry of Health, 2009). And neonatal mortality 40% of all under-five infant deaths.[13] Travel time to health facility more than 30 minutes, education level, parity, and behaviour performing antenatal care in pregnancy at this time will influence the choice between maternity delivery in non-health facilities or maternal delivery at a health facility to achieve safe delivery and simultaneously correlate with decreasing Maternal Mortality Rate.[14]

## METHODS

This study was conducted using a cross-sectional design. Mothers in 2016 who are fully registered in the Monitoring the Local Area of Maternal and Child Health in Community Health Care sub-district of Aceh Besar regency. Data were collected from July 2017 to December 2017 with all data and samples being collected with data collection in all Community Health Care in each sub-district in Aceh Besar Regency, Aceh Province, which is 23 subdistricts. The recorded data of mothers delivering labour in non-health facilities was 40 so that the study took a total of 40 maternity mothers in Faskes as a control.

## RESULTS

During the year 2016 Monitoring the Local Area of Maternal and Child Health listing that entered inclusion criteria only 14 districts. The recorded data of mothers delivering labour in non-health facilities was 40 so that the study took a total of 40 maternity mothers in Faskes as a control

**Table 1.** The Frequency Distribution of Maternity Data in Aceh Besar regency by 2016 is based on the Number of Patients Giving Birth in Non-Health Facility, and Who Gave Birth in Health Facility as Control

| Residence | Frequency | % |
|---|---|---|
| Baitussalam | 2 | 2.0 |
| BlangBintang | 4 | 5.0 |
| Darussalam | 8 | 10.0 |
| Indrapuri | 10 | 12.5 |
| Ingin Jaya | 6 | 7.5 |
| Kota Jantho | 6 | 7.5 |
| KutaBaro | 4 | 5.0 |
| KutaMalaka | 6 | 7.5 |
| LembahSeulawah | 8 | 10.0 |
| Leupung | 6 | 7.5 |
| Lhoknga | 8 | 10.0 |
| Montasik | 2 | 2.5 |
| Seulimum | 6 | 7.5 |
| SukaMakmur | 4 | 5.0 |
| Total | 80 | 100.0 |

**Table 2.** Relationship of Delivery Place with Travel Time from Home to Health Facility, Education Level, Parity, Behaviours of Antenatal Care during Pregnancy, Age, and Monthly Incomein Regency of Aceh BesarYear 2016.

| Variables | Place of Birth | | | | *P-Value* |
|---|---|---|---|---|---|
| | Health facility | | Non Health facility | | |
| | F | % | F | % | |
| **Traveling time** | | | | | |
| <30 minute | 33 | 71.7 | 13 | 28.3 | 0.000 |
| >30 minute | 7 | 20.6 | 27 | 79.4 | |
| **Education** | | | | | |
| Low | 20 | 39.2 | 31 | 60.8 | 0.011 |
| High | 20 | 69.0 | 9 | 31.0 | |
| **Parity** | | | | | |
| Primipara | 30 | 69.8 | 13 | 30.2 | 0.000 |
| Multipara | 10 | 27.0 | 27 | 73.0 | |
| **ANC** | | | | | |
| No | 15 | 37.5 | 25 | 62.5 | 0.025 |
| Yes | 25 | 62.5 | 15 | 37.5 | |
| Age | | | | | |
| Not at risk | 30 | 69.8 | 17 | 36.2 | 0.003 |
| At risk | 10 | 30.3 | 23 | 69.7 | |
| **Income** | | | | | |
| <2.5 million | 19 | 39.6 | 29 | 60.4 | 0.022 |
| > 2.5 million | 21 | 65.6 | 11 | 34.4 | |

**Table 3.** Based on Bivariate Analysis, it is Known that the Variable having the Sig Value <0.25 is the Result of Chi-Square Test that is the Time of Antenatal Care and Parity. The Variables Selected in the Final Model of Logistic Regression with the Enter Model as Tested as Follows.

| Variables | B | Sig | Exp(B) | 95% CI | |
|---|---|---|---|---|---|
| | | | | Lower | Upper |
| Time | 3.951 | 0.000 | 51.976 | 6.874 | 392.996 |
| ANC | 2.882 | 0.002 | 17.846 | 2.878 | 110.654 |
| Parity | 1.838 | 0.024 | 6.286 | 1.281 | 30.849 |
| Constant | -11.148 | 0.000 | 0.000 | | |

## DISCUSSION

This study used total sampling based on the total number of patients who delivered in non-health facilities, and equalized the total of the delivery sample in the health facilities as controls. Distribution of residential frequency, the highest sample obtained 10 patients (12.5%) from Indrapuri District. Medium 6 patients (7.5%) from Ingin Jaya Sub-district, Jantho City, Kuta Malaka, Leupung and Seulimum, and at least 2 patients (2.5%) from Baitussalam and Montasik sub-districts.

The results showed that based on the travel time from home to health facility, education level, parity, doing antenatal care, age, and income had significant relationship with the selection of place of delivery.

## CONCLUSION

Based on the results of research and discussion, it can be concluded that there is a significant relationship of travel time, education, parity, antenatal care, age, income with maternity selection in Aceh BesarRegency. The result of multivariate analysis showed that travel time was the most influential factor in choosing the delivery place with (OR = 51.976).

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**Research Article**

# The Association between Preeclampsia and Newborn Hearing Loss

## *Hubungan antara Preeklamsia dengan Penurunan Pendengaran pada Bayi Baru Lahir*

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## Abstract

**Objective :** To analyze the relationship between preeclampsia (PE) and the newborn hearing loss.

**Methods :** This cross-sectional study was conductedat RSMH Palembang since December 2016 to July 2017, obtained 48 aterm neonates born from mother diagnosed with PE (11 PE and 37 severe PE). Measurements of neonatal hearing loss then performed using emission otoacoustic (OAE) in both ears by ENT division with categories interpretation of pass and referred. The mothers were physically checked and interviewed to obtain demographic data and obstetric history. After the data normality were proved by Shapiro Wilk test, we performed bivariate analysis using X2 test on demographic and obstetric characteristics of the mother, neonatal demographic characteristics, and determine the relationship of PE with OAE result.

**Results :** There were no significant differences in maternal and neonatal demographic characteristics in neonatal hearing loss (p> 0.05). No significant relationship was found between PE and OAE of both ear (right, p = 0.437; left, p = 0.368). There was difference of mean of SBP and DBP of mother in neonate OAE of both ears (p <0.05) with cut offpoint of SBP 160 mmHg and DBP 106 mmHg.There was a significant association between DBP (≥ 106 mmHg) of the mother and birth weight of the fetus (< 2.500 g) with referred OAE.

**Conclusions :** There was a significant association between neonatal hearing loss and maternal PE, determined primarily by maternal DBP, and neonatal birth weight.

**Keywords :** maternal blood pressure, OAE, preeclampsia.

## *Abstrak*

***Tujuan :*** *Untuk menilai hubungan preeklamsia (PE) ibu dengan penurunan pendengaran bayi baru lahir.*

***Metode :*** *Penelitian observasi analitik dengan disain potong lintang dilakukan di RSMH Palembang sejak Desember 2016 sampai Juli 2017, diperoleh 48 neonatus aterm lahir dari ibu PE (11 PER dan 37 PEB). Neonatus dilakukan pengukuran pendengaran menggunakan otoakustik emisi (OAE) pada kedua telinga oleh divisi THT dengan kategori intepretasi refer dan pass. Ibu dilakukan pemeriksaan dan wawancara untuk memperoleh data demografi dan riwayat obstetri. Setelah normalitas data dibuktikan dengan tes Saphiro Wilk, dilakukan analisis bivariat menggunakan tes X2 pada karakteristik demografi dan obstetri Ibu, karakteristik demografi neonatus, dan menentukan hubungan PE dengan hasil OAE.*

***Hasil :*** *Tidak ditemukan perbedaan signifikan karakteristik demografi Ibu maupun neonatus tehadap penurunan pendengaran neonatus (p>0,05). Tidak ditemukan hubungan signfikan antara kondisi PE dengan OAE kanan (p = 0,437) dan kiri (p = 0,368). Ditemukan perbedaan rerata TDS dan TDD ibu terhadap OAE kedua telinga neonatus (p<0,05) dengan cut off point TDS 160 mmHg dan TDD 106 mmHg. Ditemukan hubungan signifikan antara TDD (>106 mmHg) ibu dan berat lahir janin (>2500 gr) dengan OAE refer.*

***Kesimpulan :*** *Terdapat hubungan bermakna antara penurunan pendengaran neonatus dengan kondisi preeklamsia ibu, yang ditentukan terutama oleh TDD ibu, serta berat lahir bayi.*

***Kata kunci :*** *OAE, preeklamsia,tekanan darah usia reproduksi tidak hamil, vitamin D.*

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## INTRODUCTION

Severe preeclampsia (PE) is a complication that affects 2-7% of pregnancies and causing vascular damaged that lead to maternal multiple organ failure and severe hypoxic conditions to the fetus in utero.[1]

A study conducted in 2008 revealed that 33% of infants from mothers with a history of severe PE experience hearing loss shortly postpartum. Other studies have also mentioned that the hearing loss also arises in the fetus of the mother with severe PE.[2]This indicates that hypoxia itself gives such a considerable influence on the hearing loss.[3]

Hearing loss of newborns from the mothers with severe PE showed a decrease in low frequency (125-500 Hz) which resembling a cochlear pathology condition. Decrease of blood flow will cause a decrease in the microcirculation of the cochlea, causing damage to the cochlear function. Decreased of blood flow to the internal hearing organ (nucleus cochlear hypoxia, cochlear nerve hypoxia, or direct cochlear damage organ) is the key of the pathogenicity of the sensorineural type hearing loss in the mother with severe PE.[4]Cochlear itself is very sensitive, especially in the apical part, to microcirculation decrease. Therefore, PE condition gives a high risk of sensorineural hearing loss.[5]

Examination with otoacoustic-emissions (OAE) has the advantage of not require expert expertise and very economical to be used as a postnatal screening tool. Having a high sensitivity and specificity (>90%) on peripheral hearing loss.[5] Thus, this study aims to analyze maternal PE relationship with the degree of newborn hearing loss with OAE.

## METHODS

A cross-sectional study was conducted at the Obgyn Department and ENT Department of RSMH Palembang since December 2016 – July 2017. The study sample was all newborns from mothers with severe PE who were treated in the Obgyn Departement of RSMH Palembang and fulfil the inclusion and exclusion criteria. Samples were taken by consecutive sampling technique.

Samples were then classified into PE group and normal (control) group. Matching was performed at the aspect of age, number of gravidity, and parity. Newborns sample will undergo a hearing function test with OAE by the ENT colleagues. The results of the examination will be presented in tabular form and analyzed with SPSS ver 17.0.

The data are presented descriptively in the form of 2x2 tables and then bivariate analysis with X2 test and unpaired T-test to assess the relationship between risk factor and the observed output based on significance (p) 0.05 (95% CI). The tendency of risks factor to the outcome of neonatal hearing loss was assessed by odds ratio (OR).

## RESULTS

Research has been conducted to assess the relationship between PE with newborn hearing loss examined with OAE. Forty eight-term neonates born, either vaginally or abdominally, form PE mother (11 PE and 37 severe PE). Normality test with the Shapiro Wilk test was obtained for all independent variable which resulted in a normal distribution (p> 0,05).

### Sample Demographic Characteristics

The characteristics of maternal demography are shown in Table 1. The number of PE mothers was in the severe PE category (77.1%) and there was no significant difference in demographic characteristics between the severe PE and PE groups (p>0.05). Both groups have similar patterns of demographic characteristics, where the majority mother give birth at the ideal age (20-35 years), take medication during pregnancy, do not consume herbs during pregnancy, have no infection during pregnancy, and all have no deafness or hearing loss family history. In terms of birth method, it was known that the majority of PE groups underwent normal labour (54.5%) while the majority of the severe PE group underwent a cesarean section (56.7%).

**Table 1.** Characteristics of Maternal & Neonatal Demographics Subject (N = 48)

| Demographic Characteristic | PE | | Severe PE | | *P- value* |
|---|---|---|---|---|---|
| | n | % | n | % | |
| **Maternal Characteristic** | | | | | |
| Maternal age (years) | 31.3636 + 4,80151 | | 31.19892 + 6.53128 | | 0.935 |
| <20 | 0 | 0 | 1 | 100 | 0.698 |
| 20-35 | 9 | 25.7 | 26 | 74.3 | (0.718 – 0.672) |
| >35 | 2 | 16.7 | 10 | 83.3 | |
| Gestational age | 36.8182 + 1.07872 | | 37.1622 + 1.16699 | | 0.388 |
| >37 weeks | 7 | 18,9 | 30 | 81.1 | 0.246 |
| <37 weeks | 4 | 36.4 | 7 | 63.6 | (0.146 – 0.346) |
| Drugs during pregnancy | | | | | |
| No | 4 | 36.4 | 7 | 63.6 | 0.208 |
| Yes | 7 | 18.5 | 30 | 81.8 | (0.228 – 0.198) |
| Herbs during pregnancy | | | | | |
| No | 9 | 28.1 | 23 | 71.9 | |
| Yes | 2 | 12.5 | 14 | 87.5 | 0.200 |
| Infection or fever during pregnancy | | | | | (0.221 – 0.196) |
| No | 10 | 22.2 | 35 | 77.8 | 0.551 |
| Yes | 1 | 33.3 | 2 | 66.7 | (0.561 – 0.540) |
| H/ deafness in family | | | | | |
| No | 11 | 22.9 | 37 | 77.1 | £ |
| Yes | 0 | 0 | 0 | 0 | |
| Delivery mode | | | | | |
| Normal | 6 | 28.6 | 15 | 71.4 | 0.389 |
| Vaginal operative | 1 | 50 | 1 | 50 | (0.409 – 0.369) |
| Cesarean section | 4 | 16.0 | 21 | 84 | |
| **Neonatal Characteristic** | | | | | |
| Birth weight (<2500 gr) | 31.3636 + 4,80151 | | 2908.11 + 565.380 | | 0.454 (-513.214 – 233.362) |
| No | 7 | 18.4 | 31 | 81.6 | 0.153 |
| Yes | 4 | 40 | 6 | 60 | (0.164 – 0.142) |
| Neonatal infection | | | | | |
| No | 11 | 22.9 | 37 | 77.1 | £ |
| Yes | 0 | 0 | 0 | 0 | |
| Hyperbilirubinemia | | | | | |
| No | 11 | 22.9 | 37 | 77.1 | £ |
| Yes | 0 | 0 | 0 | 0 | |
| Asphyxia | | | | | |
| No | 11 | 25 | 33 | 75 | 0.339 |
| Yes | 0 | 0 | 4 | 100 | (0.349 – 0.329) |
| Cephalic Trauma | | | | | |
| No | 11 | 22.9 | 37 | 77.1 | £ |
| Yes | 0 | 0 | 0 | 0 | |
| Ear Malformation | | | | | |
| No | 11 | 22.9 | 37 | 77.1 | £ |
| Yes | 0 | 0 | 0 | 0 | |
| APGAR Score | | | | | |
| Normal | 2 | 28.57 | 5 | 71.43 | 0.513 |
| Abnormal | 9 | 2 | 32 | 78 | (0.523-0.503) |
| NICU admission | | | | | |
| No | 11 | 22.9 | 37 | 77.1 | £ |
| Yes | 0 | 0 | 0 | 0 | |

** Chi Square test, 95%CI, £ Significancy cannot be evaluate*

Table 1 also showed no significant difference in neonates born from PE and severe PE groups. Nevertheless, there was asphyxia (n = 4) occurred in neonates born from severe PE mothers, but the absence of neonates treated in the NICU showed that asphyxia was mild and transient. The absence of this neonate characteristic difference indicates that severe PE and PE conditions do not significantly influence the neonatal outcomes.

## Relationship of Neonates OAE with Preeclampsia

Table 2 indicates there is no significant relationship between the degree of PE with the occurrence of neonatal hearing loss on both ears. So it can be deduced that the degree of PE does not affect the incidence of hearing loss in newborns based on OAE examination. However, the analysis of X2which uses the category data has a huge bias, mainly due to small sample sizes. So the analysis continued on the relationship of SBP and DBP to the occurrence of OAE abnormalities, as well as multivariate analysis to determine the significant risk factors of OAE abnormalities based on maternal and neonatal variables.

**Table 2.** Neonates OAE Relationship with Preeclampsia and Blood Pressure (N = 48)

| Risk Factor | OAE Dxt | | *P-value* | OAE Sin | | *P-value* |
|---|---|---|---|---|---|---|
| | Refer | Pass | | Refer | Pass | |
| Severe PE | 10 (83.3) | 27 (75) | 0.437* | 11 (84.6) | 26 (74,3) | 0.368* |
| PE | 2 (16.7) | 9 (25) | | 2 (15.4) | 9 (25,7) | |
| Sistole (mean+SD) | 167.5+14.22 | 158. 61+10.185 | 0.022§ | 166.92+13.775 | 158.57+10.331 | 0.028§ |
| Interval (min-max) | (150-200) | (140-190) | | (150-200) | (140-190) | |
| Diastole (mean+SD) | 111.67+ 11.146 | 101.11 + 7.848 | 0.001§ | 111.54+10.682 | 100.86+7.811 | <0.001§ |
| Interval (min-max) | (100-140) | (80-110) | | (100-140) | (80-110) | |
| Total | 12 (100) | 36 (100) | | 13 (100) | 35 (100) | |

* Fisher exact test, 95% CI, § Independent T Test, 95% CI

## Neonates Hearing Loss Risk Factors

Table 3 showed that only maternal risk factors for DBP (cut off point 106 mmHg) were significantly associated with neonatal OAE abnormalities, while other maternal risk factors were not significant (p> 0.250), so multivariate analysis was not performed. Similarly, the risk factors for neonatal shows only birth weight (<2500 grams) which significantly associated with neonates OAE abnormalities, while other risk factor were not significant (p> 0.250) and multivariate analysis was not performed.

**Table 3.** Bivariate Analysis of Maternal and Neonatal Risk Factors for Abnormal OAE (N = 48)

| Risk Factor | OAE | | *P-value* |
|---|---|---|---|
| | Refer | Pass | |
| **Maternal Risk Factor** | | | |
| **Maternal age** | | | |
| >35 years | 6 (46.2) | 10 (28.6) | 0.310 |
| <35 yeas | 7 (53.8) | 25 (71.4) | |
| **Sistolic blood pressure** | | | |
| >160 mmHg | 11 (84.6) | 26 (74.3) | 0.702 |
| <160 mmHg | 2 (15.4) | 9 (25.7) | |
| **Diastolic blood pressure** | | | |
| >106 mmHg | 10 (76.9) | 11 (31.4) | 0.008 |
| <106 mmHg | 3 (23,1) | 24 (68.6) | |
| **Degree of PE** | | | |
| Severe PE | 11 (84.6) | 26 (74.3) | 0.702 |
| PE | 2 (15.4) | 9 (25.7) | |
| **Infection during pregnancy** | | | |
| Infection (+) | 1 (7.7) | 2 (5.7) | 0.999 |
| Infection (-) | 12 (92.3) | 33 (94.3) | |
| **Drug consumption** | | | |
| Yes | 10 (76.9) | 27 (77.1) | 0.999 |
| No | 3 (23.1) | 8 (22.9) | |
| **Herb consumption** | | | |
| Yes | 6 (46.2) | 10 (28.6) | 0.310 |
| No | 7 (53.8) | 25 (71.4) | |
| **History of Deafness in family** | | | |
| History (+) | 0 (0) | 0 (0) | £ |
| History (-) | 13 (100) | 13 (100) | |
| **Mode of Delivery** | | | |
| Cesarean Section | 7 (53.8) | 18 (51.4) | 0.999 |
| Vaginal delivery | 6 (46.2) | 17 (48.6) | |

| | | | |
|---|---|---|---|
| **Neonatal Risk Factor** | | | |
| **Birth weight (g)** | | | |
| > 2.500 | 7 (53.8) | 31 (88.6) | 0.016 |
| < 2.500 | 6 (46.2) | 4 (11.4) | |
| APGAR score | | | |
| 10 | 3(23.1) | 4 (11.4) | 0.370 |
| < 10 | 10 (76.9) | 31 (88.6) | |
| Asphyxia | | | |
| Asphyxia (+) | 1 (7.7) | 3 (8.6) | 0.999 |
| Asphyxia (-) | 12 (92.3) | 32 (91,4) | |

*Fisher exact test, p = 0.05*

## DISCUSSION

In addition to the fetomaternal circulation, severe PE affects uteroplacental perfusion due to vasospasm. Systemic vascular insufficiency, especially the placenta, will interfere with the developmental process of fetus (hypoxic fetus). Hypoxia leads to hyperpolarization of inner hair cells that can resulting in changes in hearing neurons.[5]

Spontaneous release of the auditory neuron is the result of spontaneous release of the transmitter by hair cells. The stimulation of sound will cause depolarization of hair cells that will lead to increased release of chemical transmitters and neural jumps. In fetal hypoxia, hyperpolarization of hair cells will result in a decrease in the number of transmitters released and result in a decrease in nerve activity.[5]

Based on maternal demographic characteristics analysis no influence of maternal age, history of drug consumption, herbal medicine, infection during pregnancy and delivery method to neonatal hearing loss (p> 0.05). These findings are similar who examined maternal and placental factors for congenital hearing loss, suggesting that only funisitis (cord infection) was significantly associated with neonatal hearing loss (p = 0.05). While maternal age, parity, gestational age, delivery mode, use of antenatal drugs, and chorioamnionitis infection were statistically unrelated to neonatal hearing loss (p> 0.05).[6] The condition of funisitis was not investigated in this study, although funisitis appears to be a significant factor for congenital hearing loss.

Increase in interleukin-6 (IL-6) in umbilical cord blood, signalling a significant reduction in congenital hearing examined in neonates.[7] It was concluded that prenatal exposure to inflammation could damage the inner ear organ when a fetal inflammatory response occurs. On the other hand, the findings of chorioamnionitis did not significantly cause hearing impairment, so it is hypothesized that chorioamnionitis may not necessarily trigger a fetal inflammatory response, the outbreak of this response being confirmed only when there is an inflammatory cytokine on the umbilical cord.[6]

In some literatures, the age of preterm and low birthweight (LBW) are reportedly important facts or risks for congenital hearing loss.[7-9] A similar finding was found in this study, where birth weight <2.500 grams was significantly affected by congenital hearing loss diagnosed as *"refer"* to OAE examination. This finding is logical given that LBW conditions can be caused by premature gestational age so that the maturation of the inner ear organ has not been fully achieved, or in the case of term, the LBW condition indicates placental insufficiency and chronic fetal hypoxia occurring in preeclampsia resulting in deep hair cell hyperpolarization which may result changes in hearing neurons fetus.[5]

A contradictory finding was found in Apgar score variables, in which no significant association of Apgar scorewith congenital hearing loss was in contrast to previous studies. It has been hypothesized by previous studies that premature and LBW babies are associated with low Apgar score, so low Apgar score(which indicate fetal hypoxia) are also significantly associated with fetal hearing loss. However, this hypothesis is denied,where they found no significant relationship between Apgar scoreof 1 and 5 minutes with congenital hearing loss. It is hypothesized that Apgar score merely describe the condition of fetal well-being soon after birth and can not fully represent the intrauterine fetal hypoxia condition.[6,10] So that it can be understood when the LBW baby can have a hearing loss even though their Apgar score was good. Another

consideration of no significant association between Apgar values and hearing loss in this study was that Apgar values were assessed by different Pediatric residents so that the examiner bias could have an effect, and the Apgar 10 and <10 score categories resulted in inequality in assessments where the majority of neonates who were fit more often rated Apgar 9 instead of 10.

The next important variable in the study was drug use during pregnancy, where no significant association was found between the use of drugs during pregnancy with congenital hearing loss. The study did not specify what medications were used during pregnancy, so no analysis of the effects of each type of drug could be performed. In 2017, stated that prenatal antibiotic use has no effect on congenital hearing loss, and on the contrary, the use of corticosteroids has a positive effect which decreases congenital hearing loss in premature fetuses.[6]

The main maternal variable in this study was maternal blood pressure with a diagnosis of preeclampsia. In this study, it was found that blood pressure, especially diastolic with a *c*ut off of 106 mmHg, was significantly associated with congenital hearing loss, while systolic blood pressure with a *cut off of* 160 mmHg was not significantly related. These findings are similar to those who found a significant association between maternal blood pressure and congenital hearing loss, wherein the hearing impaired fetus was mainly from the maternal group with a mean systolic blood pressure of 156 ± 9.8 mm Hg (p <0.001) and diastolic blood pressure of 103.7 + 4.9 mmHg (p <0.001).[11]

Not many studies have described maternal blood pressure and compared women with normal preeclampsia with findings that differ from this study. For example, that there is no difference in neonatal hearing loss outcomes of the maternal group with hypertension in pregnancy and normal maternal groups;[12]Result and hypothesized that congenital hearing loss is caused by multifactorial factors, particularly environmental and genetic factors. Altuntas, however, found that women with HELLP syndrome were significantly associated with congenital sensorineural hearing loss.[2]These contradictory findings indicate that relationships between maternal blood pressure and congenital hearing loss need to be further investigated and use more detailed and comprehensive designs and tools.

Neonatal variables in this study found no significant association with congenital hearing loss, except birth weight. The same is also who states that perinatal characteristics of fetal age at delivery, birth weight, fetal sex, Apgar score, umbilical arterial pH, and postnatal neonatal decline (e.g. RDS, broncho-pulmonary dysplasia, intraventricular haemorrhage, periventricular leukomalacia, necrotizing enterocolitis, and seizures) are not associated with congenital hearing loss.[6]

This study was conducted on samples of PE mothers categorized as PE and severe PE; not much research has studied the effects of maternal preeclampsia on the outcome of hearing loss in neonates. Nevertheless, the authors acknowledge that this study has many shortcomings, among others: the number of samples is too small to be representative did not include normal mothers without PE as a comparison used cross sectionaldesign so it could not be known whether the hearing loss in some neonates is reversible or irreversible; used simple tool which was OAE that only gives the result of "refer" or "pass" without any translation of hertz level which is a problem in neonate hearing; didn't perform an analysis of the placenta using anatomical pathology examination to find out whether chorioamnionitis and funicitis were risk factors; didn't elaborate fully on research variables, for example drugs and herbs, types of prenatal infections, types of neonatal infections, Apgar score minutes 1, 5, and 10, and RDS types occured in neonates.

Further studies use prospective cohort design, larger sample size, healthy maternal as control, as well as advanced examination tools such as anatomic pathology, brainstem evoked response audiometry (BERA) ortransient evoked otoacoustic emission (TEOAE). Therefore, it is expected to provide more complete, informative, and valid relationships.

## CONCLUSIONS

We noted that there was a significant association between neonatal hearing loss and maternal PE, determined primarily by maternal DBP, and neonatal birth weight.

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**Research Article**

# Maternal Death Risk Factors In Wahidin Sudirohusodo Hospital And Its Affiliates.

## *Faktor Risiko Kematian Maternal di Rumah Sakit Umum Pusat Wahidin Sudirohusodo dan Jejaringnya*

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## Abstract

**Objective :** To identify maternal death risk factors in Wahidin Sudirohusodo Hospitals and its affiliates between 1 January - 31 December 2017.

**Methods :** This study is an observational case-control study that includes all cases of maternal death and considerable numbers of pregnancy without complications that occurred in Wahidin Sudirohusodo Hospital and its affiliates between 1 January 2016 and 31 December 2017. Data were then be analysed using *chi-square* and *logistic regression test* to know the correlations between risk factors and maternal death.

**Results :** There are 28 cases of maternal death in Wahidin Sudirohusodo Hospital and its affiliates which mostly occurred at age 20-35 years old (60.7%) and antenatal care in primary health care (71.4%). Hypertension (39.3%) and haemorrhage (35.7%) were the most frequent complications of maternal death. Age under 20 years old and older than 35 years old (odds ratio 3.882; 95% CI, 1.056-14.276; $P<0.05$), education level less than 9 years (odds ratio 3.178; 95% CI, 0.987-10.228; $P<0.05$), age and education level did not seem to affect incidence of maternal death when analysed simultaneously (odds ratio 1.842; 95% CI, $P > 0.05$).

**Conclusions :** Hypertension and haemorrhage were the most frequent causes of maternal death. Age under 20 years old and older than 35 years old as well as education level less than nine years increased the risk of maternal deaths independently. Parity, frequency of antenatal care, and location of antenatal care did not show any significant role in maternal death occurrence.

**Keywords :** age, haemorrhage, hypertension, maternal death, risk factors.

## *Abstrak*

***Tujuan :*** *Untuk mengetahui faktor-faktor risiko kematian maternal di Rumah Sakit Umum Pusat Wahidin Sudirohusodo dan jejaringnya periode 1 Januari – 31 Desember 2016.*

***Metode :*** *Penelitian ini adalah penelitian studi observasional case control dengan mengambil seluruh data kematian maternal yang terjadi di Rumah Sakit Umum Pusat Wahidin Sudirohusodo dan jejaringnya selama periode 1 Januari – 31 Desember 2016. Data dianalisis dengan Uji chi square dan regresi logistik untuk melihat faktor risiko yang diteliti dengan terjadinya kematian maternal.*

***Hasil :*** *Ada 28 kasus kematian maternal di Rumah Sakit Umum Wahidin Sudirohusodo dan jejarignya yang sebagian besar terjadi pada kelompok usia 20-35 tahun (60,7%) dan lokasi asuhan antenatal di puskesmas (71,4%). Komplikasi kehamilan terbanyak ialah hipertensi (39,3%) dan perdarahan (35,7%). Kelompok usia kurang dari 20 tahun dan lebih dari 35 tahun (odds ratio 3.882; 95% CI, 1.056-14.276; $P<0.05$) dan pendidikan kurang dari 9 tahun (odds ratio 3.178; 95% CI, 0.987-10.228; $P<0.05$) memiliki pengaruh signifikan terhadap terjadinya kematian maternal. Usia dan tingkat pendidikan secara simultan tidak mempengaruhi terjadinya angka kematian maternal (odds ratio 1.842; 95% CI; $P> 0.05$).*

***Kesimpulan :*** *Hipertensi dan perdarahan merupakan penyebab utama terjadinya kematian maternal. Kelompok usia kurang dari 20 dan lebih dari 35 tahun serta tingkat pendidikan ≤ 9 tahun secara independen berisiko meningkatkan jumlah kematian maternal. Paritas, frekuensi asuhan antenatal, dan lokasi asuhan antenatal tidak memiliki peran signifikan dalam terjadinya kematian maternal.*

***Kata kunci :*** *faktor risiko, hipertensi, kematian maternal, perdarahan, usia.*

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## INTRODUCTION

Maternal mortality rate in Indonesia is still very high, approximately 359/100 000 live births in 2012, according to the Indonesia Health Ministry register. This finding is still outreached the fifth Millenium Development Goals (MDGs) target for 2015 which was about 102/ 100 000 live births.[1,2]

Maternal deaths frequently caused by pregnancy complications such as haemorrhage, infection, and hypertension. Data registry form Maternal Health Directory in 2010-2013 revealed that maternal deaths in Indonesia were commonly associated with bleeding, hypertension, and other causes that indirectly related to pregnancy. [1,3,4]

Maternal mortality rate in South Sulawesi in 2014 was 93.20 / 100 000 live births. This finding showed greater maternal mortality rate than 2013 which was about 78.38 /100 000 live births. It seems that maternal mortality rate in South Sulawesi had achieved Millenium Development Goals (MDGs) target, but we should not feel satisfied when maternal mortality rate had achieved MDGs target because maternal death could confer a detrimental psychological and socioeconomic burden in the community. [2,3,5]

Maternal deaths in South Sulawesi were predominantly caused by haemorrhage, hypertension, and indirect cause unrelated to pregnancy. Maternal deaths were frequently occurred in labour and in the puerperium. We have to rely on this indicator to offer better risk factor identification, referral system, and labour management. [1]

Health care system in Indonesia, particularly in South Sulawesi, still needs to be fixed. Difficult access to the health care centre, low socioeconomic status, low educational level, poor antenatal care quality, and many more factors that may increase maternal mortality rate. These findings should be well identified and well-managed in order to decrease maternal mortality rates in Indonesia.[4,6,7]

## OBJECTIVES

This study aimed to identify the role of age, education level, parity, antenatal care frequency, and antenatal care location as risk factors for maternal deaths occur in Wahidin Sudirohusodo hospital and its affiliates from 01 January – 31 December 2017.

## METHODS

This study was an observational case-control study. Data were collected from Wahidin Sudirhusodo Hospital and its affiliates from 1 January – 31 December 2017 and met inclusion criteria. Inclusion criteria in this study were maternal deaths occurred in pregnancy, labour, puerperium from 1 January – 31 December 2017 in Wahidin Sudirohusudo Hospital and its affiliates. Normal labour on 1 January - 31 December 2017 in Wahidin Sudirohusodo Hospital and its affiliates. Exclusion criteria in this study were pregnant women died or underwent without the complication that occurred out of the period of study. Pregnant women underwent labour or died not in Wahidin Sudirhosudo Hospital dan its affiliates.

Pregnant women who underwent labour without complication around the study period then became control in these settings. Data collected then be analyzed with the Chi-Square test. Data analysis would be significant if $P< 0.05$. Significant risk factors then be analyzed with logistic regression analysis to assess intervariables correlation with maternal deaths occurrence.

## RESULTS

There were 28 cases of maternal death in Wahidn Sudirohusodo Hospital and its affiliates in the period 01 January – 31 December 2017. Several risk factors that could be identified in this study were age, educational level, parity, location of antenatal care, and frequency of antenatal care. [8,9]

Twenty-eight cases of maternal death that occurred in Wahidins Sudirohusodo Hospital and its affiliates between 1 January – 31 December 2017, as shown in Table 1. Maternal deaths most frequently occurred at age 20-35 years old (60.7%), multigravida (53.6%), educational level > 9 years (53.6%), and antenatal care location at primary health care (71.4%). In control, its seemed that pregnancy without complications most commonly occurred at age 20-35 years (85.7%), multigravida (64.3%), educational level

> 9 years (78.6%), and antenatal frequency < 4 times (53.6%).

Data in table 1 shows that frequency or number of antenatal care did not have significant role in predicting maternal death occurrence. Otherwise age at 20-35 years, multigravida, and educational level more than 9 years had a significant proportion in case of healthy pregnancy without complication, i.e., 85.7%, 64.3%, and 78.6% respectively.

**Table 1.** Maternal Deaths and Control Data Distribution Based on Risk Factors

| Variables | Samples | | Controls | |
|---|---|---|---|---|
| | n= 28 | (%) | n= 28 | (%) |
| **Age** | | | | |
| 20-35 | 17 | 60.7 | 24 | 85.7 |
| < 20 or > 35 | 11 | 39.3 | 4 | 14.3 |
| **Parity** | | | | |
| Primigravida | 13 | 46.4 | 10 | 35.7 |
| Multigravida | 15 | 53.6 | 18 | 64.3 |
| **Educational level** | | | | |
| < 9 years | 13 | 46.4 | 6 | 21.4 |
| > 9 years | 15 | 53.6 | 22 | 78.6 |
| **ANC frequency** | | | | |
| < 4 times | 14 | 50 | 15 | 53.6 |
| > 4 times | 14 | 50 | 13 | 46.4 |
| **ANC location** | | | | |
| Primary health centre | 20 | 71.4 | 14 | 50 |
| Hospital or Obstetrician | 8 | 28.6 | 14 | 50 |

Hypertension and haemorrhage were still the main aetiology of maternal death that occurred in Wahidin Sudirhosudo Hospital and its affiliates. These findings is shown in table 2 where maternal death proportion caused by hypertension and haemorrhage were 39.3 % and 36.7 % respectively.

**Table 2.** Pregnancy-associated Complications Leading to Maternal Death

| Complications | n | % |
|---|---|---|
| Hypertension | 11 | 39.3 |
| Infection | 5 | 17.9 |
| Haemorrhage | 10 | 35.7 |
| Other | 2 | 7.1 |

Based on risk factors analysis on two groups, maternal deaths and normal pregnancy, it seemed that age at 20-35 years (*odds ratio* 0.258; 95% CI,0.070-0.258; P> 0.05) and educational level less than or equal to 9 years (odds ratio 3.178; 95% CI, 0.987-10.228; *P*> 0.05) had a quite significant role in maternal deaths occurences. Parity, antenatal care frequency, and location of antenatal care did not have significant role in maternal death occurrences with P > 0.05.

**Table 3.** Risk Factor Analysis in Maternal Death Occurrences at Wahidin Sudirhosudo Hospital and its Affiliates between 1 January – 31 December 2017

| Variables | Sample n = 28 | Control n = 28 | *P-value* | OR | CI 95% |
|---|---|---|---|---|---|
| **Age** | | | | | |
| < 20 or > 35 | 11 | 4 | 0.035 | 3.882 | 1.056-14.276 |
| 20-35 | 17 | 24 | | | |
| **Parity** | | | | | |
| Primigravida | 13 | 10 | 0.415 | 1.560 | 0.534-4.557 |
| Multigravida | 15 | 18 | | | |
| **Educational level** | | | | | |
| < 9 years | 13 | 6 | 0.048 | 3.178 | 0.987-10.228 |
| >9 years | 15 | 22 | | | |
| **ANC frequency** | | | | | |
| < 4 times | 14 | 15 | 0.789 | 0.867 | 0.304-2.474 |
| > 4 times | 14 | 13 | | | |
| **ANC location** | | | | | |
| Primary health care | 20 | 14 | 0.101 | 2.500 | 0.828-7.548 |
| Hospital or Obstetrician | 8 | 14 | | | |

*Risk factor analysis with *chi-square*

Age less than 20 years and more than 35 years (odds ratio 0.312; 95% CI, 0.081-1.194; P>0.05) and educational level less than 9 years (odds ratio 0.384; 95% CI, 0.114-10.228; P>0.05) did not show any significant correlation in maternal death occurrence. Age and educational level (odds ratio 1.842; 95% CI; P >0.05) simultaneously did not reveal any significant correlation with maternal death.

**Tabel 4.** Regression Logistic Analyisis

| Variables | *P-value* | OR | CI 95% |
|---|---|---|---|
| **Age** | | | |
| < 20 or > 35 | >0.05 | 0.312 | 0.081-1.194 |
| 20-35 | | | |
| **Educational level** | | | |
| < 9 years | >0.05 | 0.384 | 0.114-10.228 |
| > 9 years | >0.05 | 1.842 | |

## DISCUSSION

There were 28 cases of maternal death occurred in Wahidin Sudirohusodo Hospital and its affiliates between 1 January – 31 December 2017. Most of the maternal deaths were caused by hypertension and haemorrhage. These findings is in concordance with data from South Sulawesi Maternal Health Directory. [2,10]

Maternal deaths in Wahidin Sudirohusodo Hospital and its affiliates between 1 January – 31 December 2017 most commonly occurred at age 20-35 years. This finding was different with typical assumption state that pregnancy at age 20-35 years is not a high risk pregnancy. Furthermore, normal pregnancy without complications itself seemed to occur most frequently at age 20-35 years with significant proportion, i.e., 85.7%. Risk factor analysis of age in sample and control independently revealed that age at 20-35 years was a significant risk factor (*odds ratio* 3.882; 95% *Confidence Interval* [CI], 0.070-0.947; P<0.05). This finding suggests that age still plays a role in maternal death occurrence and support the theory stated that pregnancy in women less than 20 years or more than 35 years were high-risk pregnancy.[3,4,11]

Both maternal deaths and pregnancy without complications commonly occur in multigravida, but data revealed that pregnancy without complications was slightly higher in (control) than maternal deaths group, i.e. 64.3%. Risk factors analysis based on parity revealed that there was nos significant correlation between primigravida and maternal death occurrences (*odds ratio* 1.560; 95 % CI, 0.534 – 4.557; *P*>0.05). These findings suggested that parity may play a role in maternal deaths occurrences in Wahidin Sudirhosudo Hospital and its affiliates.

Educational level may have a role in determining maternal death occurrences in Wahidin Sudirohusodo Hospital and its affiliates between 1 January – 31 December 2017. An educational level less than or equal to 9 years (*odds ratio* 3.178; 95% CI, 0.987 – 10.228; *P*<0.05) showed significant correlation with maternal deaths. This finding suggested that there was a correlation between educational level and maternal mindset of good pregnancy care. [7,8]

Antenatal care frequency less than four times during pregnancy may not have a role in determining maternal death occurrence (*odds ratio* 0.867; 95% CI , 0.304 – 2.474; *P*>0.05). This result revealed that antenatal care quantity is not significant risk factors in determining pregnancy outcome. Quality of antenatal care may pose a more significant role in determining pregnancy outcome.

Women underwent antenatal care at primary health care did not pose significant risk to develop maternal death based on risk factors analysis (*odds ratio* 2.500; 95% CI, 0.828 – 7.548; *P*>0.05). Based on the proportion found showed that 71.4% of maternal deaths occur in women who underwent antenatal care at primary health care. This finding lead us to enhance our human resources in primary health care to be able to manage pregnancy risk factors accordingly. [8]

Both age (*odds ratio* 0.312; 95% CI, 0.081-1.194; *P*>0.05) and educational level (*odds ratio* 0.384; 95% CI, 0.114-10.228; *P*>0.05) simultaneously did not revealed any significant correlation with maternal death occurrences. Based on this finding risk factor identification is much more important to decrease the maternal mortality rate in Indonesia, especially in South Sulawesi. [2,4]

## CONCLUSIONS

There were 28 cases of maternal death in Wahidin Sudirohusodo Hospital and its affiliates between 1 January – 31 December 2017.Maternal mortality most commonly occurs at age 20-35 years (60.7%), multigravida (53.6%), an educational level less than 9 years (53.6%), and antenatal care location at primary health care (71.4%). Most cases of maternal deaths were caused by hypertension (39.3%) and hemorrhage (35.7%).Educational level less than 9 years and age less than 20 years or more than 35 years independently had a significant role to maternal death occurence in Wahidin Sudirohusodo Hospital and its affiliates.

Parity, antenatal care frequency, and antenatal care location did not have significantly affect maternal mortality rate.

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**Research Article**

# The Influence of Education Level and Occupation of Pregnant Women to the use of Maternal and Child Health (MCH) Handbook

## *Pengaruh Tingkat Pendidikan dan Pekerjaan Ibu Hamil dengan Pemanfaatan Buku Kesehatan Ibu dan Anak (KIA)*

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## Abstract

**Objective :** To investigate the relationship between education level and occupation of pregnant women with MCH handbook utilization at the Pekauman Public Health Center of Banjarmasin in July–August 2018.

**Methods :** The method that was used is analytical observational research with cross-sectional design. The number of research sample is 50 people with systematic random sampling techniques, and data were analyzed by chi-square statistical tests.

**Results :** The majority of respondents were34 pregnant women (68%) with low education level, and36 pregnant women (72%) were unemployed. There were 36 pregnant women (72%) with ineffective MCH handbook utilization. The statistical result between education level of pregnant women with MCH handbook utilization is p-value = 0.005 (p < 0.05) and between occupation of pregnant woman with MCHhandbook utilization is p-value = 0.001 (p <0.05).

**Conclusions :** There a significant relationship of education leveland occupation of pregnant women with MCH handbook utilization at the Pekauman Public Health Center of Banjarmasin in July-August 2018.

**Keywords :** level ofeducation, occupation, MCH handbook.

## *Abstrak*

***Tujuan :*** *Untuk mengetahui hubungan tingkat pendidikan dan pekerjaan Ibu hamil dengan pemanfaatan buku KIA di Puskesmas Pekauman Banjarmasin Periode Juli–Agustus 2018.*

***Metode :*** *Metode yang digunakan adalah observasional analitik dengan desain potong lintang. Besar sampel penelitian adalah 50 orang dengan teknik pengambilan systematic random sampling dan data dianalisis dengan uji statistik chi square.*

***Hasil :*** *Sebagian besar responden adalah 34 ibu hamil (68%) dengan tingkat pendidikan rendah dan 36 ibu hamil (72%) yang tidak bekerja. Terdapat 36 ibu hamil (72%) dengan pemanfaatan buku KIA yang tidak efektif. Hasil uji statistik antara tingkat pendidikan ibu hamil dengan penggunaan buku KIA adalah p value = 0.005 (p < 0.05) dan antara pekerjaan ibu hamil dengan pemanfaatan buku KIA adalah p value = 0.001 (p < 0.05).*

***Kesimpulan :*** *Terdapat hubungan yang bermakana tingkat pendidikan dan pekerjaan ibu hamil dengan pemanfaatan buku KIA di Puskesmas Pekauman Banjarmasin periode Juli–Agustus 2018.*

***Kata kunci :*** *tingkat pendidikan, pekerjaan, buku KIA.*

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## INTRODUCTION

Maternal and Child Health (MCH) handbook is complete records and media information for pregnant women and her baby.[1] The government provides the MCH handbook to reduce Maternal Mortality Rate (MMR) and Infant Mortality Rate (IMR).[2]However, previous research found out that most of theMCH handbook utilization by pregnant women wasstill ineffective.[3]MCH handbook utilization as health behaviour is influenced by predisposing factors such as the level of intelligence, emotional level, information, and characteristics (age, education, occupation, and experience).[4,5]Based on this, the researcher aims to find out the relationship between education level and occupation of pregnant women with MCH handbook utilization. Based on the results of this study, it is expected that the government and health worker can conduct counselling on target.

## METHODS

The method that was used is analytical observational research with a cross-sectional

design, using a questionnaire to pregnant women who made antenatal care visits at the Pekauman Public Health Center of Banjarmasin in July-August 2018. The number of research sample is 50 people with systematic random sampling techniques according to inclusion and exclusion criteria. The data were analyzed by chi-square statistical tests and Fisher alternative test (if expected count <5). Because the data obtained one cell (25%) with expected count 4.48 at the level of higher education and effective use and one cell (25%) with expected count 3.92 in the working category and effective use, which is < 5 so that alternative tests were used with Fisher's test.

## RESULTS

The inclusion criteria for this study were pregnant women aged 20-40 years. The majority of respondents are 34 pregnant women (68%) with low education level and 36 pregnant women (72%) that were unemployed. There 36 pregnant women (72%) with ineffective MCH handbook utilization. Distribution of the respondents is presented in Table 1-3.

**Table. 1** Distribution of Respondents Based on MCH Handbook Utilization at the Pekauman Public Health Center of Banjarmasin in July-August 2018

| MCH handbook utilization | n | % |
|---|---|---|
| Ineffective | 36 | 72 |
| Effective | 14 | 28 |
| Total | 50 | 100 |

The statistical results for the relationship of education level and occupation of pregnant women with MCH handbook utilization are presented in Table 2.

**Table. 2** The Relationship of the Education level of Pregnant Women with MCH Handbook Utilization at the Pekauman Public Health Center of Banjarmasin in July-August 2018

| Education level of pregnant women | MCH handbook Utilization | | | | Total | *P-value* | OR |
|---|---|---|---|---|---|---|---|
| | Ineffective | | Effective | | | | |
| | n | % | n | % | % | | |
| Low education | 29 | 85.3 | 5 | 14.7 | 100 | 0.005 | 7.457 |
| High education | 7 | 43.8 | 9 | 56.2 | 100 | | |

**Table. 3** The Relationship of Occupation of Pregnant Women with MCH Handbook Utilization at the Pekauman Public Health Center of Banjarmasin in July-August 2018

| Occupation of pregnant women | MCH handbook Utilization | | | | Total | *P-value* | OR |
|---|---|---|---|---|---|---|---|
| | Ineffective | | Effective | | | | |
| | n | % | n | % | % | | |
| Non-working | 31 | 86.1 | 5 | 13.9 | 100 | 0.001 | 11.160 |
| Working | 5 | 35.7 | 9 | 64,3 | 100 | | |

## DISCUSSION

In this study, pregnant women with low education level have the highest number, which is 68%. Someone's education level can be influenced by the motivation of individuals to pursue education (ideals), social conditions (family and community environment), family economic conditions, parent motivation, culture, and accessibility to educational facilities (distance, travel time, road facilities and transportation).[6]

Among respondents, most pregnant women do not work, which is 72%. Occupation describes the position of a person in society and occupation also describes a person's economic ability to

meet their needs. Occupation is also related to the level of someone's busy life.[7]

Most of the respondents are ineffective in using MCH handbook, which is 72%. Green states that health behaviour is influenced by three factors, namely predisposing factors, supporting factors, and driving factors. Predisposing factors include attitudes, beliefs, knowledge, values and culture that are manifested in education, work, age, experience, culture and information. Supporting factors include the distance of health services, family economic status, and availability of facilities. The driving factors include motivation from the family and support from health workers in the form of counseling.[8,9]

The results of cross-tabulation between the level of education and the utilization of the MCH handbook by pregnant women showed that the categories that were not effective in utilizing the MCH handbook were mostly found in pregnant women with a low education level of 29 respondents (85.3%). This is in accordance with the research in 2016, which states that the level of education influences changes in attitudes and behaviour. The low level of education makes it difficult for a person to absorb information and apply it in daily life, especially in terms of health.[10,11] The less education level of pregnant women, the less the level of awareness of responsibility for health.Based on this, the lower the level of education of pregnant women, the more pregnant women are not effective in utilizing the MCH handbook.

Based on the results of statistical tests with the Fisher test at Table 2, it was found that there was a significant relationship between the level of education of pregnant women and the utilization of MCH handbook (p-value = 0.005<0.05).

This study found that most pregnant women with a low level of education and ineffective use the MCH handbook. Based on Nursalam's theory, education determines how to receive one's information. Someone with a low education level will hinder the development of one's attitude towards the acceptance of information and newly introduced values.[10] The less education level of pregnant women, the less informed in the MCH handbook that pregnant women can receive, the less the behaviour of pregnant women in carrying out information in the MCH handbook, in this case, the use of the MCH handbook becomes ineffective. Based on Table 2, it can be seen that the value of Odds Ratio = 7.457,which means pregnant women with a low level of education have a risk of 7 times ineffective in utilizing MCH handbook than pregnant women with higher education levels.

The results of cross-tabulation between occupations and utilization of MCH handbook by pregnant women showed that the categories that were ineffective in using the MCH handbook were 31 respondents (86.1%). Contrary to the results research in 2016 at the Kelasan Sleman Public Health Center stating that most pregnant women who use MCH handbook are pregnant women who do not work because there is more time to pay attention to their pregnancy and get information about maternal and child health through health workers.[12,13]

Based on the results of statistical tests with the Fisher test at Table 2, it was found that there was a significant relationship between the occupation of pregnant women and the use of MCH handbook (p-value = 0.001 <0.05).

This study found that most pregnant women as housewives in the category non-working effectively in utilizing MCH handbook because according to research in 2017 the status of a housewife cannot guarantee that pregnant women have a lot of free time to read KIA books at home. Pregnant women as housewives have quite a busy schedule taking care of their home needs, their husbands and children. Based on Table 3, the value of Odds Ratio = 11.160 means that pregnant women with non-working categories have 11 times the risk of being ineffective in utilizing MCH handbook compared with pregnant women who work.

In 2015 respondents who worked outside and had many friends were very likely to have good knowledge and be more effective in utilizing MCH handbook compared to respondents who only worked around the house or even those who did not work. Respondents who do not work and are only at home, they get little information as a result of less association with others. The status of pregnant women who work does not guarantee that pregnant women do not have time to read

the MCH handbook.[10,14,15] Pregnant women who receive sufficient information, support, and motivation from the work environment can be more effective in utilizing the MCH handbooks.

The use of the MCH handbook is more effective for working mothers, but in 2015 it is recommended for pregnant women to reduce the workload that is too heavy because it will have an adverse impact on their pregnancy.[16,17]

## CONCLUSION

We found that most of the education levels of pregnant women in the low education category were 34 people (68%) and 36 pregnant women did not work (72%) Most of the use of the MCH handbook by pregnant women was 36 people (72%) were not effective in utilizing it. There is a meaningful relationship between the level of education and occupation of pregnant women and the utilization of the MCH handbook. This research is expected to be able to inform health care workers and local governments in the upcoming counseling regarding the importance of the MCH handbook as an effort to reduce maternal and infant mortality, especially in pregnant women with low education and not working.

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**Research Article**

# Differences of Vitamin D Level in Non-pregnant Reproductive Age Women and First Trimester Pregnant Women

## *Perbedaan Kadar Vitamin D pada Perempuan Usia Reproduksi Tidak Hamil dan Perempuan Hamil Trimester Pertama*

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## Abstract

**Objective :** To compare vitamin D level in non-pregnant reproductive age women and first-trimester pregnant women.

**Methods :** This was acomparative cross-sectional study. The vitamin D serum level of two groups, the first one wasnon-pregnant reproductive age women (18-35 years), and the second one was first-trimester pregnant women,was collected. Samples were examined by Electro Chemiluminescence Immunoassay (ECLIA) method. The study was conducted in Dr. Hasan Sadikin Hospital in February-April 2018.

**Results :** The mean of vitamin D level in the non-pregnant reproductive age women group was 18.73 (6.93) ng/mL, while the first-trimester pregnant women group was 13.87 (4.04) ng/mL. The difference in mean of vitamin D level in both groups was significant with *p-value*<0.001.

**Conclusions :** Vitamin D level in the non-pregnant reproductive age women group is higher than the first-trimester pregnant women group.

**Keywords :** first-trimester pregnant women, non-pregnant reproductive-age women, vitamin D.

## *Abstrak*

***Tujuan :*** *Membandingkan kadar vitamin D pada perempuan usia reproduksi tidak hamil danperempuan hamil trimester pertama sehingga dapat mencegah berbagai komplikasi kehamilan.*

***Metode :*** *Penelitian analitik komparatif potong lintang terhadap 60 perempuan yang dibagi menjadi 2 kelompok, kelompok perempuan usia reproduksi tidak hamil (18-35 tahun) dan kelompok perempuan hamil trimester pertama. Pada kedua kelompok dilakukan pemeriksaan kadar vitamin D dengan metode Electro-chemiluminescence immunoassay(ECLIA). Penelitian ini dilakukan di RSUP Dr. Hasan Sadikin pada bulan Februari-April 2018.Data diproses menggunakan program SPSS versi 24.0.*

***Hasil :*** *Kadar vitamin D rata-rata pada kelompok perempuan usia reproduksi tidak hamil adalah 18,73 (6,93) ng/mL, sedangkan pada kelompok perempuan hamil trimester pertama adalah 13,87 (4,04) ng/mL. Perbedaan kadar rata-rata vitamin D pada kedua kelompok tersebut bermaka dengan nilai p<0,001.*

***Kesimpulan :*** *Kadar vitamin D pada kelompok perempuan usia reproduksi tidak hamil lebih tinggi dibandingkan dengan kelompok perempuan hamil trimester pertama.*

***Kata kunci :*** *perempuan hamil trimester pertama, perempuan usia reproduksi tidak hamil, vitamin D.*

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## INTRODUCTION

Vitamin D is a fat-soluble vitamin that plays an important role in overall health. Vitamin D deficiency is widespread among women worldwide, particularly in Indonesia and Malaysia, with the prevalence up to 63%. Approximately 504 ofreproductive age women (18-40 years) is found the mean of 25-hydroxy-vitamin D (25[OH] D) serum level is 48 nmol/L.[1] Forty-eight percent of first trimester pregnant women in US also have vitamin D deficiency, with the mean of 25(OH)D serum level is 40 nmol/L.[2] Vitamin D deficiency has been widely discussed as a health problem that affects not only musculoskeletal health but also the problem of acute and chronic diseases as well as an increased risk of cancer, autoimmune disease, diabetes, and cardiovascular disease.[3]

Vitamin D deficiency is defined as 25-hydroxy-

vitamin D serum level< 20 ng/mL (50 nmol/L), while vitamin D insufficiency is vitamin D serum level 21-29 ng/mL (52-72 nmol/L).[4] Factors that affect vitamin D deficiency in non-pregnant reproductive age women and first trimester pregnant women include the changes of organ functions involved in the synthesis of 25 (OH) D such as skin, liver, kidney, and intestines; lifestyle that tend to avoid sunlight; use of sunscreen; and low intake of foods containing vitamin D. Whereas in these groups need to get attention because they are vulnerable to nutritional problems due to the physiological role of menstruation and childbirth.[5] Increased Body Mass Index (BMI) is also another factor that can affect vitamin D levels.[6]

The effect of vitamin D on muscle strength and muscle function has been shown in various studies of skeletal muscles in animals and humans. Pelvic floor weakness can manifest clinically in symptoms of pelvic floor dysfunction, including urinary incontinence, faecal incontinence, and pelvic organ prolapse. Thus there appears to be a relationship between the low serum vitamin D concentration which causes reduced skeletal muscle mass and muscle strength. The clinical relation of vitamin D deficiency and pelvic floor disorders is thought to be due to reduced skeletal muscle mass and muscle strength throughout the body, including the pelvic floor muscles of pelvis.[7]

Study shows that most of the reproductive age women in Indonesia have vitamin D deficiency.[8] Pregnancy and childbirth causes damage to the pelvic muscles due to stretching some pelvic muscles. After the birth, the pelvic muscles damaged need to repair, for about 3 months. Various causes influence the healing of pelvic muscles, and one of them is vitamin D level in reproductive age women and first trimester pregnant. Providing vitamin D supplementation tonon-pregnant reproductive age women and first trimester pregnant are not routinely given in Indonesia. The normal value of vitamin D levels in non-pregnant reproductive age women and first trimester pregnant in Indonesia remains unknown. In addition, study on the cause of vitamin D deficiency has never been done in Indonesia.

Considering these problems, this study aimed to compare vitamin D level in non-pregnant reproductive age women and first-trimester pregnant women in order to prevent some complications in pregnancy and the pelvic floor weakness, both in non-pregnant reproductive age women and pregnant women.

## METHODS

This was a comparative cross-sectional study. Subjects were non-pregnant reproductive-age women in Bandung and first-trimester pregnant women (18-35 years) in Dr. Hasan Sadikin Hospital Bandung with a timeline of February to April 2018. Samples were collected by consecutive sampling. The total population were 60 women, divided into two groups: 30 non-pregnant reproductive age women, and 30 first trimester pregnant women that match the inclusion and exclusion criteria.

The inclusion criteria were age 18-35 years old, BMI 18-30 kg/m$^2$, have no vitamin D supplementation, no smoking, exposed to sunlight between 8.00-3.00 p.m, have no chronic illness and malignancy. The exclusion criteria were women who did not continue the examination and those who were not included in the inclusion criteria.

Blood sample of vitamin D from subjects was collected and examined by Electro-chemiluminescence immunoassay (ECLIA) method.

Data were analyzed by T-test and processed with the help of Statistical Product and Service Solutions (SPSS) for Windows version 24.0.

## RESULT

**Table 1.** Characteristics of Age, BMI, Calories Intake, and Sunlight Exposure in both Groups

| Characteristics | Groups | | *P-Value* |
|---|---|---|---|
| | Non-pregnant reproductive-age women (n=30) | First-trimester pregnant women (n=30) | |
| **Age (year)** | | | |
| Mean (SD) | 23.9 (4.6) | 25.7 (4.6) | |
| Median | 21.5 | 26.5 | 0.153* |
| Range | 19–34 | 19–34 | |
| **BMI (kg/m2)** | | | |
| Mean (SD) | 22.6 (2.8) | 23.8 (3.1) | |
| Median | 21.9 | 24.4 | |
| Range | 18.3–29.9 | 18.7–29.5 | 0.101** |
| **Calories intake (kcal)** | | | |
| Mean (SD) | 2053.3 (179.5) | 2223.3(170.6) | |
| Median | 2050 | 2250 | |
| Range | 1700 – 2500 | 1800–2500 | <0.001** |
| **Sunlight exposure (minute)** | | | |
| Mean (SD) | 18.0 (4.1) | 17.7 (3.4) | |
| Median | 20 | 17.5 | 0.736* |
| Range | 10–25 | 10–25 | |

Interpretation : Calories intake in first trimester pregnant women was higher than non-pregnant reproductive age women (p<0.05), *analyzed by Mann-Whitney; ** analyzed by unpaired t-test.

**Table 2.** Differences of Vitamin D Level in both Groups

| Variable | Groups | | *P-Value* |
|---|---|---|---|
| | Non-pregnant reproductive-age women (n=30) | First-trimester pregnant women (n=30) | |
| **Vitamin D level (ng/ml)** | | | |
| Mean (SD) | 18.73 (6.93) | 13.87 (4.04) | |
| Median | 17.58 | 12.34 | 0.004* |
| Range | 10.39 – 36.26 | 8.48 – 24.65 | |
| **Vitamin D level after calories intake adjusted** | | | |
| Mean (SE) | 19.71 (1.03) | 12.89 (1.03) | <0.001** |
| Confident interval 95% | 17.64 – 21.78 | 10.82 – 14.96 | |
| **Vitamin D status** | | | |
| Deficiency (< 12) | 5 | 14 | |
| Insufficiency (12-20) | 11 | 13 | 0.003*** |
| Sufficiency (> 20) | 14 | 3 | |

Interpretation:Vitamin D level in non-pregnant reproductive age women was higher than first-trimester pregnant women (p <0.001), *analyzed by Mann-Whitney; **analyzed by ; ***analyzed by Chi-square.

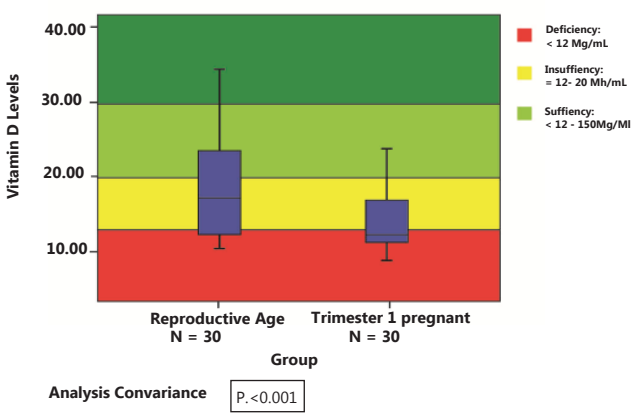


**Figure 1.** Differences of vitamin D level in non-pregnant reproductive age women and first-trimester pregnant women

**Vitamin D level**

Our study showed that the significant difference of vitamin D level in both groups (p <0.001). Vitamin D level in non-pregnant reproductive age women was 18.73 (6.93) ng/mL, while in the first-trimester pregnant women was 13.87 (4.04) ng/mL. The mean of vitamin D level both before and after calories intakeadjusted in non-pregnant reproductive age women was higher than first-trimester pregnant women. Based on vitamin D status, non-pregnant reproductive age women have vitamin D sufficiency (46.7%), while first-trimester pregnant women have vitamin D deficiency (46.7%).

## DISCUSSION

The characteristics of the subjects compared in this study were age, Body Mass Index (BMI), sunlight exposure and number of calories intake. This was based on the assumption that these factors can be confounding factors on the results of this study. So to be able to compare the two groups of studies, the characteristics of subjects between non-pregnant reproductive age women and first-trimester pregnant women must be homogeneous. It was found that there were no significant differences in the characteristics of the subjects, the age of patients (p=0.153), BMI (p=0.101) and duration of sunlight exposure (p=0.736), while the number of calories intake (p<0.001). This study concluded that both groups are homogeneous; thus, it was expected that bias due to age, BMI, and duration of sunlight exposure could be removed so that both groups could be compared.

The number of calories intake in this study was similar to the study suggested that non-pregnant reproductive age women have a daily calorie intake of 1,800-2,000 kcal for mild daily activities and 2,000–2,200 for moderate to heavy daily activities. In the first trimester pregnant women, the need for daily caloric intake increases by 150-200 kcal. This is caused by rapid fetal formation needs.[9]

**Vitamin D Level in Non-pregnant Reproductive Age Women and First-Trimester Pregnant Women**

The mean of vitamin D level in non-pregnant reproductive age women in this study was found to be significantly higher than first-trimester pregnant women. All subjects in this study had vitamin D level below normal (<30 ng/mL).

Vitamin D has an important role in calcium homeostasis as well as bone development and mineralization. Exposure to ultraviolet B (290-320 nm) is the main source of vitamin D.[10] For bone health, at least the level of 25-hydroxy-vitamin D3 20 ng/mL is needed.[11] Vitamin D deficiency is very common however, the magnitude of D hypovitaminosis could vary depending on the population studied, regional and seasonal considerations. Study in US found that the prevalence of vitamin D deficiency in non-pregnant reproductive age women was 52% up to 87% in winter and depends on height.[12] In a systematic review of 195 studies conducted in 44 countries with participants of approximately 168,000 people, the mean of 25-hydroxy-vitamin D3 serum level was <20 ng/mL for about 37.3% of the study subjects. Vitamin D deficiency in African-American, Turkish, and Chinese were 42.4%, 81.4%, and 79.7%, respectively.[13]

Vitamin D deficiency is a factor in the pathophysiology of several types of cancer, cardiovascular disease, hypertension, diabetes and morbidity in pregnancy.[4, 14-16] Data from the 2005-2006 NHANES survey showed that 69% of pregnant women and 78% of non-pregnant reproductive age women in U had levels of 25-hydroxy-vitamin D3 <30 ng/mL. In pregnancy, the placenta is an extra-renal source of calcitriol (1,25-dihydroxy-vitamin D).[12]

In 504 women of childbearing age (WUS) aged 18-40 years found that serum concentrations of 25-hydroxy-vitamin D3 were 48 ng/mL with a prevalence of vitamin D deficiency of 63%. As many as 63% of WUS in Jakarta aged 18-40 years have vitamin D deficiency with the mean level of 25-hydroxy-vitamin D3 concentration of 19.2 ng/mL.[1]It was found that vitamin D deficiency can be caused by lifestyle tend to avoid sunlight exposure, use of sunscreen and low food intake of vitamin D. People who live near the equator exposed to sunlight without using a kind of sunscreen protector have 25-hydroxy-vitamin D3 level >30 ng/mL.[1, 17]

Vitamin D is deposited mainly in adipose tissue and muscle. Vitamin D has been detected in different adipose tissue compartments, such as

the subcutaneous abdomen, omental, pericardial and perirenal.[18, 19]High-fat levels can also cause low levels of vitamin D in the circulation due to the trapping of vitamin D in fat cells.[20]A study found that 70.4% of obese women had 25(OH)D circulation between 25 and 75 nmol/L, compared to 86.1% of reproductive-age women.[21]Obese women had 25 (OH) D lower than normal-weight women in the first trimester of pregnancy. Similarly, a study by Bodnar et al. found that obese women (based on pre-pregnant BMI) had lower serum concentrations of 25(OH)D compared to normal-weight women in first-trimester pregnancy.[22]

Pregnancy can increase the concentration of Vitamin D Binding Protein (VDBP) in circulation. Estrogen metabolism can be disrupted in obese women, and this can potentially affect hepatic production of VDBP. Circulating VDBP concentrations are influenced by the VDBP phenotype, and a relationship between DBP, gene polymorphism, and fat mass has been demonstrated. In an in vitro study, interleukin-6 (IL-6) increases the expression of messenger ribonucleic acid (mRNA) inside, and VDBP secretion from hepatic cells. Higher levels of circulating IL-6 in obese women are found and could possibly affect DBP hepatic production. Interestingly, DBP concentrations are positively associated with serum lipids and high sensitive C-reactive protein (hs-CRP).[18]The possible reason for low 25(OH)D in first-trimester pregnant women is low vitamin D intake. In a food intake survey by Riksmaten showed that intake of vitamin D in women, the age group of 18-30 years and 31-44 years was 5.2 and 6.2 µg/day respectively.[18]

Concentrations of 1α,25-(OH) 2D and DBP circulation increase during pregnancy. 1α,25-(OH)2D increases due to increased renal 1α-hydroxylase activity and increased DBP due to increased estrogen levels that affect hepatic production. Both VDR and the enzymes responsible for converting 25 (OH) D to 1α, 25 (OH) 2D are present in the placenta, making it at least have an autocrine or paracrine effect. In observational studies, low vitamin D levels during pregnancy have been associated with an increased risk of preeclampsia, diabetes mellitus in pregnancy, and fetal growth restriction.[18]

The limitation in this study was the mean of vitamin D level in the population in Southeast Asia, especially in Indonesia, was still very limited, so there was no reference value for vitamin D levels for the mean of vitamin D level in Indonesian women. This study was cross-sectional, so it could not be concluded about the causes of differences in vitamin D levels in both groups. Further study was needed in the form of longitudinal studies that assess differences in vitamin D levels by giving vitamin D supplementation.

## CONCLUSION

Vitamin D level in non-pregnant reproductive-age women is higher than first-trimester pregnant women.

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**Research Article**

# Postoperative Pain Survival and Correlating Factors in Endometriosis Patients

## *Kesintasan Keluhan Nyeri Pascapembedahan pada Pasien Endometriosis serta Faktor-Faktor yang Mempengaruhi*

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## Abstract

**Objective :** To determine the survival of pain complaints at 3, 6, 9 and 12 months and the correlation between age at diagnosis, age of menarche, parity, stage of disease and post-operative medication in endometriosis patient at RSUPN Dr. Cipto Mangunkusumo.

**Methods :** This was a prospective cohort study with survival analysis method of 139 women of productive age with endometriosis who came to gynecology outpatient clinic in Dr. CiptoMangunkusumo Hospital from January 2015 to January 2017. The patients were observed at 3 months, 6 months, 9 months and 12 months after the surgery.

**Results :** Survival of pain complaints at 3, 6, 9 and 12 months after endometriosis operation was 99.2%, 96.6%, 93% and 88.4% respectively. There was no significant correlation between post-operative pain survival and age of diagnosis (p=0.138), age of menarche (p=0.492), parity (p=0.110) and stage of disease (p=0.908). There was a significant correlation between post-operative medical therapy and pain complaints survival. Subjects who were given medication had a risk of 0.26 times (CI 95% 0.081-0.857) pain recurrence compared to those who were not.

**Conclusions :** Pain complaints survival were significantly associated with post-operative medical therapy, but not associated with age, age of menarche, parity and stage of disease.

**Keywords :** endometriosis, postoperative medical therapy, postoperative pain, survival.

## *Abstrak*

***Tujuan :*** *Mengetahui kesintasan keluhan nyeri pada 3, 6, 9 dan 12 bulan dan hubungan antara usia saat diagnosis, usia menarke, paritas, stadium penyakit dan terapi medisinalis pascapembedahan pada pasien endometriosis di RSUPN Dr. CiptoMangunkusumo.*

***Metode :*** *Penelitian kohort prospektif pada 139 perempuan usia produktif dengan metode analisis kesintasan pada pasien endometriosis yang dating ke poliklinik ginekologi RSUPN Cipto Mangunkusumo pada bulan Januari 2015 hingga Januari 2017. Pasien kemudian diobservasi pada bulan ke 3, 6, 9 dan 12 setelah operasi.*

***Hasil :*** *Kesintasan keluhan nyeri pada bulan ke 3, 6, 9 dan 12 berturut-turut adalah 99,2%, 96,6%, 93% dan 88,4%. Tidak ada hubungan yang bermakna antara kesintasan nyeri pascapembedahan dengan usia saat diagnosis (p=0,138), usia saat menarke (p=0,492), paritas (p=0,110) dan stadium penyakit (p=0,908). Terdapat hubungan yang bermakna antara terapi medisinalis pascapembedahan dan kesintasan keluhan nyeri. Subyek yang mendapatkan terapi medisinalis pascapembedahan memiliki risiko 0,26 kali mengalami kekambuhan nyeri dibandingkan dengan yang tidak.*

***Kesimpulan :*** *Kesintasan keluhan nyeri memilki hubungan yang bermakna dengan terapi medisinalis pascapembedahan namun tidak memiliki hubungan dengan usia saat diagnosis, usia menarke, paritasdan stadium penyakit.*

***Kata kunci :*** *fendometriosis, kesintasan, nyeripascapembedahan, terapi medisinalis pascapembedahan.*

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## INTRODUCTION

Endometriosis is defined as abnormal implantation of endometrial tissue outside the uterine cavity. This ectopic tissue may lead to chronic inflammation process that depends on estrogen hormone.[1-7] Endometriosis is found in up to 176 million people all over the world. It affects around 5-10% women of reproductive age.[5,7,8]This disease is one of the leading causes of pain complaints; which includes dysmenorrhea, dyspareunia, chronic pelvic pain, dysuria and dyschezia.[4] In Dr. Cipto Mangunkusumo Hospital, most endometriosis patients came with the complaint of pelvic pain (82.5%), followed by dysmenorrhea (81%), *low back pain* (32.5%),

dyspareunia (20,9%) and dyschezia (4.6%). These pain complaints lead to low quality of life; therefore,treatment is required.[7,9,10]

There are two modalities in treating endometriosis patients which are conservative and surgical therapy. Until today, the treatment of choice to treat endometriosis is laparoscopy. This treatment has several purposes such as to lessen the pain, recurrence rate and to maintain fertility.[11,12]

Endometriosis has a high recurrence rate of 21.5%, 46.7% and 55.4% at the second, fifth and seventh year after surgery.[13] A study 23 studies, the recurrence rate of endometriosis after surgery is as high as 40-50% at the fifth year.[14,15]This study also stated that the risk factors of this high recurrence include age when diagnosed, stage of disease and history of previous treatment.

These data imply that pain recurrence in endometriosis patients is an essential aspect. Therefore, it is important to know what factors could affect pain survival. Considering that, we are interested to know the recurrence rate of pain in endometriosis patients through survival analysis and its correlating factors in Dr. Cipto Mangunkusumo Hospital.

## METHODS

This research was a prospective cohort study. Subjects were women 18-49 years old who came to Gynecology Outpatient Clinic from January 2015 to January 2017. A total of 154 patients obtained consecutively who were diagnosed with endometriosis underwent surgery in Dr. CiptoMangunkusumo Hospital at that time. Only 139 out of 154 patients metthe inclusion criteria of this research. Inclusion criteria were endometriosis patients who had a psychosocial activity limitation, use of analgesic medication, and visual analogue scale (VAS) of 4 or more. The VAS was 4 or more on dysmenorrhea, dyspareunia, pelvic pain, dysuria or dyschezia symptoms with a minimum of once at the measurement period. Exclusion criteria were patients who had a history of abdominal surgery (except appendectomy), who had other diseases than endometriosis which could lead to pelvic pain, diagnosed with neurotic disease and/or psychiatric diseases and had a history of tubectomy.

Data were analyzed using SPSS®softwarefor IOS version 22.0. The survival rate of pain complaints was analyzed using Kaplan-Meier analysis. All variables meet the proportional hazard assumption, therefore the analysis was done using cox regression. Patients were followed up to 12 months.

## RESULT

**Table 1.** Characteristics of Postoperative Endometriosis Patients in Cipto Mangunkusumo from January 2015 to January 2017

| Characteristics | | Description (n=139) |
|---|---|---|
| Age (years) | | 40 (17 – 49) |
| Age category | <30 | 18 (12.9%) |
| | ≥30 | 121 (87.1%) |
| Age of menarche | <11 | 4 (2.9%) |
| | ≥11 | 135 (97.1%) |
| Parity | 0 | 66 (47.5%) |
| | 1 | 23 (16.5%) |
| | 2 | 29 (20.9%) |
| | 3 | 19 (13.7%) |
| | 4 | 2 (1.4%) |
| Parity category | 0 | 66 (47.5%) |
| | 1-2 | 53 (38.1%) |
| | ≥3 | 20 (14.4%) |
| Stage of disease | Minimal | 1 (0.7%) |
| | Mild | 24 (17.8%) |
| | Moderate | 47 (37.8%) |
| | Severe | 67 (48.2%) |
| Stage of disease category | Minimal andmild | 25 (18%) |
| | Moderate and severe | 114 (82%) |
| Medical therapy | No | 91 (65.5%) |
| | Yes | 48 (34.5%) |
| Post-operative medical therapy | No medicinal therapy | 91 (65.5%) |
| | Progestin | 28 (20.1%) |
| | GnRH agonist | 11 (7.9%) |
| | Progestin + GnRH agonist | 2 (1.4%) |
| | COC | 6 (4.3%) |
| | COC + progestin | 1 (0.7%) |
| Pain after surgery | Did not recur *(censor)* | 126 (90.6%) |
| | Recur *(event)* | 13 (9.4%) |

In this study, the age of subject sranges from 17-49 years old with the median of 40 years old. Most subjects (87.1%) are 30 years and above. One hundred and thirty-five subjects (97.1%) had menarche at the age of 11 or more. Most subjects (66 patients) were nullipara, 23 subjects (16.5%) were primipara, 29 subjects (20.9%) had 2 parity, 19 subjects (13.7%) 3parity and only 2 subjects had 4 parity.

Endometriosis degree of patients in this study was assessed into four stage. One subject (0.7%) had minimal disease, 24 subjects (17.8%) had mild disease, 47 subjects (37.8%) had moderate disease and 67 patients (48.2%) had severe disease. Forty-eight subjects (34.5%) were given medical therapy after the surgery. Most of them (20.1%) were given progestin medication. After a 3 months regular follow-up up to a year, 126 patients (90.6%) stated the pain did not recur.

**Survival Rate**

The pain survival rate were acknowledged every three months. On the third months, the pain survival rate were 99.2%. However this percentage were decreased to 96.6% after 6-month follow-up and 93% after 9 months follow up. After 12 months of follow-up, the pain survival rate was 88.4%. From the Kaplan-Meier curve, the survival rate decreased over time. However, this research did not reach the median time because the observation is limited to 12 months.

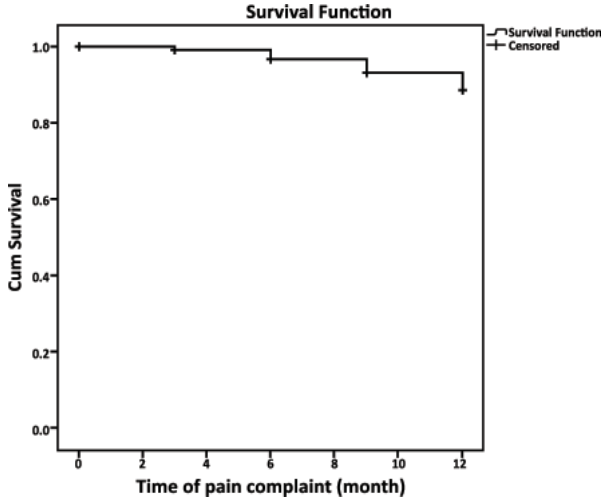


**Figure 1.** Kaplan Meier Curve of Overall Pain Survival in Endometriosis Patients

Subjects who were under 30 years old and 30 years above had the pain survival rate at 12 months follow-up of 63% and 87%, respectively. However, the log-rank test analysis showed there was no significant association between pain survival and the age category (p=0.152). In this study, subjects who had menarche on the age of 11 years old and above had the pain survival rate of 86% after 12 months follow-up. Below 11 years old, the pain survival was 50% after 12 months follow up, while 11 years oldhas pain survival for 86% after 12 months follow-up, This study also analyzed the association between age of menarche and pain survival and it is found that there was no significant association between both variables (p=0.286). Subjects with 0, 1-2, and 3 or more parity had the pain survival rate after 12 months follow-up of 83%, 93% and 68%, respectively. However, both groups were statistically insignificant, with the p value= 0.061. At 3 months follow up, subjects with 0, 1-2, and 3 or more parity had an almost similar percentage of survival 98%, 100%, and 100% respectively, however, significant decrease after six months follow up were subjects with three or more parity (87%).

In this study, subjects with a minimal-mild stage of endometriosis experienced pain survival of 90% and subjects with moderate-severe stage's pain survival were 83%. Nevertheless, this result is statistically insignificant (p=0.908).

The pain survival rate of patients who received postoperative medical therapy was started from 100% on 3 months follow up to 73% after 12 months follow-up, and those who did not receive had the pain survival rate was started from 99% on the first 3-month follow-up to 91%. From the analysis, the post-operative medical therapy category and pain survival had no significant association.

Variables were also analyzed using bivariate analysis to find the hazard ratio. The hazard ratio (HR) of age when diagnosed, age of menarche, parity, stage of the disease and post-operative medical therapy were 2.46, 2.85, 0.44 and 0.03, 0.92 and 0.26, respectively. Variables who had the p-value < 0.25, which were age, age of menarche, parity and post-operative medical therapy, were then included in the multivariate analysis. From the multivariate analysis, it was found that post-operative medical therapy had the p-value of 0.027 and HR of 0.26 (CI 95% 0.081-0.857).

**Table 2.** Multivariate Analysis Result

| Variables | HR | | | |
|---|---|---|---|---|
| | Model 1 | Model 2 | Model 3 | Model 4 (last) |
| Age category | 3.31 | 3.83 | 2.39 | 3.31 |
| Age of menarche category | 2.22 | - | - | 2.22 |
| Parity category | 1.92 | 1.89 | - | 1.92 |
| Post-operative medical therapy | 0.25 | 0.24 | 0.27 | 0.25 |

## DISCUSSION

From 139 subjects, 13 subjects had censor (loss to follow up). Overall, the pain survival rate reduces over time from 99.2% at three months to 88.4% at 12 months. The median time of pain survival was 24 months. Therefore, this study needed a longer follow-up time.[16]

### Pain Survival and Age when Diagnosed

Pain survival in postoperative endometriosis patients with the age < 30 years old when diagnosed at 3, 6, 9 and 12 months were 100%, 100%, 92% and 63%. While the group of age 30 and above had the pain survival of 98%, 96%, 92% and 87%. This showed that pain recurrence was found more in patients age 30 and above. Though statistically insignificant, this variable was included in the multivariate analysis because it was clinically significant. However, at the third model, this variable did not affect the pain complaints.

This result was similar that age and pain survival is statistically insignificant but patients with younger age (29,9±5,4 years old vs 32.6±6.1 years old) had clinically significant pain survival and recurrence of endometriosis with the HR = 0.935 (CI 0.895-0.977).[16,17] Endometriosis patients who were diagnosed at a younger age were linked with lesser estrogen and therefore may reduce the recurrence rate. The low survival rate of 63% at subjects <30 years old may be due to limited number of samples in this category.

### Pain Survival and Age of Menarche

Patients who had menarche at the age of <11 years old had pain survival at 3, 6, 9 and 12 months of 100%, 100%, 100% and 50%. While the other group had the pain survival of 99%, 96%, 93% and 86%. However, this variable is clinically insignificant after the Log rank test. This variable was included in the multivariate analysis because its p value=0.315 but at the end of the analysis, this variable showed no effect in pain complaints. This result showed that patients who had menarche at a younger age had a higher risk of pain complaints recurrence. This was supported by other literature that stated patients who had menarche at an earlier age is at higher risk of pain recurrence in endometriosis.[16]

### Pain Survival and Parity

Subjects with 0-1 parity had the highest pain survival rate at 3, 6, 9 and 12 months among the group, which were 100%, 100%, 98% and 93%. From the log-rank test, parity was not significantly associated with pain survival. However, this variable was found to be clinically significant and was included in the multivariate analysis. This result was different from several studies that found pregnancy before endometriosis surgery as a protective factor of pain survival with the OR=0.759 ($p<0.05$).[12,18-20]Infertility was found to have a linked with more prolonged estrogen exposure and therefore could trigger the occurrence of endometriosis. In contrast, pregnancy could cause regression of endometriosis lesion.[21,22]

### Pain Survival and Stage of Disease

In this study, the stage of disease was categorized into minimal-mild and moderate-severe. Patients with minimal-mild disease had the pain survival after 3, 6, 9 and 12 months of 95%, 95%, 90% and 90%. While patients with the moderate-severe disease had the pain survival of 100%, 97%, 94% and 83%. From the log-rank test, this variable was found to be statistically unassociated with the pain survival rate. Bivariate analysis showed that this variable in clinically insignificant, so this variable was not included in the multivariate analysis.

From other literature, high recurrence rate was found in subjects with moderate to severe stage of endometriosis. Besides the stage, the surgery technique was also associated with the recurrence rate. Conservative operations could lead to progressive growing of endometriosis and therefore subjects can experience chronic pelvic pain.[13,16,23-27]

**Pain Survival and Medical Therapy**

Forty-eight subjects received medical therapy after the surgical procedure in this study. From the 48 subjects, 20.1% received progestin, 7.9% received Gn-RH agonist, 1.4% received progestin and Gn-RH agonist, 4.3% received combined oral contraceptives (COC); 0.7% received COC and progestin. The pain survival of subjects receiving medical therapy was 100%, 93%, 86% and 73% at 3, 6, 9 and 12 months follow-up. From the bivariate analysis, this variable was found to have a significant association with pain survival (HR=0.26, CI 95% 0.08-0.86; p=0.027).

From a systematic review, though still inconsistent, it was found that hormonal therapy suppression after surgery compared to surgery alone reduced pain complaints after 12 months.[28] Some studies showed that patients who were treated with laparoscopic excision and cyclic oral contraceptives (such as desogestrel, gestodene and dianogest) had significant reduction of pain than those treated with laparoscopic excision alone. Progestin prevented implantation and endometriosis growth by inhibiting the expression of metalloproteinase matrix and angiogenesis thus reducing inflammation.[29-31]

Besides progestin, COC could also be used. COC worked by reducing the frequency of menstrual period, inducing endometriosis to become atrophy, reducing prostaglandin production that plays a role in pain and reducing cell proliferation.[29,32] Gn-RH agonist is another treatment method of endometriosis;however, it should not be used for longer than 6 months due to its effect of estrogen deficit.[33]

## CONCLUSIONS

In conclusion, the 3, 6, 9 and 12 months follow-up of post-operative endometriosis patients showed a pain survival of 99.2%, 96.6%, 93% and 88.4%, respectively. Age, age of menarche, parity and stage of the disease have no significant association with the pain survival of post-operative endometriosis patients. However, postoperative medical therapy was significantly associated with reduction of pain. Longer study and *randomized controlled trial* (RCT) study is needed to reduce selection bias and indication bias.

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**Research Article**

# Profile of D-dimer in Uncomplicated Pregnancy

## *Profil D-dimer Kehamilan tanpa Komplikasi*

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## Abstract

**Objective :** To obtain the profile of D-dimer in uncomplicated pregnancy.

**Methods :** A cross sectional study was done on 90 uncomplicated pregnant women consisted of 30 women in each trimester and 30 healthy, nonpregnant women as control group from July to August 2012. D-dimer level was measured by particle enhanced immunoturbidimetry method using Innovance D-dimer and Sysmex CA 1500 in the Department of Clinical Pathology, Dr. Cipto Mangunkusumo Hospital, Jakarta.

**Results :** All women in the control group showed normal D-dimer level (<0.,5 mg/L FEU). The median and range of D-dimer level in the 1st trimester, 2nd trimester, and 3rd trimester were 0.42 mg/L FEU and 0.1-1.07 mg/L FEU, 0.97 mg/L FEU and 0.6-3.34 mg/L FEU, and 1.56 mg/L FEU and 0.69-3.75 mg/L FEU, respectively. Increased D-dimer level was found in 27% of pregnant women in 1st trimester, 87% in 2nd trimester, and 100% in 3rd trimester.

**Conclusions :** Increased D-dimer level was found in 27% of pregnant women in 1st trimester, 87% in 2nd trimester, and 100% in 3rd trimester. The range of D-dimer level in the 1st trimester was 0.1-1.07 mg/L FEU, in the 2nd trimester was 0.6-3.34 mg/L FEU, and in the 3rd trimester was 0.69-3.75 mg/L FEU.

**Keywords :** D-dimer, trimester, uncomplicated pregnancy.

## *Abstrak*

***Tujuan :*** *Untuk mendapatkan profil D-dimer pada kehamilan tanpa komplikasi.*

***Metode :*** *Penelitian potong lintang dilakukan pada 90 perempuan hamil tanpa komplikasi yang terdiri atas 30 perempuan pada tiap trimester dan 30 perempuan sehat yang tidak hamil, sebagai kelompok kontrol dari bulan Juli sampai Agustus 2012. Kadar D-dimer diukur dengan cara particle enhanced immunoturbidimetry menggunakan reagen Innovance® D-dimer dan koagulometer Sysmex® CA 1500 di Deparemen Patologi Klinik, Rumah Sakit Umum Pusat Nasional Dr. Cipto Mangunkusumo, Jakarta.*

***Hasil :*** *Seluruh perempuan dalam kelompok kontrol mempunyai kadar D-dimer dalam batas normal (<0.,5 mg/L FEU). Median (rentang) kadar D-dimer pada trimester pertama, kedua, dan ketiga berturut-turut 0.42 mg/L FEU (0.1-1.07 mg/L FEU), 0.97 mg/L FEU (0.6-3.34 mg/L FEU), dan 1.56 mg/L FEU (0.69-3.75 mg/L FEU). Peningkatan kadar D-dimer ditemukan pada 27% perempuan hamil trimester pertama, 87% trimester kedua, dan pada 100% trimester ketiga.*

***Kesimpulan :*** *Peningkatan kadar D-dimer ditemukan pada 27% perempuan hamil trimester pertama, 87% trimester kedua dan 100% pada trimester ketiga. Rentang kadar D-dimer level pada trimester pertama adalah 0.1-1.07 mg/L FEU, pada trimester kedua 0.6-3.34 mg/L FEU, dan pada trimester ketiga 0.69-3.75 mg/L FEU.*

***Kata kunci :*** *D-dimer, kehamilan tanpa komplikasi, trimester*

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## INTRODUCTION

The incidence of Venous Thromboembolism (VTE) in pregnant women is 4-5 folds higher than nonpregnant women.[1] Obstetric complications that associated with thromboembolisms are recurrent abortus, preeclampsia, and fetal growth retardation.[2] Increased risk of VTE in pregnancy is associated with venous stasis due to uterus enlargement and hypercoagulable state.[1,3] Many experts think that hypercoagulable state in pregnancy is anaturally occurring mechanism to anticipate bleeding during labour.[3]

The clinical manifestations of VTE are Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE). The accuracy of VTE diagnosis solely based on clinical manifestations is low. Venography is the gold standard in the diagnosis of DVT, but this procedure is invasive, and now compression ultrasonography and D-dimer are used as a modality in the diagnosis of DVT after clinical probability has been determined.[4]

D-dimer is a degradation product of cross-linked fibrin by the action of plasmin during fibrinolysis process. Since cross-linked fibrin is formed as the end product of coagulation process, D-dimer can be used as a marker of coagulation activation as well as fibrinolysis.[5] Elevated D-dimer level is found in many conditions where activation of coagulation occurs such as VTE, disseminated intravascular coagulation (DIC), malignancy, sepsis, postoperative condition, post-traumatic injury, myocardial infarction, heart failure, liver diseases, pregnancy, and in elderly. Since increased D-dimer is very sensitive but not specific for VTE, normal level of D-dimer isused to exclude the diagnosis of VTE.[5]

Measurement of D-dimer level in pregnancy is vital to predict VTE and associated obstetric complications. However, this approach is hampered due to increased D dimer in normal pregnancy.[3] D-dimer level in Caucasian women using MDA® Immunoturbidimetric, Organon Teknika reported that D-dimer level increased above normal value starting from first trimester in pregnancy.[6] At second trimester normal D-dimer level only found in 22% of pregnant women, and in the third trimester all pregnant women showed increased D-dimer level.[6]On the other hand who measured D-dimer in Nigerian women using ELISA technique with Technozym®, Technoclone GmDH reported that 63.3% of pregnant women had normal D-dimer values (0-200 ng/mL),[7] 26.7% of the pregnant women had elevated D-dimer values (201-499 ng/mL), while 10.0% were found to be at risk of thrombosis (D-dimer >500 ng/mL). This discrepancy may be caused by different population race and different method in measuring D dimer. To date, there is no data regarding the D-dimer level in Indonesian pregnant women. This situation prompts us to determine D-dimer level in Indonesian uncomplicated pregnant women in each trimester. The objective to study is to obtain the profile of the D-dimer level of uncomplicated pregnancy.

## METHODS

This study had been approved by the Ethics Committee, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo Hospital (No.396). Written informed consents were obtained from all subjects. This study was designed as a cross-sectional study and was performed from July to August 2012.

### Subject and Control

Based on results, the minimum number of subjects in each trimester was 29 [6]. In this study 30 subjects in each trimester wererecruited from the Obstetric clinic in Dr. Cipto Mangunkusumo Hospital, and from several Community Health Centres in Matraman, Jatinegara, Cakung, and Pulogadung. Inclusion criteria were pregnant women on the first, second, and third trimester. Control group were 30 healthy, nonpregnant women of the same reproductive age that were recruited from students and laboratory technician. Exclusion criteria were hypertension, leg oedema, seizures, leukocyte count more than 12 000/mL, proteinuria, and diabetes mellitus. Additional exclusion criteria for the control group were positive in pregnancy test, inflammation, and oral contraceptive users. Samples collection were done consecutively.

### Samples and Measurement

Samples for this study comprised blood and urine. Blood was collected by veni puncture at fossa cubiti, 3 mL of blood was mixed with

trisodium citrate 0.109 M as an anticoagulant for D-dimer determination and 3 mL was mixed with $K_3$EDTA for hematology examination. Citrate bloodwas centrifuged at 1500 x g for 15 minutes to obtain platelet-poor plasma for D-dimer measurement. Hematology examination was done using hematology analyzer Sysmex XE-2100. Proteinuria and glucosuria were examined by semi quantitative method using AIM URI-TEST®according to manufacturer instruction.

**Determination of D-dimer Level**

Determination of D-dimer level was performed using Innovance® D dimer Kit, Sysmex consisted of Innovance D-dimer Reagent which contains polystyrene particle coated with monoclonal mouse antibodies against D-dimer, Innovance D-dimer Buffer is buffer saline solution which contains detergent and carbohydrate polymer, Innovance D-dimer Supplement is buffer saline solution which contains blocking reagent to inhibit nonspecific reaction against heterophilic antibodies such as rheumatoid factor and anti-mouse antibody, Innovance D-dimer Diluent is buffer saline solution which contains detergent to dilute sample, control, and calibrator. Principle of Innovance® D-dimer assay is particle-enhanced immunoturbidimetric assay. D-dimer in the plasma reacted with specific monoclonal antibody-coated bead and resulted in agglutination and increased turbidity. Increased turbidity was measured by Sysmex CA1500.[8,9] Before measuring D-dimer in plasma samples, precision and accuracy tests were done by measuring Innovance® D-dimer control 1 (normal control) with assign value 0.26 – 0.38mg/L FEU and Innovance® D dimer control 2 (abnormal control) with assign value 2.22 – 3.32 mg/L FEU.

**Statistical Analysis**

The result of precision test was analyzed by calculating the mean, standard deviation and Coefficient of Variation (CV). Accuracy was analyzed by calculating the difference between the smallest and largest value obtainedfrom the target value.

Data analyses of D-dimer of pregnant and control groups were done based on data distribution. Distribution of continuous data was analyzed.[10]Data with normal distribution would be presented as mean and standard deviation, while data with abnormal distribution would be presented as median and range. The difference between groupswith normal distribution was analyzed by one way ANOVA. If there was a significant difference, ANOVA was followed by Post-Hoc analysis. If abnormal distribution was obtained, logarithmic transformation should be done and the distribution oftransformed data would be checked. If data distribution was still abnormal, then analysis was used to analyze the difference between groups.[11] Statistical analyses were done using SPSS version 12.

## RESULTS

The results of within run precision test using Innovance® D-dimer normal control and abnormal control revealed CV 2.5% and 1.36%, respectively. While the results of accuracy test revealed d=(-12,5%) – (-6.2%) for normal control and d= (-0.9%) – (5.0%) for abnormal control. Data distribution of D-dimer in the pregnant group as well as in control group were abnormal; thus, data were presented as median and range from minimum to maximum (Table 1).

**Table 1.** The Level of D-dimer in Pregnant Women and Control Group

| Group | n | Median (mg/L FEU) | Range (min-max) (mg/L FEU) |
|---|---|---|---|
| Control | 30 | 0.21 | 0.11 – 0.50 |
| 1st trimester | 30 | 0.42 | 0.17 – 1.07 |
| 2nd trimester | 30 | 0.97 | 0.31 – 3.34 |
| 3rd trimester | 30 | 1.56 | 0.69 – 3.75 |

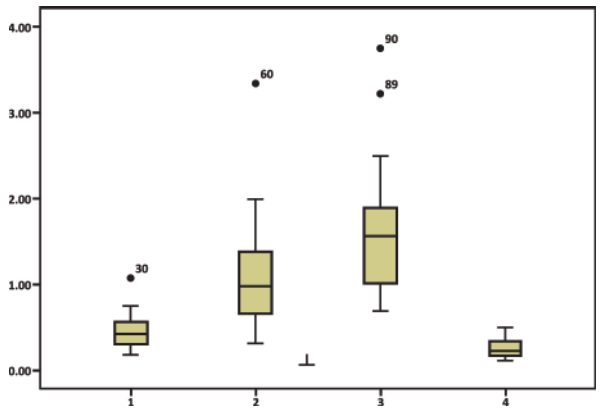


**Figure 1.** Boxplot of D-dimer Level in Pregnant Women and Control Group

Based on 0.5 mg/L Fibrinogen Equivalent Unit (FEU)as the upper limit of normal range, increased D-dimer level was found in 8 out of 30 (27%) pregnant women in first trimester, 26 out of 30 (87%) pregnant women in second trimester, and all (100%) pregnant women in third trimester (Table 2). There was nosubject who showed increased D-dimer level in the control group.

**Table 2.** The Proportion of Women with Increased D-dimer Level

| Group | Proportion of subjects with increased D-dimer level (%) |
|---|---|
| Control group | 0 |
| 1st trimester | 27 |
| 2nd trimester | 87 |
| 3rd trimester | 100 |

After logarithmic transformation, it was found that datadistribution of D-dimer in all trimester was normal. The result of one way ANOVA revealed that p = 0.00, so Post-Hoc analysis was done. Post-Hoc analysis between the control group, first trimester, second trimester, and third trimester revealed p=0.00.

## DISCUSSION

The results of within run precision using normal and abnormal control revealed CV=2.5% and 1.36%, respectively. These values were still lower than allowable CV mentioned by the manufacturer, i.e.: 4.1% for normal control and 1.4% for abnormal control.

The results of accuracy test indicated d=(-12.5%) - (-6.2%) using normal control and d=(-0.9%) - (5.0%) using abnormal control. Both values were still lower than allowable value mentioned by manufacturer 18.75% for normal control and 19.85% for abnormal control. Based on precision and accuracy, Ddimer measurement in this study is valid.

The level of D dimer in the control group showed that median was 0.21 mg/L FEU with range 0.11 – 0.50 mg/LFEU. Increased D dimer level was not found in the control group. In pregnant women median and range of D dimer level in the first, second, and third trimester were 0.42(0.17– 1.07)mg/L FEU, 0.97(0.31 – 3.34) mg/L FEU, and 1.56(0.69 -3.75)mg/L FEU,respectively. Comparisonof the results of this study with data from the literature presented in table 3.

It was shown that the increased D dimer level during pregnancy was obtained by other studies. The difference of D dimer level in pregnancy, as shown in table 3 might be caused bydifferent method, reagent, cutoff value, and population. The study who measured D- dimer level in the same samples of pregnant women using 5 different reagents confirmed that different reagents and methods caused variability of D-dimer level (Table 4).[15]

**Table 3.** Comparison of the Results of This Study with Data from the References

| Author Country | Method | Reagent | Cut off | 1st trimester mg/L or µg/mL | 2nd trimester mg/L or µg/mL | 3rd trimester mg/L or µg/mL |
|---|---|---|---|---|---|---|
| Kline[6] et al US | Immunoturbidimetric | MDA | 0.5 | 0.58±0.36* | 0.83±0.46* | 1.16±0.57* |
| Kawaguchi[11] et al Japan | Latex agglutination | Mitsubishi Kagaku Iatron Inc, Tokyo | 1.0 | 0.82±0.79* | 1.78±1.67* | 2.48±2.36* |
| Reger[12] et al Hungary | Not mentioned | IL, Milano | 0.250 | 0.250 (0.152-0.607)** | 0.309(0.191-0.874)** | 0.541(0.260-1.036)** |
| Hedengran[13] et al Denmark | Latex agglutination | STA Liatest D-DI | 0.5 | 0.2–0.9 | 0.2–1.5 | 0.4--2.8 |
| Elst[5] et al Belgium | ELFA | Vidas, Biomerieux | 0.5 | 0.18–0.30 | 0.18-1.29 | 0.28-2.08 |
| Morse[14] et al UK | Not mentioned | IL- Test™ D dimer | 0.280 | 0.191±0.025* | 0.393±0.072* | 0.544±0.096* |
| This Study Indonesia | Immunoturbidimetric | Innovance, Sysmex | 0.5 | 0.42(0.17 – 1.07)** | 0.97(0.31 – 3.34)** | 1.56(0.69 – 3.75)** |

*mean±SD, ** median (range)

**Table 4.** Median and Range of D-dimer Level at Pregnancy Determined by Various Methods[15]

| Reagents (unit) | Method | 1st trimester | 2nd trimester | 3rd trimester |
|---|---|---|---|---|
| Vidas® (µg/mL FEU) | ELFA | 0.6 (0.15 – 1.35) | 0.71 (0.55 – 0.95) | 1.48 (0.97 – 2.05) |
| Asserachrome® (µg/mL FEU) | MicroELISA | 0.65 (0.19 – 1.17) | 0.66 (0.51 – 0.89) | 1.25 (0.84 - 2.19) |
| Dimertest® (µg/mL FEU) | Latex agglutination | 0.27 (0.21 – 0.34) | 0.42 (0.29 – 0.70) | 0.82 (0.47 – 1.04) |
| Liatest® (µg/mL FEU) | Latex agglutination | 0.48 (0.22 – 1.06) | 0.52 (0.33 – 0.82) | 0.99 (0.67 – 1.77) |
| Innovance D-dimer (µg/mL FEU) | Immunoturbidimetry | 0.80 (0.21- 1.51) | 0.93 (0.74 – 1.17) | 1.56 (1.10 – 2.67) |

The results of our study in the second and third trimester as shown in table 3 were similar with the result when using Innovance D-dimer (the same reagents that were used in this study).This indicated that D dimer level was not affected by population race.[15]

Many studies reported that D-dimer level increased during pregnancy, some studies revealed that increased D-dimer was started at the first trimester, but the others started at the second trimester. In our study increased D-dimer level was found in 27% of pregnant women in the first trimester, 87% in the second trimester and 100% in the 3rd trimester. It means that activation of coagulation started from the first trimester of pregnancy and was progressively increased. This result that increased D-dimer was started in the first trimester, found in 78% in the second trimester and all pregnant women in the third trimester.[6] Increased D-dimer was found in 21.2% in gestational week 4-13, 59.4% in gestational week 14-27, 85.2% in gestational week 28-35, and 92.3% in gestational week 36-42.[11] On the other hand, reported that increased D dimer was found in more than 25% of pregnant women in gestational week 13-20, and by weeks 36-42, all of the pregnant women had D-dimer level above threshold.[13]

This discrepancy may be caused by different specificity of D-dimer reagent and different unit in expressing the result. The performance of each D-dimer reagent differs, depending on the specificity of the monoclonal antibodies used in the kit, variability in the cutoff value to identify positive results, and heterogeneity of the patient population[16]. Monoclonal antibodies used in the kit recognize neoepitopes on D-dimer that are not expressed on D domains of non-cross-linked fibrin. In addition, up to now, there is no international standard as a reference in measuring D-dimer level.

The result of our study indicated that coagulation cascade had been activated since the first trimester. This condition might be caused by thromboplastin substances released by placenta, which trigger coagulation cascade by activating factor VII.[17]As reported by many authors, changes in the balance of coagulation and fibrinolysis occur in pregnancy.[1,17,18] Increased level of some coagulation factors such as fibrinogen, factor VII, VIII, X, and von Willebrand factor, and reduced protein S, a natural anticoagulant, result in hypercoagulability in pregnancy.[1,17] In addition, fibrinolytic activity is depressed in pregnancy due to increased plasminogen activator inhibitor 1 and plasminogen activator inhibitor 2.[1,17,18]All of these changes cause an imbalance of hemostasis, which favours to thrombotic tendency.

In many studies, all pregnant women in the third trimester showed increased D-dimer level and the highest D-dimer level was found in the third trimester. It means that activation of coagulation reached the peak at the third trimester.

The impact of this study is the upper limit of the normal range of 0.5 mg/L FEU cannot be used as a cutoff value to rule out thrombosis in pregnancy. It is recommended to determinea new cutoff value of D dimer in pregnancy that can be used to exclude VTE.

The strength of this study is the first study in Indonesia which determine D dimer level in pregnancy while the weakness of the study measures D dimer only performed using 1 reagent while there are many reagents available in the market in Indonesia.

## CONCLUSION

Increased D-dimer level in pregnant women was started in the first trimester, and it was found in 27% of pregnant women in the first trimester, 87%in the second trimester, and in 100% in the third trimester. To exclude VTE in pregnancy, determination of a new cutoff value of D-dimer is recommended.

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**Research Article**

# The 45° Mediolateral Episiotomy: Does it Reduce to the Incidence of Extended Laceration Incidence and Postlabour Pain?

## *Episiotomi Mediolateral 45 Derajat terhadap Kejadian Perluasan Cedera dan Nyeri Pascasalin pada Primigravida*

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## Abstract

**Objective :** To investigate the relationship of 45° to 60° mediolateral episiotomy and the incidence of extended laceration and post labour pain in primigravida.

**Methods :** This study used simple randomization design which was conducted in the Department of Obstetrics and Gynecology, Teaching Hospital, Faculty of Medicine, Universitas Hasanuddin from April 2018 to September 2018. There were 80 samples for the 45° mediolateral episiotomy group and 80 samples for the 60° group.

**Results :** After the Chi-Square correlation test has been carried out, the research result indicates that there is a higher incidence in 60° mediolateral episiotomy group in extended perineal laceration (p=0.002), and Fisher Exact test shows that post-labour pain (p=0.000) higher in the same group compared to the 45 o group.

**Conclusions :** Mediolateral episiotomy 45° have lower extended perineal laceration and post-labour pain compared to the 60 o group.

**Keywords :** episiotomy, mediolateral 45°, mediolateral 60°, perineal laceration, post-labour pain, primigravida.

## *Abstrak*

***Tujuan :*** *Mengetahui hubungan episiotomi mediolateral 45° dan 60° terhadap kejadian perluasan cedera dan nyeri pascasalin pada primigravida.*

***Metode :*** *Simple randomization. Penelitian dilaksanakan di Rumah Sakit Pendidikan Departemen Obstetri dan Ginekologi Fakultas Kedokteran Universitas Hasanuddin periode April 2018 – September 2018. Total sampel yang diperoleh adalah 80 untuk kelompok 45° dan 80 sampel untuk kelompok 60°.*

***Hasil :*** *Setelah dilakukan uji hubungan dengan Chi Square terdapat hubungan yang signifikan pada episiotomi 60° dengan kejadian perluasan cedera (p=0,002) dan uji Fisher menyatakan hubungan bermakna nyeri pascasalin pada kelompok yang sama (p=0,000) dibandingkan episiotomi 45°. Episiotomi mediolateral 45° memiliki luaran lebih sedikit menyebabkan kejadian perluasan cedera dan nyeri pascasalin dibandingkan episiotomi 60°.*

***Kata kunci :*** *episiotomi, mediolateral 45°, mediolateral 60°, nyeri pascasalin, primigravida, ruptur perineum.*

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## INTRODUCTION

An episiotomy is one of the most usual surgical procedures in obstetrics to accelerate the delivery time of the baby. The episiotomy itself has been carried out almost all over the world to avoid the occurrence of extensive perineal tears such as third or level four perineal rupture. There are several ways to do an episiotomy, such as medial, mediolateral and lateral episiotomy. A medial episiotomy is rarely done since the tear can extend to the anus[1]. What is often done almost all over the world is a mediolateral episiotomy[2].

A consensus was carried out on the European continent where no clear and firm definition was agreed upon between one country and another, as well as between one hospital and another so that a joint decision was needed to agree on what episiotomy angle should be used[3]. A 45° mediolateral episiotomy has been carried out to avoid a tear in the sphincter. In fact, after repairing the perineum, the episiotomy scar of 45° angle changes to 10-15°, so the mediolateral episiotomy of 45° is feared to injure the anal sphincter muscle[4]. A mediolateral episiotomy is done to prevent the occurrence of tears in the

sphincter muscle, but there is still a possibility of sphincter injury after mediolateral episiotomy, that is, after perineal repair, the episiotomy scar angle of 60° changes to 45° so that the sphincter muscle can be avoided. The question is which angle is taken for episiotomy, is it 45° or 60°?[5]

The objective of this study is to investigate the relationship of 45° and 60° mediolateral episiotomy and both extended laceration incidence and post-labour pain in primigravida.

## METHODS

This study was conducted at the Khadijah I Hospital, Pertiwi Hospital and Fatimah Hospital, Makassar. Spontaneous deliveries are attended by midwives, whereas instrumental deliveries by physicians. In our hospitals, all spontaneous deliveries are attended by midwives and instrumental deliveries by the resident doctor. The routine hospital practice is to perform an examination before vaginal delivery to see whether the labour is indicated for an episiotomy to avoid anal sphincter lacerations. If there was an extended vaginal laceration after episiotomy, the residentwould examine and evaluate every case and suture the laceration of second-degree perineal tears. If the third or fourth-degree perineal laceration occurs, the experienced consultant was called to repair the laceration.

Recruitment took place over a 6-month period from January to June 2018. All primigravida with an indication of episiotomy, who were available for recruitment in the maternity ward, were approached before delivery and invited to participate by signing the informed consent form. The inclusion criteria were primigravida, mother's age is in the range of 15-35 years, single pregnancy with normal presentation, no sign of infection, no vulvar or vaginal abnormalities or genital infections, not having history of vaginal surgery procedures or a history of antepartum bleeding, no contraindication for vaginal delivery, the interpretation of fetal weight between 2.500 grams to 4.000 grams, has an indication of an episiotomy. A total of 160 primigravida were invited to participate and agreed to enrol in the study and signed informed written consent. All the participants were examined within 24 hours postpartum. Episiotomy was performed when the fetal head had been in crowning position, with the special device with whether 45° or 60° in 2 cm length of episiotomy. After the procedure, we check whether there are additional perineal tears or not that are marked by the edges of uneven wounds or the addition of tears outside the episiotomy site. After 24 hours, perineal pain was assessed with VAS and categorized into 3 categories, namely mild (VAS 0-3), moderate (VAS 4-6), and severe (VAS 7-10). They were shown VAS and explained that 0 represented "no pain at all" and 10"the worst pain ever."Statistical calculations were performed with SPSS. Bivariate analyses were performed by chi-square test and Fisher exact test. Ap value of <0.05 was chosen as a statistical significance level.

## RESULTS

In this study, there were 160 subjects in total, 80 each for both mediolateral episiotomy groups. The characteristics of the research subject can be seen in table 1. It can be seen that in both groups homogeneous and not significant differences between the two episiotomy groups. A total of 49 (61.25%) subjects who underwent 60° mediolateral episiotomy treatment experienced an extension of injury. Meanwhile, only 29 (36.25%) subjects had 45° mediolateral episiotomy who experienced an extension of injury (table 2). The degree of episiotomy is related to the extent of injury (p = 0.002).38 (47.5%) subjects who underwent 60° mediolateral episiotomy experienced moderate pain. Meanwhile, only 1 (1.25%) subjects had 45° mediolateral episiotomy who experienced moderate pain (table 2). No subject experienced severe pain. The degree of episiotomy is related to the degree of pain (p = 0.000).

**Table 1.** Characteristics of the Study Sample

| Sample | Episiotomy 45° | | Episiotomy 60° | | *P-value* |
|---|---|---|---|---|---|
| **Characteristic** | **n** | **%** | **n** | **%** | |
| **Age (year)** | | | | | |
| Low risk | 66 | 82.5 | 67 | 83.7 | 0.833 |
| High risk | 14 | 17.5 | 13 | 16.3 | |
| **Education** | | | | | |
| Basic | 16 | 20 | 14 | 17.5 | 0.685 |
| High | 64 | 80 | 66 | 82.5 | |
| **BW* (gram)** | | | | | |
| BW | 2969.37 | ± 254.5 | 3019.38 | ± 299.13 | 0.257 |
| **Head Circumference (cm)** | | | | | |
| HC | 32.11 | ± 0.914 | 32.09 | ± 1.009 | 0.870 |

*BW: birth weight

**Table 2.** Expansion of Injuries and O of Pain Based on Episiotomy

| Variable | Mediolateral Episiotomy | | | | *P-value* |
|---|---|---|---|---|---|
| | 45° | | 60° | | |
| | **n** | **%** | **n** | **%** | |
| **Extended Laceration** | | | | | |
| Yes | 29 | 36.25 | 19 | 61.25 | 0.002 |
| No | 51 | 63.75 | 31 | 38.75 | |
| **Pain** | | | | | |
| Mild | 79 | 98.75 | 42 | 52.5 | 0.000 |
| Moderate | 1 | 1.25 | 38 | 47.5 | |

## DISCUSSION

Episiotomy in primigravida patients can reduce the incidence of perineal trauma[6]. Therefore, there were no differences in risk factors for both groups of subjects to experience perineal trauma. In this study, there were no significant differences between maternal age at delivery, birth weight, and head circumference in the two subject groups. Subjects in this study gave birth to a baby with a median birth weight of 3.000 (2.500-3.900) grams. Previous research stated that high birth weight could increase the risk of perineal trauma[7]. However, there were no subjects who gave birth to babies > 4.000 grams. Therefore, there are no differences in the risk factors of both subjects for the possibility of perineal trauma.

A large baby's head circumference is a risk factor for perineal trauma. Each increase of 1 cm in the head circumference of a baby will increase the risk of perineal trauma by 1.22 times[8]. The greater the head circumference of a baby born by vaginal delivery will increasingly cause strain on the perineum and will increase the risk of perineal trauma. Subjects in this study gave birth to babies with an average head circumference of 32 (30-35) cm, and there were no significant differences between the two groups of subjects. Therefore, differences in the head circumference of babies born by subjects do not affect the results of the study.

In this study, a mediolateral episiotomy was carried out 45° and 60° with the same episiotomy length of 2 cm, but the area produced was certainly different due to the use of the episiotomy angle. A 45° angle of 2 cm will add a circle diameter of 1.41 cm (cos 45°), while an angle of 60° with the same length results in an expansion of a diameter of 1 cm (cos 60°) so that the mediolateral episiotomy of 60° will experience more injury expansion than 45 o due to the expansion of smaller diameters.

Moderate pain was experienced by 38 (47.5%) subjects who underwent a 60° mediolateral episiotomy. Meanwhile, only 1 (1.25%) subjects underwent a mediolateral episiotomy of 45°. There is a significant difference between the degree of pain in the mediolateral episiotomy 60° compared to 45°. This is in line with previous studies which stated that moderate / severe pain after 4 hours and one day was more experienced by subjects treated with episiotomy 60°.[9] In terms of anatomy, the perineal area is innervated by the pudendal nerve. In the perineum, there are many ends of nerve fibres so that the episiotomy can cause pain. A 60° mediolateral episiotomy can make a wound longer than a mediolateral

episiotomy 45°. This can make the pain in the 60° mediolateral episiotomy have a higher degree of pain than the mediolateral episiotomy 45°.[10]

This study has several limitations, such as the expansion of injuries reaching the level 3 and 4 perineal rupture not found in both groups so that it is not certain which is more superior to the incidence of anal sphincter rupture. Six months of post-episiotomy pain and coital pain have not been studied. The post-suturing angle is also not measured, so there is no possibility of a possible risk of anal sphincter injury in subsequent pregnancies if vaginal delivery is carried out without episiotomy procedure.

## CONCLUSION

In this study, it can be concluded that the expansion of perineal injury in the mediolateral episiotomy group is 45° less than the episiotomy of 60°. The degree of pain is lighter in the mediolateral episiotomy 45° compared to 60 ° where there are more stitches than the 45° mediolateral episiotomy.

## CONFLICT of INTEREST

None.

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**Research Article**

# Improvement Knowledge and Attitude about Adolescent's Reproductive Health through Education Intervention in Junior and Senior High

## *Peningkatan Pengetahuan dan Sikap tentang Kesehatan Reproduksi Remaja melalui Intervensi Penyuluhan pada Siswa Sekolah Menengah Pertama dan Sekolah Menengah Atas Negeri*

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## Abstract

**Objective :** To determine the changes in point of view and positive attitudes towards adolescent reproductive health in junior and senior high school students in Southeast Sulawesi after counselling interventions.

**Methods :** Experimental Research with The One Group Pretest-Posttest Design. The population in the study were all adolescents aged between 12-19 years as students in Southeast Sulawesi. The sampling was performed by Simple stratified random sampling technique with a sample of 300 people for middle and high school students. The instrument used was a questionnaire with data analysis by using the t-test.

**Results :** Showed that the level of knowledge and attitudes of students about adolescent reproductive health was differed between pretest & posttest in junior and senior high school students ($\rho<0.05$),because the students who were given counselling interventions with lecture methods, powerpoint, and discussion, will add to the broader understanding and insight and tend to generate positive responses from students so that they have good basic knowledge and attitudes about adolescent reproductive health.

**Conclusions :** The study was the increase in knowledge and positive attitudes about adolescent reproductive health after counselling interventions.

**Keywords :** adolescent, counselling, knowledge and attitude, reproductive health.

## *Abstrak*

***Tujuan :*** *Untuk mengetahui perubahan pengetahuan dan sikap yang positif tentang kesehatan reproduksi remaja pada siswa SMP dan SMA Negeri di Sulawesi Tenggara setelah dilakukan intervensi penyuluhan.*

***Metode :*** *Penelitian Eksperimen (pre-experiment) dengan rancanganThe One Group Pretest-Posttest Design. Populasi dalam penelitian adalah keseluruhan remaja yang berusia antara 12-19 tahun yang sementara berstatus sebagai siswa SMP dan SMA Negeri di Sulawesi Tenggara. Pengambilan sampel dilakukan dengan teknik Simple stratified random sampling dengan jumlah sampel 300 orang untuk siswa SMP dan SMA. Instrumen yang dipakai adalah angket dengan analisis data menggunakan uji-t.*

***Hasil :*** *Menunjukkan tingkat pengetahuan dan sikap siswa tentang kesehatan reproduksi remaja berbeda antara pretest dan posttest pada siswa SMP dan SMA Negeri di Provinsi Sulawesi Tenggara ($\rho$ value < 0,05).Hal ini disebabkan karena pada siswa SMP dan SMA Negeri di Provinsi Sulawesi Tenggara yang diberikan intervensi penyuluhan dengan metode ceramah, visualisasi (power point), dan tanya jawab, akan menambah pemahaman dan wawasan yang lebih luas dan cenderung menimbulkan respon yang positif dari siswa sehingga memiliki pengetahuan dan sikap yang baik tentang kesehatan reproduksi remaja.*

***Kesimpulan :*** *Terjadi peningkatan pengetahuan dan sikap yang positif tentang kesehatan reproduksi remaja setelah intervensi penyuluhan.*

***Kata kunci :*** *kesehatan reproduksi , pengetahuan dan sikap, remaja, penyuluhan.*

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## INTRODUCTION

Adolescent problems are social realities that exist in society. Currently, there has been a shift in sexual behaviour among adolescents whose causes are not merely due to cultural shifts or social influences, but also the progress in improving nutrition in Indonesia has triggered a shift in sexual behaviour among adolescents[1-3]. The problem of sexual relations among teenagers is actually a global problem because almost all countries in the world show similar trends[4,5]. Reproductive health in adolescents includes sexually transmitted diseases (STDs), including increased HIV/AIDS infections, sexual violence, early pregnancy and childbirth at risk of maternal and infant death, and unwanted pregnancies that often lead to unsafe abortions[2,3].

Negative factors such as the spread of pornographic themed information in the mass media, lack of cultivation of moral and religious values, the influence of promiscuity, and the lack of parental attitudes toward children, as well as the strength of hormonal influences, are a series of causes of teenagers having free sex[6,7]. Based on information from the cumulative number of HIV/AIDS cases currently in Indonesia reported up to September 2008, the number of people with HIV was 6.277 patients, and the number of AIDS cases was 15.136 patients with 3.197 deaths. Based on data from the Directorate General of PPM and Ministry of Health of Indonesia with HIV/AIDS aged 15-19 years in 2007, there were 279 patients and increase of 484 patients in 2008[8].

Cases of HIV/AIDS in Southeast Sulawesi Province cumulatively from 2004 to 2010 have found 127 cases, which 73 people have HIV and 54 have AIDS with details of Kendari City 58 cases, Muna 24 cases, Wakatobi Regency 13 case, Buton Regency 8 cases, Kolaka Regency 8 cases, Bau-Bau City 6 cases, Bombana Regency 5 cases, South Konawe Regency 4 cases, Konawe District 3 cases and North Konawe District 2 cases. Based on data from the public health office in Southeast Sulawesi it shows a significant increase of HIV/AIDS cases in the 2010-2012 by 15 cases (2010), 69 cases (2011) and 125 cases (2012). While in 2013 was 103 people and January-October 2014 was 158 people. If one patient detected was equivalent to one hundred people who were not detected, then HIV/AIDS sufferers in Southeast Sulawesi during 2014 were estimated at 158.000[9].

Based on a survey of adolescent sexual behavior in Kendari (2007) by KPA(HIV/AIDS Commission), it was found that there were variations in sexual trends among adolescents, namely 2% having sex, 1% having oral sex, 2% only attaching genitals and 10 % just holding a sensitive areas and the highest sex trends of 85% were other sexual behaviour. Adolescent sexual behaviour has the potential to pose a risk for them to be infected with HIV/AIDS and other sexually transmitted diseases due to their ignorance of knowledge and attitudes about reproductive health. It was found that the level of knowledge in senior and vocational high school students in Kendari city about reproductive health was very low and tends to do the negative sexual behavior. This was supported by the increasing number of nightlife facilities that provide exclusive entertainment services for customers, including sexual services. Based on the results of observations, it was found that many nightclubs employed teenagers as a special attraction for visitors[10].

Information about adolescent reproductive health, especially in junior and senior high school students in the current era of globalization is very easy to obtain. It could through print-out and electronic media or the internet[11], but due to the limited curriculum content in schools related to reproductive health problems make the students find out for themselves and get inappropriate information from their friends who are basically lack of knowledge too[12]. In connection with the above facts and linked to the 2013-2018 Southeast Sulawesi by Regional Medium-Term Development Plan with the vision of Realizing Prosperous, Independent and Competitive, one of its missions is to improve the quality of human resources in the health sector to improve community health. The goal is to reduce morbidity, so the problem of adolescents, especially those related to reproductive health problems of junior and senior high school students in Southeast Sulawesi Province, could get serious attention from the government. The purpose of this study was to determine the increase in knowledge and changes in positive attitudes about adolescent reproductive health in junior and senior high school students in Southeast Sulawesi after counselling interventions.

## METHODS

Experiment (pre-experiment) with One Group Pretest-Posttest Design was used in this study. The research conducted on March-August 2016 in North Kolaka, Kolaka, Konawe, Kendari, and Bau-Bau Regencies, Southeast Sulawesi Province. The research divided into 2 (two) groups, Reference population (all adolescents aged between 12-21 years) and the target population (all adolescents aged between 12-19 years as middle and high school students).

The Simple stratified random sampling techniquefrom each class for junior high school (class VII, VIII, IX) and high school (class X, XI, XII) was used. So each sample was obtained 30 people for each middle school and high school (North Kolaka, Kolaka, Konawe, Kendari and Bau-Bau) and the total number of samples was 300 students (respondents). The variables in this study consisted of two; independent variables (counselling interventions about adolescent reproductive health) and dependent variables (the level of knowledge and attitudes of adolescents about reproductive health).

A questionnaire was used in this study. The data collection was the primary data obtained through a list of questions that have been prepared previously based on the research objectives then provided and filled in by the respondent before and after the intervention was conducted (pretest & posttest). As for secondary data, it was obtained from the Office of Education, Youth and Sports (Junior &Senior high school) from each research location in Southeast Sulawesi Province. To analyze the statistical analysis was performed(t-test) by using the analyze menu that contained in the main menu of SPSS For Windows Release 14.013.

## RESULTS

### Knowledge of Adolescent Reproductive Health

**Table 1.** Knowledge about Adolescent Reproductive Health in State and Junior High School Students

| City/District | Category | Knowledge of an adolescent reproductive health | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Junior high school 1 and 9 | | | | Senior high school 1 and 4 | | | |
| | | Pretest (n=30) | | Posttest | | Pretest (n=30) | | Posttest | |
| | | n | % | n | % | n | % | n | % |
| North Kolaka | High | 9 | 30 | 26 | 86.7 | 14 | 46.7 | 21 | 70 |
| | Medium | 21 | 70 | 4 | 13.3 | 16 | 53.3 | 9 | 30 |
| | Low | - | - | - | - | - | - | - | - |
| Kolaka Regency | High | 14 | 46.7 | 23 | 76.7 | 20 | 66.7 | 29 | 96.7 |
| | Medium | 16 | 53.3 | 7 | 23.3 | 10 | 33.3 | 1 | 3.3 |
| | Low | - | - | - | - | - | - | - | - |
| Konawe District | High | 17 | 56.7 | 20 | 66.7 | 17 | 56.7 | 23 | 76.7 |
| | Medium | 13 | 43.3 | 10 | 33.3 | 13 | 43.3 | 7 | 23.3 |
| | Low | - | - | - | - | - | - | - | - |
| Kendari City | High | 6 | 20 | 13 | 43.3 | 23 | 76.7 | 30 | 100 |
| | Medium | 24 | 80 | 17 | 56.7 | 7 | 23.3 | - | - |
| | Low | - | - | - | - | - | - | - | - |
| Bau-Bau City | High | 18 | 60 | 22 | 73.3 | 23 | 76.7 | 30 | 100 |
| | Medium | 12 | 40 | 8 | 26.7 | 7 | 23.3 | - | - |
| | Low | - | - | - | - | - | - | - | - |

**Table 2.** T-test Analysis of Knowledge about Adolescent Reproductive Health in School Students in Southeast Sulawesi Province

| School | The Influence of Counseling on Knowledge of Adolescent Reproductive Health | Mean | SD | t-hit | df | *P-value* |
|---|---|---|---|---|---|---|
| Public | Pretest | 19.740 | 2.815 | | | |
| Middle | Posttest | 21.473 | 2.689 | | | |
| School | Difference | 1.733 | 126 | -7.880 | 149 | 0.000 |
| Students | | | | | | |
| High | Pretest | 21.633 | 3.478 | | | |
| School | Posttest | 23.207 | 4.060 | | | |
| Students | Differences | 1.574 | 582 | -4.661 | 0.000 | 149 |

Based on table 2, the results of public middle school students was t = -7.880 and p = 0.000 were obtained with α = 0.05 and df = 149, then t table = 1.960 was obtained. This shows t count> t table (p <0.05), so that Ho was rejected and H1 was accepted, it means that there was a significant influence of counselling interventions on increasing knowledge about adolescent reproductive health in students of Public Middle Schools in Southeast Sulawesi Province.The results of high school students was t = -4.661 and p = 0.000 were obtained with α = 0.05 and df = 149, then t table = 1.960 was obtained. This shows t count> t table (p <0.05), so that Ho was rejected and H1 was accepted, it means that there was a significant influence of counselling interventions on increasing knowledge about adolescent reproductive health in students of High Schools in Southeast Sulawesi Province.

## Attitude of Adolescent Reproductive Health

**Table 3.** Attitude of Adolescent Reproductive Health in Junior and Senior High School Students

| Distric | Category | Attitudes about adolescent reproductive health | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Junior high school 1 and 9 | | | | Senior high school 1 and 4 | | | |
| | | Pretest (n=30) | | Posttest | | Pretest (n=30) | | Posttest | |
| | | n | % | n | % | n | % | n | % |
| North Kolaka | Good | 11 | 36.7 | 21 | 70 | 25 | 83.3 | 25 | 83.3 |
| Regency | Medium | 16 | 53.3 | 9 | 30 | 5 | 16.7 | 5 | 16.7 |
| | Less | 3 | 10 | - | - | - | - | - | - |
| Kolaka | Good | 13 | 43.3 | 17 | 56.7 | 28 | 93.3 | 28 | 93.3 |
| Regency | Medium | 13 | 43.3 | 13 | 43.3 | 2 | 6.7 | 2 | 6.7 |
| | Less | 4 | 13.4 | - | - | - | - | - | - |
| Konawe | Good | 21 | 70 | 20 | 66.7 | 22 | 73.3 | 22 | 73.3 |
| District | Medium | 9 | 30 | 10 | 33.3 | 7 | 23.3 | 8 | 26.7 |
| | Less | - | - | - | - | 1 | 3.3 | - | - |
| Kendari City | Good | 19 | 63.3 | 17 | 56.7 | 28 | 93.3 | 29 | 96.7 |
| | Medium | 11 | 36.7 | 12 | 40 | 2 | 6.7 | 1 | 3.3 |
| | Less | - | - | 1 | 3,3 | - | - | - | - |
| Bau-Bau City | Good | 26 | 86.7 | 25 | 83.4 | 26 | 86.7 | 29 | 96.7 |
| | Medium | 4 | 13.3 | 4 | 13.3 | 4 | 13.3 | 1 | 3.3 |
| | Less | - | - | 1 | 3.3 | - | - | - | - |

**Table 4.** T-test Analysis of Attitudes about Adolescent Reproductive Health in Junior and High School Students in Southeast Sulawesi Province

| School students | Effect of Counseling on Attitudes About Adolescent Reproductive Health | Mean | SD | t-hit | *P-value* | df |
|---|---|---|---|---|---|---|
| Junior high school | Pretest | 14.240 | 4.679 | | | |
| students | Posttest | 15.093 | 3.161 | | | |
| | Differences | 853 | 1.518 | -2.301 | 0.023 | 149 |
| High school | Pretest | 16.647 | 3.308 | | | |
| students | Posttest | 16.867 | 2.806 | | | |
| | Differences | 220 | 502 | -2.174 | 149 | 0.034 |

Based on table 4, the results of junior high school students was t = -2.301 and p = 0.023 were obtained with α = 0.05 and df = 149, then t table = 1.960 was obtained. This shows t count> t table (p <0.05), so that Ho was rejected and H1 was accepted, it means that there was a significant influence of counselling interventions on attitudes about adolescent reproductive health in students of State Junior High Schools in Southeast Sulawesi Province. The results of high school studentswas t = -2.174 and p = 0.034 were obtained with α = 0.05 and df = 149, then t table = 1.960 was obtained. This shows t count> t table (p <0.05), so that Ho was rejected and H1 was accepted, it means that there was a significant influence of counselling interventions on attitudes about adolescent reproductive health in high school students in Southeast Sulawesi Province.

## DISCUSSION

### Overview Knowledge of Adolescent Reproductive Health

Adolescent reproductive health knowledge is information that explains the impacts and problems often faced by adolescents due to the lack of knowledge about reproductive health and ways to prevent from also occurring the number of adolescents who obtained reproductive health knowledge from print/media electronics, even though most of the information was unfiltered[1,14.]

Knowledge about adolescent reproductive health is critical so that adolescents have responsible for their attitudes and behaviors[5,11]. Debriefing knowledge about changes that occur physically, psychologically and sexually will make it easier for teenagers to understand and overcome various confusing conditions that will appearing later. Knowledge is influenced by several factors, including education level. Health education brings changes to knowledge[6]. Varied knowledge can be caused by different learning abilities of each person[11].

The results of the analysis data regarding knowledge about adolescent reproductive health with t-test (p <0.05) has significant differences in the level of knowledge between pretest and posttest. Posttest tend to have high knowledge about adolescent reproductive health, while at pretest generally have intermediate knowledge. Based on the results of this study, it indicate that counselling on adolescent reproductive health was needed to increase knowledge about adolescent reproductive health in both junior and senior high schools, especially in Southeast Sulawesi Province. This where there was a significant influence between the provision of health education to increase adolescent knowledge[5,14].

### Overview Attitudes about Adolescent Reproductive Health

Attitude is a readiness to react to objects in a particular environment as an appreciation of the object[15]. Based on data analysis with t-test (p <0.05), there is a difference between pretest and posttest. At the pretest, respondents had sufficient attitudes about adolescent reproductive health. While at posttest, respondents tend to have a good attitude about adolescent reproductive health. This was evident from the results of research data that at the pretest only has a small portion of sufficient attitudes towards reproductive health, whereas at the posttest most of them had a good basic attitude. This is due to attaining an attitude that supports not only knowledge but also influenced by emotional factors, personal experience, mass media, educational institutions, religious institutions, influences of others, and culture[16].

### The Effect of Intervention on Counseling on Increasing Knowledge of Adolescent Reproductive Health

Knowledge is the result of knowing after sensing a particular object. Sensing occurs through the five senses of human; the sense of sight (the eye), the sense of hearing (the ear), the sense of smell (nose), the sense of taste (tongue) and the sense of touch (hand). Much of the knowledge is obtained from the eyes and ears[15]. Knowledge is influenced by several factors including education level. Health education could changes the knowledge[6.] Varied knowledge can be caused by different learning abilities of everyone[17].

The results of the study on junior and senior high school students in Southeast Sulawesi (pretest & posttest) had significant differences in knowledge after given a counseling interventions.

This means that there was a significant influence between counselling with students in level of knowledge about adolescent reproductive health. It could be said counselling with lecture and slide methods is a combination of methods and media of counselling that more effective because it uses more than five senses and more leads to attractiveness and interest of respondents so the information delivered is more easily accepted. According to previous research, the senses that turn the most knowledge into the brain are the eyes. Approximately 75% - 87% of human knowledge is obtained or channelled through the eyes. While 13% - 25% is channeled through other senses. From this, it was concluded that visual tools made it easier to convey and receive information or educational material[10].

The results of this study were relevant to the results of research by Socony in America which shows that by telling 70% can be remembered three hours later, and only 10% was remembered three days later. Then, by Showing 72% can be remembered three hours later, and only 20% was remembered three days later. By telling and showing at once it can be remembered three hours later 85%, and 65% can be remembered three days later. Based on data analysis by using t-test with a significance level α = 5% (0.05) obtained t-count> t-table and ρ<0.05. This means that the extension intervention (treatment) has a significant effect on increasing knowledge about adolescent reproductive health.

### The Effect of Intervention on Counseling on Attitudes about Adolescent Reproductive Health

Attitude is a readiness to react to objects in a particular environment as an appreciation of the object[17]. The results showed that there were significant differences between the pretest and posttest attitudes of adolescents about reproductive health after being given counselling interventions. This is due to attaining an attitude that supports not only knowledge but also influenced by emotional factors, personal experience, mass media, education, religious, influences of others who are considered important, and culture[16]. The results of the t-test, with a significance level of α = 5% (0.05) obtained the results of t-count> t-table and ρ<0.05. This means that there was a significant influence between counselling interventions and changes in positive student attitudes toward adolescent reproductive health.

## CONCLUSION

The level of students knowledge about adolescent reproductive health was different (pretest & posttest) between junior and senior high school students (ρ<0.05) or there was an increase in knowledge about adolescent reproductive health after counselling interventions. This was because the students of junior and senior high schools in Southeast Sulawesi who were given counselling interventions by lecture method, powerpoint, and discussion will increase understanding and broader insight about adolescent reproductive health. Based on the results of the study, it is recommended for all the educator of Junior and Senior High Schools in Southeast Sulawesi Province to always provide counselling on adolescent reproductive health through biology teachers as local content, so that adolescents do not fall into knowledge and attitudes about reproductive health, wrong and incorrect. In addition, collaboration with various stakeholders can be conducted to provide counselling to students at least once a month, and also provide adequate facilities and time for health counselling at school.

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**Research Article**

# Postoperative Catheterization after Total Vaginal Hysterectomy: Six versus Twenty Four Hours. A Randomized Controlled Trial

## *Kateterisasi Pascaoperasi Total Vaginal Histerektomi: Enam Jam versus Dua Puluh Empat Jam. Sebuah Penelitian Randomisasi Terkontrol.*

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## Abstract

**Objective :** To find out whether urinary bladder catheterization after total vaginal hysterectomy is more advantageous.

**Methods :** Forty-six subjects were included. Subjects were divided into two groups. In one group (n = 24), a transurethral catheter was removed after six hours post-surgery. In the other group (n = 24), the catheter was removed after twenty-four hours. A few hours after removal of the catheter, patients were asked to urinate. Then residual volumes were measured by measuring cylinder, using 12F catheter. Pain was measured using visual analogue scale (VAS) score. Patients' length of stay was also compared. Data were analyzed using Student T-test if distributed normally or Mann-Whitney Rank if data was abnormal.

**Results :** Mean age for each group was 63.21 ± 8.73 and 62.38 ± 7.52 (6 hours, 24 hours respectively). Median score for 6 hours group was 50.00 (range 5 - 80) and for 24 hours was 100 (range 30 - 250) (P = 0.000). Pain perception and hospital stay were not statistically different in both group (p = 0.134 and P = 0.377).

**Conclusions :** In this study, difference in postoperative catheterization time is associated with residual volume.

**Keywords :** bladder catheterization, postoperative catheterization, residual volume, total vaginal hysterectomy.

## *Abstrak*

***Tujuan :*** *Untuk membandingkan lama waktu pemasangan kateter pascaoperasi total vaginal histerektomi yang lebih menguntungkan.*

***Metode :*** *Empat puluh enam pasien ikut serta dalam penelitian. Secara acak dibagi menjadi 2 kelompok. Pada grup I (n = 24), pelepasan kateter dilakukan setelah enam jam pascaoperasi. Pada grup II (n = 24), kateter dilepas setelah dua puluh empat jam. Beberapa jam setelah pelepasan kateter, pasien diminta untuk buang air kecil. Lalu residu urin diukur setelahnya menggunakan gelas ukur, memakai kateter no. 12 F. Skor nyeri menggunakan skor Visual Analogue Scale (VAS). Lama rawat inap juga dibandingkan. Analisis data menggunakan student's T-test. Jika terdistribusi tidak normal, analisis memakai Mann-Whitney Rank.*

***Hasil :*** *Rerata usia untuk tiap grup adalah 63,21 ± 8,73 dan 62,38 ± 7,52 (6 jam, 24 jam, secara berurutan). Skor median untuk grup 6 jam adalah 50,00 (range 5 – 80) dan grup 24 jam adalah 100 (range 30 – 250) (P = 0,000). Tidak ada perbedaan signifikan secara statistic pada rasa skor nyeri dan lama rawat inap (p = 0,134 dan p = 0,377).*

***Kesimpulan :*** *Pada penelitian ini, perbedaan waktu pemasangan kateter pascaoperasi memiliki hubungan dengan volume sisa urine.*

***Kata kunci :*** *kateterisasi urine, kateterisasi pascaoperasi, volume sisa urine, total vaginal histerektomi.*

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## INTRODUCTION

Transurethral catheterization following uncomplicated vaginal prolapse surgery is a standard method of practice for bladder treatment to enable drainage and prevent overdistension of the bladder. However, its implementation was relatively custom based, hospital policy-based and personal preference-dependent; therefore the duration varies markedly.[1-3] Although a necessary procedure, catheterization has a certain complication such as increasing the symptomatic and asymptomatic urinary tract infection (UTI), discomfort, and pain.[4] The risk of catheter-related UTI increase with the length of time a catheter is in situ.[5] Bladder catheterization increases the occurrence of UTI and is likely to have a negative impact on the well-being of patients after surgery and to prolong hospital stay.[6] That disadvantages of prolonging catheterization outweigh the advantages.[7] That patients who underwent catheter removal at 6 hours after the surgery did not need recatheterization and a lower incidence of UTI.[3]

In RSUP Prof. Dr. RD Kandou, the duration for catheterization following uncomplicated total vaginal hysterectomy varies based on operator preference. This study was undertaken to know whether urinary bladder catheterization after total vaginal hysterectomy is more advantageous.

## METHODS

This study was a randomized controlled clinical trial that was conducted from January 2016 to April 2017 in Prof dr. RD Kandou General Hospital and its satellite. Ethical approval for the study had been obtained. Written informed consent was obtained from all patients before the randomization process. Women who were included in the study underwent an uncomplicated total vaginal hysterectomy.

Patients are divided using double-blinded randomized principal and concealment using SNOSE method into two groups (24 women for each group). All patients received a single dose of antibiotic prophylaxis before the operation. 12F latex catheters with a 10 ml balloon were used. Catheters were inserted before the operation for the duration of the surgical procedure. Then, the catheter was removed either six hours or twenty-four hours after the operation. The time of the completion of skin/vagina closure was designated at the zero hours.

The following variables were assessed for each group: post voiding residual volume, pain, and length of hospital stay. After urinary catheter removal, patients were invited to spontaneously void their bladder. After voiding, residual volume was checked using on-off urinary catheterization. If they could not void or when there was no urge within 6–8 hours after the catheter removal, no 12F catheter was reinserted. Pain score was asked when we performed the on-off urinary catheterization and categorized using Visual Analogue Scale (VAS) score. The length of hospital stay was defined as the time interval between the completion of surgery and hospital discharge.

Numerical variables were evaluated using unpaired student's T-test. IBM SPSS Statistic Version 20 was used for the data analysis. Categorical variables were evaluated by Chi-square analysis. A P-value < 0.05 was considered statistically significant.

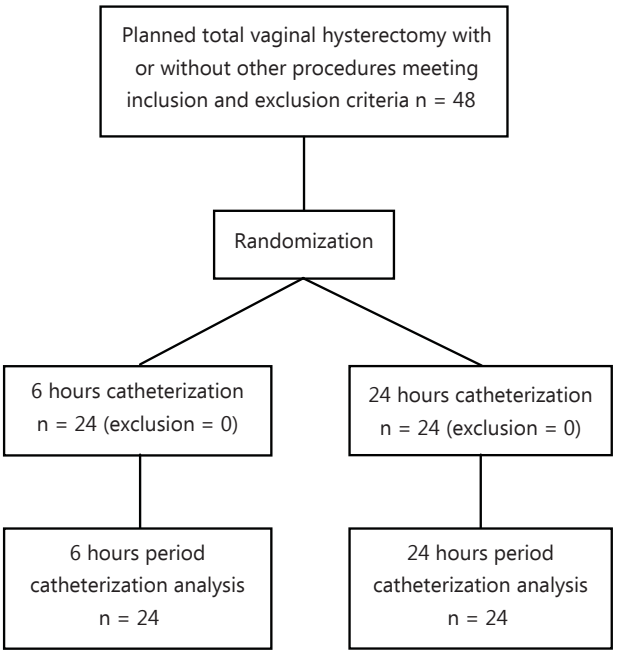


**Figure 1.** Flow Chart of Progress through the Trial

## RESULTS

A total of 48 women were enrolled in the study and 24 were assigned to each group. There were no single subjects that excluded.

**Table 1.** Demographics/ Clinical Characteristics of Patients

| Variable | Description | | *P-value* |
|---|---|---|---|
| Catheterization duration | 6 hours (n = 24) | 24 hours (n = 24) | |
| Age | 63.21 ± 8.73 | 62.38 ± 7.52 | 0.725* |
| Body Mass Index | 24.28 ± 2.75 | 25.49 ±3.49 | 0.192* |
| Operation duration (minutes) | 90 (65 – 150) | 90 (70 – 150) | 0.571** |

*Abnormally distributed numeric variable was written in median (minimum-maximumum range).*
**Student T-tests **Mann Whitney Rank test*

**Table 2.** Outcome Results

| | 6 hours (n=24) | | 24 hours (n=24) | | *P-value* |
|---|---|---|---|---|---|
| | **Median** | **Range** | **Median** | **Range** | |
| Residual volume | 5.,00 | 5 – 80 | 100.00 | 30–250 | 0,000 |
| VAS score | 3.00 | 0–6 | 4.50 | 1–6 | 0.134 |
| Hospital stay | 3.00 | 2–4 | 3.00 | 2–5 | 0.377 |

All women had similar demographic characteristics; age, body mass index, and duration of surgery (Table 1). The median age was 63 (range 44 – 86 years). Of the patients in both groups, all cases in the groups could void after its removal.

The purpose of this study is to find out whether urinary bladder catheterization is more advantageous. Based on table 2, using Mann Whitney Rank Test, we found a significant difference in residual volume (P = 0,000), but there was no significant difference in VAS score (pain perception) and hospital stay (P = 0.134 and P = 0.377, respectively).

## DISCUSSION

In-dwelling urinary catheterization is not a harmless procedure, commonly used to assess urinary output, to prevent postoperative urinary retention, and to reduce the possibility of injury to the urinary system during the surgery.[1]In-dwelling catheter after gynecological operation has been shown to affect the length of hospitalization, the occurrence of febrile morbidity and the incidence of urinary tract infection.[8] Such infections not only prolong hospital stay and are expensive to treat but also cause unpleasant symptoms.[9]

Currently, it is standard for in-dwelling catheters to be placed for 24 hours after standard gynecologic surgeries. However, found that patients who had immediate removal of indwelling catheters had no adverse outcomes and reported significantly less pain than patients who had their catheters removed after 24 hours.[8] Having difference, stated that a high rate of recatheterization was observed in the group of immediate removal of the catheter,[3] whereas all subjects in the group of 6 hours catheter removal could void after its removal. In this study, lesser residual volume was found in the 6 hours group and had significant difference in comparative test using Mann Whitney Rank test. Also concluded that short term catheterization is more beneficial to prevent bladder over filling after vaginal prolapsed surgery.[4]

Pain scoring using VAS score had no difference statistically. Maybe it was caused by the use of analgesics and antibiotics pre- and post-operative, lowering the rate of infection. Though standard antibiotic treatment during or after removal of the catheter is not indicated in urogynecology patients as many have no bacteriuria or appear to clear bacteriuria without antibiotics.[2] Duration of hospital stay was also had no significant difference statistically. Though that shorter indwelling catheterization time was associated with shorter hospital admission.[3,7]

## CONCLUSION

In this study, shorter transurethral catheterization is associated with lower urine residual volume.

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**Research Article**

# Administration Oral Misoprostol after Radical Hysterectomy Due to Cervical Cancer in the Early Stage Decrease Urinary Retention Incident

## *Pemberian Misoprostol Per Oral Pascahisterektomi Radikal pada Karsinoma Serviks Stadium Awal untuk Menurunkan Insiden Retensio Urin*

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## Abstract

**Objective :** To determine the effect of oral Misoprostol after Radical Hysterectomy in the early stage Cervical Cancer to reduce the incidence of urinary retention.

**Methods :** The study was conducted with a prospective cohort method, randomized control trial and double-blind to the patients with early-stage cervical cancer who performed Radical Hysterectomy in Dr. Zainoel Abidin hospital, Banda Aceh. There are 34 subjects who agreed to participate in the study. Subjects were divided into 2 groups. The first group who received Misoprostol orally as the intervention group and the other group that received placebo as the control group.

**Results :** The incidence of urinary retention after Radical Hysterectomy in Dr. Zainoel Abidin hospital, Banda Aceh, decreased significantly in the intervention group compared to the control group (P 0,049). In the intervention group Misoprostol reduce residual urine. Ability to void spontaneously and urine volume were increase. The duration of catheterization and length of hospital stay for the patients were shorter.

**Conclusions :** Administration of Misoprostol orally reduce the incidence of urinary retention after Radical Hysterectomy. Oral Misoprostol can be recommended as an additional procedure to reduce urinary retention.

**Keywords :** cervical cancer, misoprostol , radical hysterectomy, urinary retention.

## *Abstrak*

***Tujuan :*** *Untuk mengetahui pengaruh pemberian Misoprostol per oral pascaoperasi Histerektomi Radikal pada pasien karsinoma Serviks stadium awal terhadap insidensi retensio urin.*

***Metode :*** *Penelitian dilakukan dengan metode kohort prospektif, randomized control trial dan double blind, pada pasien karsinoma serviks stadium awal yang dilakukan Histerektomi Radikal di RS dr. Zainoel Abidin, Banda Aceh. Terdapat 34 pasien yang telah menyetujui mengikuti penelitian, yang dibagi dalam 2 kelompok yaitu kelompok yang mendapat Misoprostol tablet per oral sebagai kelompok perlakuan dan kelompok yang mendapat plasebo sebagai kelompok kontrol. Residu urin pada kedua kelompok diukur dan faktor-faktor lain yang terkait dilakukan pendataan untuk dilakukan analisis.*

***Hasil :*** *Kejadian retensio urin pascahisterektomi Radikal di RS dr. Zainoel Abidin, Banda Aceh, menurun secara bermakna pada kelompok perlakuan dibandingkan kelompok kontrol (P0,049). Pada kelompok perlakuan Misoprostol menurunkan residu urin. Peningkatan kemampuan berkemih spontan dan volume urin .lama pemakaian kateter transuretra dan lama perawatan menjadi lebih singkat.*

***Kesimpulan :*** *Pemberian Misoprostol per oral mengurangi insiden retensio urin pascahisterektomi Radikal.*

*Saran : Misoprostol per oral dapat direkomendasikan sebagai prosedur tambahan untuk mengurangi retensio urin.*

***Kata kunci :*** *karsinoma serviks, histerektomi radikal, misoprostol, retensio urin.*

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## INTRODUCTION

Cervical cancer ranks second in Indonesia due to the number of cancer patients in women but as a cause of death was the first rank. Based on WHO data (World Health Organization) in 2008 it is estimated that every day there are 38 new cases of Cervical Carcinoma and 21 women who died of Cervical Cancer in Indonesia.[1] Based on 2013 Riset Kesehatan Dasar (Riskesdas) conducted by the Ministry of Health Litbangkes, prevalence of sufferers cervical cancer in Aceh Province is equivalent to prevalence of Indonesian national cervical cancer, which is 1.4 / 1,000 population or two people per 1,000 population.[2] Based on secondary data from Zainoel Abidin General Hospital Banda Aceh in 2013, the majority of cases of Cervical Cancer (61%) wherein the early stages (stadium 1A, stadium 1B and stadium IIA).[3]

Urinary retention is the most frequent complication of surgery Radical Hysterectomy of the Early-stage Cervical Cancer and causes voiding dysfunction with an incidence of 8% - 80%. Twenty of percent of patients who have had a Radical Hysterectomy developed Vesika Urinary dysfunction up to 3 months postoperatively.[4-6]

Misoprostol is a drug that is often used for the treatment of urinary retention. The effects of these drugs can increase Detrusor muscle contractions. Misoprostol is a PGE1 derivative. Pharmaco kinetic Oral administration of Misoprostol is more rapidly absorbed than intravaginal administration.[7-9] The authors want to prevent the occurrence of Urinary Retention by administering Misoprostol orally as a prophylaxis to reduce bladder dysfunction morbidity. Therefore the authors are interested in assessing the effectiveness of Misoprostol per oral administration to reduce the incidence of urinary retention after Radical Hysterectomy.

## METHODS

This research design is a Randomized Control Trial, Double blind study. The group was given oral Misoprostol tablets with a catheter after Radical Hysterectomy was called the intervention group and the group was given a placebo with a catheter as the control group. The study was conducted after the ethical clearance approved by ethical committee, at the Division of Gynecology Oncology, Zainoel Abidin general Hospital Banda Aceh and started from January 2017 to October 2018. The target population in this study were all patients who have had Radical Hysterectomy in the early stage Cervical Cancer (stage 1A, 1B, 2A).

Inclusion criteria were: patients after radical hysterectomy in the early stage cervical cancer and agreed to take part in the study by signing an informed consent. Exclusion criteria were patients with a history of urinary retention before surgery, urinalysis and LEA tests showing urinary tract infections, hydronephrosis, chronic urinary retention and urinary incontinence, Urethral stricture and history of Vesika Urinary injury. The number of subjects in this study were 34 patients consisting of 17 intervention groups and 17 control groups. The randomization method used SNOSE (sequentially, numbered, opaque, sealed, sealed envelope) or using sequential, numbered envelopes, envelopes that are not transparent and closed.

Patients were given oral misoprostol tablets 200 µg per 12 hours, within 24 hours after radical hysterectomy. All patients have a transurethral catheter placed after surgery hysterectomy for emptying the bladder for 1 x 24 hours. After the catheter is removed the patient is observed, as follows: Within 6 hours of observation, the patient is given a drink water 100 cc per hour. If the patient wants and able to void spontaneously, perform measurement for residual urine using a catheter. If residual urine is less than 100 ml, then the patient is considered capable of spontaneous voiding. If residual urine is 100-500 ml or more, the patient has urinary retention and continue to urinary retention management. If within 6 hours observation the patient is unable to void spontaneously, the patient's urine will be removed by transurethral catheter for 24 hours. Observation of the research will be carried out until the patient can spontaneously urinate again with urine residue less than 100 ml and suitable for discharged from the hospital. Data collection of factors related to urinary retention after radical hysterectomy were: bladder capacity, spontaneous voiding time, urine volume, length of stay, intraoperative blood loss, time of surgery for radical hysterectomy and side effects of Misoprostol. Data will be analyzed using the SPSS 22 software with significance P-value <0.05.

## RESULT

During the study period, we included 34 research subject who met our inclusion and exclusion criteria. General characteristics of study subject are shown in table 1.

**Table 1.** General Characteristic of Research Subject

| Variable | Frequency (n) | (%) |
|---|---|---|
| Intervention group (Misoprostol) | 17 | 50 |
| Control group (Placebo) | 17 | 50 |
| **Urinary retention** | | |
| Control | 13 | 38.2 |
| Intervention | 3 | 8.8 |
| **Without urinary retention** | | |
| Control | 4 | 11.7 |
| Intervention | 14 | 41.3 |
| **Age** | | |
| 40-45 | 4 | 11.7 |
| 46-50 | 4 | 11.7 |
| 51-55 | 12 | 35.3 |
| 56-60 | 11 | 32.3 |
| 61-65 | 2 | 5.8 |
| 65-70 | 1 | 3.2 |
| underweight | 0 | 0 |
| Normal | 27 | 79.4 |
| Overweight | 5 | 14.7 |
| Obesity | 2 | 5.9 |
| **Parity** | | |
| Parity 1 | 0 | 0 |
| Parity 2-4 | 15 | 44.1 |
| Parity>4 | 19 | 55.9 |
| **Cervical Cancer Staging** | | |
| Stage 1A | 1 | 2.9 |
| Stage 1B | 15 | 44.1 |
| Stage 2A | 18 | 53 |
| **Able to void spontaneously** | | |
| Control | 11 | 32.3 |
| Intervention | 17 | 50.1 |
| **Unable to void spontaneously** | | |
| Control | 6 | 17.6 |
| Intervention | 0 | 0 |
| **Intraoperative bleeding ≥500 cc** | | |
| Urinary retention | 12 | 35.3 |
| Without urinary retention | 7 | 20.5 |
| **Intraoperative bleeding <500 cc** | | |
| Urinary retention | 4 | 11.7 |
| Without urinary retention | 11 | 32.5 |

### Correlation between Administration Misoprostol Tablets and placebo to Residual Volume after Catheter Removal

In 34 patient, 6 research subject were found in the control group who were unable to void spontaneously after catheter removal, only 11 research subject residual urine could be measured. All intervention groups were able to void after catheter removal, resulting in 17 research subject of residual urine that could be measured. The statistical calculation showed that the independent sample test results with P-value 0.049, which means there are significant differences. Based on the data that the administration of misoprostol after radical hysterectomy can reduce the residual urine.

**Table 2.** Correlation between the Administration of Misoprostol Tablets with Mean Urine Residual Volume

| Group | Total Case | Mean urine residual volume | SD |
|---|---|---|---|
| Intervention | 17 | 52.6 ml | 47.9 |
| Control | 11 | 159.5 ml | 155.6 |
| P=0.049 | | | |

### Correlation between Administration of Misoprostol Tablets and Volume of Residual Urine 100 ml or more (Urinary Retention)

In 34 patient who has had radical hysterectomy, there were 16 research subject with residual urine 100 ml or more after transurethral catheter removal. Thirteen (38.2%) cases were from the control group and 3 cases (8.8%) from the intervention group. In the statistical calculation using the Chi-square test, the difference between the occurrence of urine residual volume of ≥ 100 ml between these groups is significant with P-value 0.002. These findings show that administration of misoprostol tablets after radical hysterectomy can reduce residual urine volume to less than 100 ml.

**Table 3.** Correlation between the Administration of Misoprostol Tablets and Volume of Residul Urine ≥ 100 ml (urinary retention)

| Group | Urine residual volume ≥ 100 ml | Urine residual volume < 100 ml |
|---|---|---|
| Control | 13 Cases (38.2%) | 4 Cases (11.7 %) |
| Intervention | 3 Cases (8.8 %) | 14 Cases (41.3 %) |
| Total Cases | 16 | 18 |
| P= 0.002 | | |

### Correlation between Administration of Misoprostol Tablets with Spontaneous Voiding ability

There were 6 research subject unable to void spontaneously (17.6%) all of which occurred in the control group. All patients (17 research subject (50.1%)) in the intervention group were able to void spontaneously, whereas in the control group there were 11 research subject were able to void spontaneously (32.3%). Statistical calculations

using the Chi-square test, the difference between the administration of misoprostol tablets and the ability to void spontaneously after catheter removal between these groups were significant with P-value 0.018.

**Correlation between Administration Misoprostol Tablets and Bladder Capacity**

In the control group there were 11 research subject were able to void spontaneously with mean bladder capacity 327,2 ml. All patient in the intervention group were able to void spontaneously with mean bladder capacity 360,5 ml. In the statistical calculation of this study using the independent sample test, the P-value 0.479. It means that there is no significant difference in bladder capacity between the intervention group and the control group. It can be concluded that administration Misoprostol after radical hysterectomy has no effect on bladder capacity.

**Correlation between Administration Misoprostol Tablets and the First Time of Voiding Postradical Hysterectomy**

Based on the data of the first voiding response after radical hysterectomy, it shows the first time of voiding after radical hysterectomy in the intervention group more faster than the control group (117.6 vs 237.2 minutes). In the statistical calculation using the independent sample test obtained P 0.001, which means there are significant differences.

**Correlation between the Administration of Misoprostol Tablets with Length of Hospital Stay**

Based on statistical calculations using the independent sample test, the difference in length of hospital stay between the intervention and control groups was significant with a P-value of 0.001. The mean length of hospital stay in the intervention group was 3.3 days, while the average length of the control group was 4.8 days. The data showed that the length of hospital stay in the intervention group was more shorten than the control group.

**Correlation between Retention of Urine and Amount of Intraoperative Bleeding**

In this study, an amount of intraoperative bleeding depends on the stage of cervical cancer and the extent of the operating area. Urinary retention with the amount of intraoperative bleeding> 500cc was found in 12 (35%) research subject and 7 (20.5%) research subject without urinary retention. In the case of radical hysterectomy with intraoperative bleeding ≤ 500, 4 (11.7%) research subjects have had urinary retention and 11 without urinary retention (32.3%). The results of statistical analysis using the Chi-square test obtained P-value 0.07 this data showed no significant differences.

**Side Effect**

The administration of misoprostol orally 200 micrograms every 12 hours did not have serious side effects, and no patients dropped out from this study. Three of the 17 patients were administered misoprostol, complained of cramping in the abdominal wall with mild intensity and transient abdominal pain. These side effects do not require treatment and always self-limiting. Other side effects such as diarrhoea, chest pain, hypotension, arrhythmia and shivering were not found in both groups.

## DISCUSSION

Residual urine is affected by Detrusor muscle contractions. The physiology of voiding and bladder emptying process play a role in decreasing residual urine. Misoprostol, a PGE1 analogue causes open calcium channels so that extracellular calcium will easily enter the intracellular and bind to calmodulin which will activate the formation of MLC Kinase which facilitates the formation of P-Myosin. The myosin crossbridge to bind the actin filament to allow contraction of the detrusor muscle. Oral administration of misoprostol after radical hysterectomy can reduce residual urine volume. This condition is caused by the ability of prostaglandin to improve tone recovery and detrusor bladder muscle activity so that the

bladder's ability to empty all of the urine more better. Normal voiding requires an adequate Detrusor tone and low resistance to the bladder neck and urethra.[10,11] This study shows that misoprostol can increase the contraction of detrusor muscle.

Administration of misoprostol tablets after radical hysterectomy can reduce residual urine volume to less than 100 ml and increase spontaneous voiding ability.[12,13]This also corresponds with research that prostaglandin can accelerate recovery and activate detrusor bladder muscle tone. Existing literature found significant differences after vaginal hysterectomy procedure which given a prostaglandin 1.5 mg analogue intravaginally. Regarding to the study the mean residual urine significantly decrease.[14,15]

Pathophysiology mechanism of lower urinary tract function changes after radical hysterectomy. The urinary bladder wall undergoes decline in the elastic muscular properties caused by surgical injury and partial damage from the autonomic bladder innervation.[16-18] Literature revealed that the rate of postoperative voiding dysfunction depends on the resection of vaginal, paravaginal and parametrial tissue.[19,20] In Literature, 47% of women in the early stage cervical cancer post radical hysterectomy undergo urinary retention with residual urine ≥ 100 ml. In general, the initial transient changes after radical hysterectomy consist of reduced bladder capacity, detrusor hypoactivity, and reduced bladder sensation.

Literature has shown that decline in bladder compliance occurs after radical hysterectomy.[21,22] The data shows the first time of voiding after radical hysterectomy in the intervention group more faster than the control group (117.6 minutes vs 237.2 minutes, P <0.001). The administration of misoprostol can shorten the first time of voiding after radical hysterectomy, improve compliance and increase the proprioceptive sensation and bladder sensation.

In this study showed a significant increase in urine volume in the intervention group after radical hysterectomy (312.6 ml vs. 201.3 ml). Based on statistical calculations, there are significant differences so that oral administration of misoprostol after radical hysterectomy can increase urine volume.

Administration of misoprostol tablets after radical hysterectomy can reduce the length of stay and reduce residual urine. This data corresponds that length of stay postoperative ranging from 1 to 6 days. Bergman's research stated that giving Misoprostol will shorten the length of stay.[23]

An amount of intraoperative bleeding after radical hysterectomy showed that there was no significant difference in cases of bleeding more than 500 cc or less than 500 cc due to occurrence of urinary retention, so it can be concluded that the incidence of urinary retention was not related to an amount of intraoperative radical hysterectomy. Urinary retention was associated with an amount of intraoperative bleeding correspond to the research which stated that urinary retention was not caused by intraoperative bleeding, but was probably due to an expansion of the operating area which could cause innervation of Pelvicus nerve in the lower urinary tract.[24,25]

## CONCLUSION

Oral administration of misoprostol tablets can reduce the incidence of urinary retention after radical hysterectomy. Oral administration of misoprostol tablets can reduce residual urine volume, increase spontaneous voiding ability, increase urine volume, shortening the first time of voiding after radical hysterectomy and reduce length of hospital stay. There was no significant correlation with oral misoprostol tablets with decreased bladder capacity. An amount of intraoperative bleeding has no significant correlation with the incidence of urinary retention.

## RECOMMENDATION

The author recommend that a larger sample group can yield more accurate study result. Expanding research variables and conducting pre-operative examinations to measure detrusor muscle strength and urethral resistance.

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**Case Series**

# Cryotherapy versus Cold Coagulation for Treating Cervical Precancerous Lesions

## *Krioterapi versus Cold Coagulation untuk Menatalaksana Lesi Prakanker Serviks*

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## Abstract

**Objective :** Elaborating the results and comparison of cryotherapy and cold coagulation for cervical pre-cancer lesion cases in West Cakung Primary Health Center, Jakarta, Indonesia.

**Methods :** Observation was conducted from cervical pre-cancer lesion cases which were found by visual inspection with acetic acid (VIA) method. Those cases were directed into cryotherapy or cold coagulation based on randomization sampling. After 6-months post-therapy, the lesions were assessed. This study was administered on Cakung Barat Health Center, Jakarta, Indonesia, on April-December 2018. Of 10 cases, five were treated using cryotherapy and the rest with cold coagulation.

**Results :** After six months follow up, 1 of 5 patients from each therapy still had VIA positive result. The side effect in form of spotting after 1 month of cryotherapy and cold coagulation were 1/5 and 3/5, respectively. There were no other side effects reported during the 6-months follow up for both treatments.

**Conclusions :** The result of both treatments are relatively the same in converting VIA positive into negative, proved with each therapy have turned 4 for 5 patients with prior VIA positive into negative. The side effects endured by respondents were minimal in 1-month post-therapy, while there were no significant side effects after six months post-therapy.

**Keywords :** cervix, cold coagulation, cryotherapy, precancer lesion.

## *Abstrak*

***Tujuan :*** *Memberikan informasi hasil terapi dan perbandingan antara krioterapi dan cold coagulation pada kasus lesi prakanker serviks dan efek samping yang ditimbulkanpada responden di wilayah puskesmas Cakung Barat, Jakarta, Indonesia.*

***Metode :*** *Penelitian bersifat observasi pada beberapa kasus lesi prakanker serviks yang ditemukan dengan pemeriksaan inspeksi visual dengan asam asetat (IVA). Lesi tersebut diterapi dengan krioterapi atau cold coagulation secara acak. Setelah 6 bulan setelah terapi, lesi diperiksa ulang. Penelitian berlangsung di wilayah Puskesmas Kelurahan Cakung Barat, Jakarta, Indonesia pada bulan April – Desember 2018. Total kasus yang dinilai berjumlah 10 kasus dengan pembagian 5 kasus diterapi krioterapi, 5 kasus diterapi cold coagulation.*

***Hasil :*** *Setelah 6 bulan pascapengobatan, 1 dari 5 pasien 1 dari 5 orang yang diterapi krioterapi atau cold coagulation dinyatakan masih IVA positif. Efek samping pengobatan setelah 1 bulan adalah spotting sebesar 1/5 dan 3/5, masing-masing. Tidak ada efek samping yang dikeluhkan pasien setelah 6 bulan paska pengobatan krioterapi dancold coagulation.*

***Kesimpulan :*** *Hasil terapi lesi prakanker serviks dengan krioterapi atau cold coagulation relatifsama, hal ini dibuktikan dengan masing-masing terapi telah mengubah 4 dari 5 pasien dengan IVA positif menjadi IVA negatif. Efek samping minimal dirasakan responden pada 1 bulan pasca pengobatan, sedangkan tidak ada efek samping yang dirasakan setelah 6 bulan pengobatan pascaterapi.*

***Kata kunci :*** *serviks, cold coagulation, krioterapi, lesi prakanker serviks.*

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## INTRODUCTION

Data of GLOBOCAN, International Agency for Research on Cancer (IARC) on 2018 revealed that the number of incident and mortality of cervical cancer ranked in fourth position on women cancer globally.[1]In Indonesia this position become the second, after breast cancer.[2]

Cervical cancer caused by the Human Papilloma Virus (HPV) infection sub-type oncogenic.[3]The efforts to prevent cervical cancer could be administered in the early stages of HPV infection. Several methods are available to help the diagnosing of HPV infections in pre-cancer lesion stages; visual inspection with acetic acid (VIA), pap smear test, HPV DNA test and others.[4]If compared with pap smear or HPV DNA test, VIA method are more likely used in limited and low-resource setting like primary health center or other private first level of health facilities since it require minimum source of human resource and do not require comprehensive laboratory.[5,6]

After early detection, further therapy is needed if lesion found. One of the treatments is cryotherapy which has been included in cervical cancer early detection Indonesian national agenda through See and Treat program. In high-income countries, the incidence and mortality of cervical cancer decreased until 75% from early detection and lesion treatment before invasive cancer developed.[7]If single visit treatment were done, the potential incidence of cervical would be decreased by 26% more.[8]

On the Indonesian See and Treat program the roughest challenge is about the procurement of $CO_2$or $N_2O$ gas.[4]Thus similar method like cold coagulation could be used to tackle this challenge, since it require electricity instead of gas. Cold coagulation therapy were adopted in many countries like Asia and Africa for its relatively simple features.[4]But in Indonesia; cold coagulation method are the least popular compared to cryotherapy. Therefore, a study to assess and compare the result of both treatments is needed. This study fulfills those aspects in comparing the result of VIA after treatments.

## CASE

Among 5 of 10 patients received pre cancer lesion treatment of cryotherapy and the rest received cold coagulation based on randomization sampling. Their age average was 28 years old. All of patients were diagnosed with VIA positive and 3 of them has cervicitis (treatment: 2 cryotherapy and 1 cold coagulation). Cryotherapy technique was conducted with 3 minutes double freeze – 5 minutes rest between, while cold coagulation technique use single heater for 1 minute. After those treatments, patients were asked for 1 month sex abstinence and should do the follow up on 1 and 6-month post therapy.

Patient 1, 2 and 3 were diagnosed with VIA positive but no cervicitis and treated with cryotherapy. There were no significant side effects after treatment. The ice remaining were found 1 month post therapy and 6-months post treatment the remaining were not visible and VIA result turn into negative. Patient 4 and 5 were diagnosed with VIA positive and cervicitis and treated with cryotherapy. Spotting were detected just in patient 4 on 1-month post therapy 5. After 6 months, patient 4 and 5 reported that no side effects occurred and the VIA turn into negative, while patients 5 still has VIA positive with no cervicitis.

Patient 6, 7, 9, 10 were diagnosed with VIA positive, no cervicitis and treated with cold coagulation. Patient 6 and 9 reported no side effects endured while patient 7 and 10 has spotting in the first month and disappeared after. One of them were still diagnosed with VIA positive on 6 months post therapy. Patients 8 with VIA positive and cervicitis were also treated with cold coagulation. Spotting were occurred in the first month and disappeared after. The result after 6 month were both negative for VIA and cervicitis.

**Table 1.**Treatment, Result and Side Effects

| Case | Age (year) | VIA Diagnosis | Treatment | Result (6 months post) | Side Effect (1 month post) | Side Effect (6 month post) |
|---|---|---|---|---|---|---|
| 1 | 36 | Positive | Cryotherapy | Negative | Watery discharge | No |
| 2 | 44 | Positive | Cryotherapy | Negative | Watery discharge | No |
| 3 | 36 | Positive | Cryotherapy | Negative | Watery discharge | No |
| 4 | 33 | Positive, Cervicitis | Cryotherapy | Negative, Cervicitis (-) | Watery discharge, Spotting | No |
| 5 | 22 | Positive, Cervicitis | Cryotherapy | Positive,Cervicitis (-) | Watery discharge | No |
| 6 | 25 | Positive | Cold Coagulation | Negative | No | No |
| 7 | 27 | Positive | Cold Coagulation | Negative | Spotting | No |
| 8 | 43 | Positive, Cervicitis | Cold Coagulation | Negative, Cervicitis (-) | Spotting | No |
| 9 | 23 | Positive | Cold Coagulation | Positive | No | No |
| 10 | 30 | Positive | Cold Coagulation | Negative | Spotting | No |

## DISCUSSION

As this study, cryotherapy and cold coagulation were focused to treat cervical cancer pre-cancer lesion and cervicitis. Since 1964, cryotherapy has been used to cure chronic cervicitis and precancer lesion, while cold coagulation begin 2 years after it.[9]Cryotherapyuse $N_2O$gas since it colder than $CO_2$gas (freezing poin of -89 °C compared to-78 °C), while cold coagulation use electricity.[10]The objective of these abrasive treatment are to freeze the transformation zone. Thus cellular necrosis affects the development of pre cancer lesion.

The success rate in this study were 80% in resolving VIA positive both using cryotherapy and cold coagulation. This finding is coherence with the study from India about effectivity of cryotherapy in precancer lesion which revealed the almost 80% clearance confirmed by biopsy histology on Cervical Intraepithelial lesion (CIN).[11]On 2014 the effectivity of cold coagulation with the 94% success rate on CIN 1-3.[12]

Complication and significantside effects were not likely occurred in this study. The safety of cryotherapy were reported through study from India and coagulation from Brazil.[11,13] Both studies highlighted that the minimal side effects happened after treatment, including abdominal cramp, heat sensation and spotting. In this study, all patient with cryotherapy were reporting watery discharge as general side effect after treatment with cryotherapy and 1 of themalso were reporting spotting during 1 month post therapy.

Excision methods Loop Electrosurgical Excision Procedure (LEEP), Large Loop Excision Transformation Zone (LLETZ), laser conization, and cold knife conization) are highly efficacious than ablative treatment (cryotheraphy and cold coagulation). Unfortunately, they are unsuitable for low-level providers and remote areas, higher risk of complications, and quite costly.

In Indonesia, as a nation with separated island and do not have enough obgyn in every area, ablative treatment is a solution for treat patient with lesion of cervical cancer. See and treat program is an national program combination between community screening with VIA examination and treat with cryotherapy. In the implementation, Cryotherapy has minimum side effects and the simplicity tools so can be used by well-trained general practioner or midwive. However, in the process, the constrain of cryotherapy is the availibility of gas ($N_2O$ or $CO_2$) especially for transport the gas to isolated area. Other than that, gas could block the duct which resulting in temperature inconsistency.[14]So, there is needed the alternative methods which has same usability and can answer the challenges.

**Table 2.** Cervix Documentation on Patients with Cryotherapy

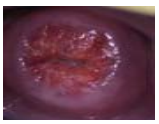
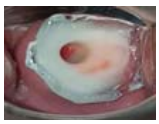
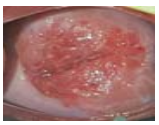
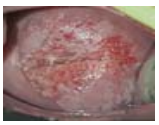
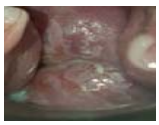
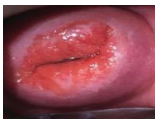
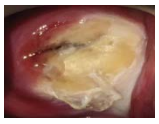
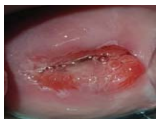
| No. Patient | Pre IVA | Post IVA | Post Cryotherapy | Post 6 month treatment |
|---|---|---|---|---|
| 1 |  |  |  |  |
| 3 |  |  |  |  |
| 5 |  |  |  |  |

**Table 3.** Cervix Documentation on Patients with Cold Coagulation

| No. Patient | Pre IVA | Post IVA | Post Cold Coagulation | Post 6 months treatment |
|---|---|---|---|---|
| 6 |  |  |  |  |
| 8 |  |  |  |  |
| 10 |  |  |  |  |

Another affordable alternative method to treat precancer lesion and cervicitis and similarities in the implementation likes cryotherapy is cold coagulation.[4] The tool used generates heat from electric energy to destroy the lesion in cervical tissue: the superficial epithelium disappears after treatment, and the destruction of stroma and glandular due to drying.[15] The duration of treatment were about 30-60 seconds.

The cold coagulation therapy is relatively easy to perform, requiring only the small device and electricity. With all the convenience provided by cold coagulation method, the dependency of electrical source might become the shortfall. Temperature and optimum application has been not determined yet in consensus to assess the Depth of Necrosis (DON). A research of 80 patients stated that the average of necrosis depth after single application with flat tip were 2,6 mm (100°c for 20 seconds) until 3,5 mm (120°c for 30 seconds).[16]Compared with cryotherapy, the average of necrosis depth after a double freeze techniquea 3-min freeze followed by a 5-min thaw and a 3-min freeze is similar.[17]The pain generated during the procedure of cold coagulation should be noted. Further study should be administered to determine the parameter for optimum therapy and the tolerance of the patients.

In this study, 1 of 5 patients with cryotherapy or cold coagulation was reported pregnant until 3-4 months post therapy. The review from WHO stated that abortus rate on patients with cryotherapy is not likely higher that the common population. [18]Another study also stated that cold coagulation has no effect on fertility, proven by 94% women were pregnant during 2 year post therapy.[19]

Cold coagulation are currently not included in WHO 2013 cervical cancer treatment guideline for its limited source of study material. While this treatment gained popularity in some low and

middle income countries (LMICs) during the rising abrasive treatment in Asia and Africa countries for its simplicity features, cold coagulation were slowly replaced by *Loop* Electrosurgical Excision Procedure (LEEP).[4] Therefore, this study aimed to add the information about the effectivity and safety of cold coagulation if compared with cryotherapy.

## CONCLUSION

The results of cervical precancer lesion treatment with cryotherapy or cold coagulation were relatively same in converting VIA positive to VIA negative, both 4 of 5 patients in every treatment were recovered. The side effects on both therapy after 1 month were minimal only spotting were reported. While after 6 months therapy, there were no side effects reported.

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**Research Article**

# Nasal Congestion and its Management in Pregnancy Rhinitis

## *Hidung Tersumbat dan Penatalaksanaannya pada Rinitis Kehamilan*

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## Abstract

**Objective :** To elaborate on the pathomechanism of pregnancy rhinitis and the proper management of rhinitis symptoms, particularly nasal obstruction.
Methods: Literature review.

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**Result:** Placental Growth Hormone has a similar effect as progesterone in pregnancy, which is peripheral vasodilatation and increases extracellular volume. Increased estrogen during pregnancy enhances the parasympathetic activity, thus increasing vascular permeability and glandular activity.Plasma leakage from vascular bed to stroma results in edematous turbinates, causing nasal congestion. This mucosal swelling is exaggerated with the presence of thick and profuse secretion.

**Conclusions :** Pregnancy rhinitis, manifested as nasal congestion, is considered a phenomenon and may become a serious condition. Persistent nasal congestion acts as a potential risk factor in affecting fetal growth and development through gradual hypoxia process. This condition can lead to various complications such as maternal hypertension, preeclampsia, impaired fetal growth, and low APGAR scores. In-depth knowledge of pathomechanism is essential as guidance to proper treatment, including conservative and medical therapies, which will lead to an optimal outcome for both mother and baby.

**Keywords :** estrogen, nasal congestion, placental growth hormone, pregnancy rhinitis.

## *Abstrak*

***Tujuan :*** *Untuk memaparkan patomekanisme rinitis kehamilan dan tatalaksana yang tepat dalam mengatasi gejala rinitisnya, terutama hidung tersumbat.*

***Metode :*** *Tinjauan pustaka.*

***Hasil:*** *PGH dan progesterone memiliki efek serupa yaitu vasodilatasi perifer dan peningkatan volume ekstraselular. Peningkatan estrogen selama kehamilan menstimulus aktivitas sistem parasimpatetik, yang mana terjadi peningkatan permeabilitas vaskular dan aktivitas kelenjar. Kebocoran plasma dari pembuluh darah ke stroma akan menyebabkan edema konka yang bermanifestasi sebagai kongesti hidung. Kondisi pembengkakan mukosa ini diperberat dengan adanya hipersekresi.*

***Kesimpulan :*** *Rinitis kehamilan, dengan manifestasi kongesti hidung, dianggap sebagai suatu fenomena yang dapat menjadi fatal. Kongesti hidung persisten merupakan faktor risiko terjadinya gangguan tumbuh kembang janin melalui proses hipoksia bertahap. Kondisi ini dapat berlanjut menimbulkan komplikasi seperti hipertensi maternal, preeklamsia, gangguan tumbuh janin, dan skor APGAR yang rendah. Memahami patomekanisme sangat utama dalam membimbing klinisi memberikan tatalaksana yang tepat, termasuk terapi konservatif dan farmaka, yang akan memberikan keluaran yang optimal baik bagi ibu dan bayi.*

***Kata kunci :*** *estrogen, kongesti hidung, placental growth hormone, rinitis kehamilan.*

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## INTRODUCTION

Rhinitis is a common problem during pregnancy, affecting up to 30% of pregnant women.[1]Rhinitis during pregnancy might occurs as allergic rhinitis, drug-induced rhinitis, rhinosinusitis, anatomical variations, and gestational or "pregnancy" rhinitis.[2] In women with prior history of allergic rhinitis, nasal symptoms might improve or worsen during their pregnancies.[3, 4]Demoly[1] quoted that around 10–30% pregnant women suffer more from their AR symptoms. However, some women experience rhinitis symptoms only asepisodes in their pregnancies. Thus, pregnancy rhinitis is defined as nasal congestion present during the last six weeks or more of pregnancy, without other signs of respiratory tract infection and no known allergic cause.Pregnancy rhinitis usually disappears within two weeks after delivery[1, 3]

Pregnancy rhinitis is reported in one of five pregnant women.[3] The incidence rate from small groupsof pregnant women were respectively 30% of 79 women, 18% of 66 women, and 21% of 160 women. The prevalence of pregnancy rhinitis as 17.17%, with the description as follows: 0% in the first trimester, 9.38% in the second trimester, and 38.89% in the third trimester.[3,4]

In a questionnaire study, 22% of 599 pregnant women reported having nasal congestion during their midwife visits. Rhinitis symptoms occurred in their 7th to 36th week of pregnancies and disappeared in second to the fourth week after delivery. Fourty two percent of 2.264 pregnant women had nasal obstruction on the 36th week of pregnancies.[3]

Pregnancy rhinitis is considered as the result of hormonal changes and fluctuation during pregnancy, which might manifest as nasal congestion as the most bothersome symptom. During pregnancy, elevated estrogen and progesterone levels are associated with nasal mucosal hyperreactivity. These hormones also induce mucosal swelling, glandular secretion, and dilatation of turbinate capillaries, resulting in worsening of symptoms, especially nasal obstruction.[1, 3, 5]

It is believed that placental growth hormone (PGH) may stimulate mucosal growth and thus induce nasal congestion.Other than that, physiological changes during pregnancy also attribute to symptoms severity. Increased circulating blood volume during pregnancy, up to 40% of pre-pregnancy, is related to increased nasal airway resistance.[5]

Due to similar symptoms with other inflammatory diseases of the nose, pregnancy rhinitis should be suspected by the exclusion of other causes of rhinitis.6, 7 Rhinitis symptoms in pregnancy might not be considered as fatal, however, worsen symptoms during pregnancy may impair maternal daily activities and emotional well being. Persistent nasal congestion resulting in sleep disturbance during pregnancy is related to intrauterine growth retardation and lower APGAR scores.3 Proper management of pregnancy rhinitis must not raise problems, and worth consider the risk-benefit ratio for mothers and infants. [3, 6, 7]

**The Effects of Pregnancy Hormones to Nasal Physiology**

Throughout the pregnancy, hormonal changes affect the physiologic nasal cycle in many ways. Pregnancy-related hormonal changes and neuropeptides are causing this alteration to the mucosa of the nose.[8]

**Estrogen**

Estrogen production dramatically increases during pregnancy. Estrogen tends to inhibit acetylcholine esterase leading to the production of acetylcholine and induces Parasympathetic activity.

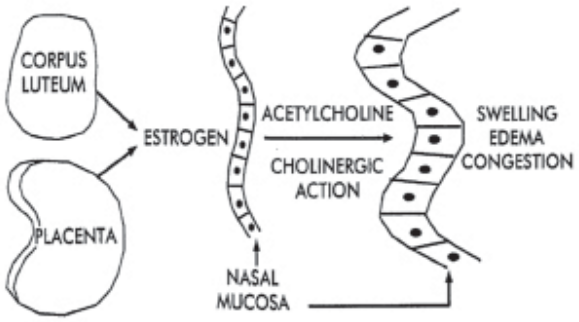


**Figure 1.** Estrogen Effects during Pregnancy[11]

This cholinergic activity causesvasodilatation and oedema to the nasal mucosa.[9, 10] (Figure 1)

In general, estrogen causes nasal turbinates to be edematous, leading to nasal obstruction, nasal discharge flowing into the throat (postnasal drip). Untreated conditions may cause olfactory function disturbance. These rhinitis symptoms also occur in women with birth control pills and hormonal replacement therapy.[12, 13]

Other known effects of estrogen are increased of vascular permeability, protein synthesis, glandular activity and increase the sensitivity of vasomotor properties in the autonomic nervous system. Increase of protein synthesis and hyaluronic acid in the nasal mucosa causes the mucus to thicken and disrupt the mucociliary clearance of the nasal cycle.[9,10]In addition, increase of blood pooling due to decreasedα-adrenergic smooth muscle tonus in the venous sinusoid, or oedema caused by plasma leakage from the vascular bed to the stroma.[3]

Excessive mucus production gives a sensation to the throat as post nasal drip, thus enhance nasal congestion. Studied nasal mucosa biopsies from pregnant women and those who consumed birth control pills, which he found glandular hyperactivities and increased phagocytosis. Nasal congestion is the initial side effect of high dose estrogen contraceptive pill intake.[14] Conducted a cohort study of 568 patients and found a significant correlation between the incidence of asthma and rhinitis during pregnancy. Furthermore, β-estradiol and progesterone have receptors in nasal mucosa that contribute to the nasal congestion pathophysiology in pregnant women.[12, 13, 15]

The significant rise of the plasma volume in pregnant womenoccur during the 6 – 8 weeks of gestation and reach its peak at week 32. Volume may increase to 4700 to 5200 ml (45% increase to unpregnant women). This occurrence happened due to an increase of estrogen secretion and renin angiotensin aldosterone system stimulation, which attract water and retent natrium. Water retention produces oedema of the mucosa thus resulting nasal congestion.[11]

Estrogen may trigger an immune reaction through the α-estrogen receptor on the mast cell. This reaction peak during the menstrual period, pregnancy, oral contraception consumption and hormone replacement therapy. A hypothesisstates that estrogen and progesterone act as antigen bound to a different protein producing Th2 cell, which regulates IgE synthesis and other antibodies. The antibody linked to mast cells as well as appropriate antigens (hormone or metabolites) will cause degranulation of the mast cell or basophil. Thus releasing histamine, Th2 cytokines, and leukotrienes.[16, 17]

**Progesterone**

There was no difference in blood progesterone levelbetween women with and without pregnancy rhinitis. Other study showed an increase of circulatory blood volume, possibly from vasodilatation occurringdue to the increased level of progesterone in pregnant women, which may induce nasal congestion2. Nasal vascular pooling from smooth muscle relaxation related to the increase of progesterone. An increase of vasoactive intestinal peptide (VIP) release, stimulated by progesterone and oxytocin, may enhance nasal congestion. Progesterone-related fibroblast in the nasal mucosa may also affect the extracellular matrix.[10]

**Prolactin**

Production of prolactin by pituitary increases during pregnancy, which suggests the possibility of its role in the pathogenesis of pregnancy rhinitis; however, this is contradicted by the absence of sinus pathology in patients who have prolactinomas. Furthermore, bromocriptine and quinagolide reduce prolactin production which eventually develops nasal congestion.[3]

**Neuropeptides**

A vasoactive intestinal polypeptide (VIP) is associated with other forms of rhinitis, and a possible mediator for nasal mucosa vasodilation, which is responsible for nasal congestion during pregnancy. Nasal biopsies of postmenopausal women showed an increased immunopositivity for estradiol, estradiol receptor, VIP, and substance P (SP) after six months of hormone replacement therapy. Whereas, there was a reduction in neuropeptide Y(NPY). Nasal application of hormone replacement therapy induced stronger VI P changes than did the transdermal application. Mucociliary transport time and subjective nasal congestion decreased, but anterior rhinomanometry was unchanged. The investigators proposed that estrogen action in the nasal mucosa is mediated by neuropeptides an increase of gland secretion and vasodilatation by VIP and SP and a decrease of NPY-induced vasoconstriction.[3] VIP relaxes the blood vessels to the upper airways, trachea, bronchi, and pulmonary vessels.

Innervation of the nasal mucosa is mainly organized and complex. The autonomic system regulates the mucosal vasculature and glandular secretion. The efferent nasal reflex arc consists of sympathetic and parasympathetic nerves. Parasympathetic nerve stimulates the release of acetylcholine, norepinephrine, and VIP. Postganglionic parasympathetic nerve innervates serous and mucous glands, arteries, veins and arteriovenous anastomoses. The distribution of VIP-immunoreactive fibres corresponds to the cholinergic distribution system. VIP stimulates

serous cell secretion, dilates nasal vessels, and may also regulate mucociliary clearance in the nose.[18]

The mechanism of hyperactivity of the nose remains unknown. The proposed hypothesis is increased permeability and increased the sensitivity of sensory nerve endings and imbalance of autonomic nerve regulation caused by changes of the nasal mucosa neuroreceptors.[18]Substance P is produced by the afferent sensory neurons of the trigeminal nerve within the nasal mucosa. Neurotransmitter promotes vasodilatation, increase blood vessels permeability, and hypersecretion of submucosal glands, leading to all sorts of nasal symptoms. The exact role of this neuropeptide in pregnancy rhinitis remains unclear.[19]

Small-diameter of the unmyelinated sensory fibres which areextensively branched, densely innervate the walls of submucosal vessels and glandular acini to form the neurosecretory varicosities within the vascular and glandular area. Neuronal wave evoked by histamine immediately extends to the peripheral sensory neurons, and the central, brain, as well. Hence, various neuropeptides are released from the nerve endings into the spaces near submucosal vessels and gland to elicit its rapid reactions.[19]

**Placental Growth Hormone**

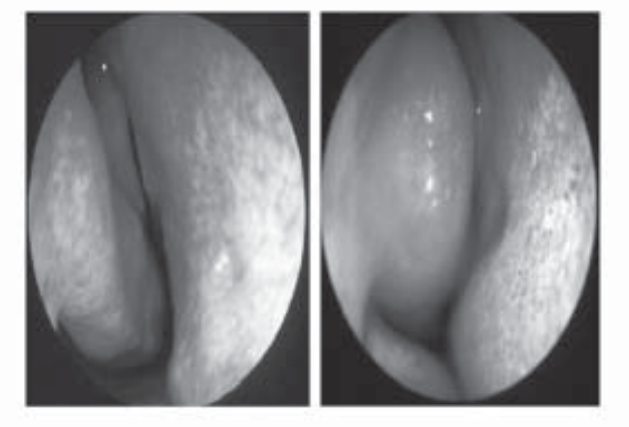

**Figure 2.** nasoendoscopic finding right inferior turbinate in pregnancy rhinitis pre (right) and post (left) decongestant.[3]

Human Growth Hormone (hGH) is secreted in an episodic burst in low levels between peaks. This pattern is later replaced by continuous secretion of Placental Growth Hormone (PGH) after the first trimester of gestation. That placental growth hormone (PGH) was significantly high during pregnancy. A significantly higher level of PGH in women with pregnancy rhinitis group on all occasions throughout the pregnancy. Presumably, PGH stimulates nasal mucosa similar to progesterone, thus inducing pregnancy rhinitis. PGH has a similar effect as progesterone in pregnancy, which is peripheral vasodilatation and increases extracellular volume.[20] The mechanism is still unknown; further study is warranted.[3, 20]

**Risk Factors**

According to a questionnaire study done, the incidence of pregnancy rhinitis is significantly higher among smoking women than non-smoking women (odds ratio: 1,7; CI 95% 1,1-1,5)[2,3]. Thus, smoking is considered an irritant agent that most probably stimulates nasal congestion. In vitro test to 10 airborne allergensin 165 pregnant women, in which 83 women had pregnancy rhinitis[14]. Overall sensitization was not increased in women with pregnancy rhinitis, yet sensitization to house dust mites frequently occurred in this group.Therefore, subjects with a high level of IgE to house dust mites are considered prone to develop pregnancy rhinitis. However, to differentiate pregnancy rhinitis to allergic rhinitis in pregnancyis still a challenge.[2, 3, 14]

## DIAGNOSIS

The diagnosis of pregnancy rhinitis is made by history taking, consisting thorough information regarding symptoms and physical examination to eliminate other cause of other nasal disorders. This shall exclude allergic rhinitis, vasomotor rhinitis, septal deviation, polyposis, rhinosinusitis and many more. It is difficult to differentiate allergic and nonallergic rhinitis. The common triggering factor of nonallergic rhinitis may be weather or temperature changes, food, perfume, strong odour and smoke. Additional symptoms may include allergic conjunctivitis (itching, watery, redness and swelling of the eye).[21]

A comprehensive head and neck examination starting with a simple rhinoscopy or nasoendoscopic examination to exclude other cause of rhinitis (Figure 2). The mucosa of the nasal and nasal turbinates may appear swollen and covered with serous to seromucoid discharge. There are no other specific further findings (laboratory or other means) to diagnose

pregnancy rhinitis.Pregnancy rhinitis is diagnosed based on subjective findings of symptoms and physical examination.[21]


**Figure 3.** Visual Analog Scale (VAS)[22]

The evaluation of subjective nasal obstruction using a Visual Analog Score (VAS) and Nasal Obstructive Symptom Evaluation (NOSE) scale may assess the quality of daily life (Figure 3 and Table 1). Both tools are highly specific and sensitive, validated by previous studies on many other nasal pathologies. VAS and NOSE scale are patient-centred quantitative diagnostic tools. VAS score more than 5 and NOSE scale more than equal to 5 in pregnant women presumably to be pregnancy rhinitis.[22]

**Table 1.** Nasal Obstructive Symptom Evaluation Scale23

| | Mild | Moderate | Fairly bad | Severe |
|---|---|---|---|---|
| Nose obstruction and stuffiness | 0 1 | 2 | 3 | 4 |
| Nose obstruction | 0 1 | 2 | 3 | 4 |
| Trouble breathing through my nose | 0 1 | 2 | 3 | 4 |
| Trouble of sleeping | 0 1 | 2 | 3 | 4 |
| Unable to get enough air through my nose during exercise or exertion | 0 1 | 2 | 3 | 4 |

Over the past month, how much of a problem were the following conditions for you? Please circle the most correct response.

Discharge Inflammation Polyps/Oedema (DIP) score is a clinician-based examination validated by previous researches (Table 2). DIP score quantifiesnasoendoscopic findings (more than 5 to be considered as pregnancy rhinitis). A correlation between VAS, NOSE, and DIP scores toward gestation in evaluating pregnancy rhinitis.[4]

**Table 2.** Discharge Inflammation Polyps/Edema (DIP) Scoring System24

| | Absent 0 | Moderat 1 | Severe 2 |
|---|---|---|---|
| Discharge Inflammation Polyps/Edema | | | |

Nasal congestion may also be objectively assessed by rhinomanometry, acoustic rhinometry, or peak nasal inspiratory flowmetry (PNIF). Those examinations assess nasal congestion by measuring nasal resistance, nasal volume, and nasal airflow.[24]

## DIFFERENTIAL DIAGNOSIS

Pregnancy rhinitis is a subtype of non-allergic non-infectious (NANIR). Allergic rhinitis shows similar symptoms to pregnancy rhinitis, but the underlying pathology occurred due to immunoglobulin E-mediated hypersensitivity. A definitive diagnosis of allergic rhinitis is established by skin prick test or specific IgE serology results.[2, 3, 25]

Rhinitis medicamentosa is another differential diagnosis but may also become a complication of pregnancy rhinitis. Most women do not directly disclose a history of prolonged usage of intranasaldecongestant. Therefore it is essential to obtain this information in the history taking. Healthy individuals with rhinitis medicamentosa no longer have nasal congestion in 2 days after they stop using decongestants. During pregnancy, if congestion persists for more than a week or so after reducing intranasal decongestant, the diagnosis should be pregnancy rhinitis.[3]

Other differential diagnosis includes upper respiratory tract infection and anatomical variation (septal deviation and hypertrophic turbinates) which disrupt the mucociliary clearance. Infection may occur due to a virus which causes direct damage to the nasal epithelial barrier and indirectly by hyperactivity of nasal mucosa, thus disrupts mucociliary clearance. It is important to exclude sinusitis by the clinical finding of purulent discharge in the middle meatus, facial pain, and olfactory dysfunction. Sinusitis during pregnancy (common in the second trimester) may not improve with conservative treatment such as nasal saline irrigation. Secondary bacterial infection may also occur. Typical organisms found in such conditions are Streptococcus pneumonia, Haemophilus influenza, and Moraxella catarrhalis.[26]

## IMPACT OF PREGNANCY RHINITIS

Impact of pregnancy rhinitis to the fetus is indirectly related to sleeping disturbance

experienced by pregnant women.Besides nasal congestion due to placental hormones, lying down in bedtime (supine position) also cause more nasal congestion due to the effect of gravitation. Difficulty in breathing through the nose increases the risk of snoring and mouth breathing during sleep. Twenty three percent of 502 postpartum women reported having to snore at the last weeks of their pregnancies. Snoring gives a higher risk of developing hypertension, pre-eclampsia, intrauterine growth retardation (IUGR), and low APGAR scores. Mouth breathing in pregnancy rhinitis affects lung vascular tonus or mother/ and fetus oxygenation. Pregnancy rhinitis might induce the presence of obstructive sleep apnea (OSA).[2,3] Physiologically, inhaled nitric oxide, which is highly produced inside the maxillary sinuses, decreases lung vascular resistance and increases lung oxygenation. Nasal congestion might disturb nitric oxide production.

Another study stated that pregnancy rhinitis impaired women's quality of life and might cause OSA, which in turn disturb pregnancy outcome[25]. Quality of life impairment was most significant at the third trimester than the second trimester. In addition, there is a significant difference in the quality of life between women with and without pregnancy rhinitis. Prolonged nasal congestion may lead to sinusitis development. Furthermore, it may cause cognitive and concentration impairment, fatigue, and headache. Pregnancy rhinitis is also associated with increased anxiety. Mouth breathing, on the other hand, causes dry mouth and decreases saliva secretion, leading to dental caries due to loss of salivary protection effect.

Quality of life in pregnancy rhinitis has not been fully evaluated, yet in severe cases, women showed difficulty in achieving optimum respiratory needs during the delivery process. Nasal congestion acts as a potential risk in hampering fetal growth and development by gradual hypoxia.[27]

## MANAGEMENT

### Conservative treatment

In the conservative approach, it is essential to elaboratetreatment options and goals to women with pregnancy rhinitis, which is to alleviate symptoms rather than cure the disease. Doctors must ensure pregnant women that nasal congestion is a common occurrence during pregnancy. Such information should be given at the first antenatal care visit, along with several treatment options to choose.[2, 3]

*Physical Exercise*

Physical exercise has been known to have a decongestant effect on the nasal mucosa. Head elevationat 300– 450 when laying down reduce the likelihood of vena cava syndrome and snoring. Another mechanical mean is using dilator fornostrils. This device dilates the narrowest part of the upper airways that is valve area of the nose. External type dilator may improve nocturnal nasal congestion related to breathing in pregnant women, while internal type dilator may reduce snoring in men as effective as a nasal decongestant. The adverse effect from dilator usage would be local irritation of the skin due to pressure.[28]

*Nasal Saline Irrigation*

Nasal saline irrigation is effective in improving symptoms, by repairing mucociliary clearance, reducing mucosal oedema, reducing inflammatory mediators, and cleaning mucus or triggering agents. Nasal irrigation is performed using isotonic saline solution 30–500 ml (average 200 – 250 ml), pH range is 6.2-8.4. Higher volume irrigates a wider area in the nasal cavity. Hypertonic solution (3% sodium chloride solution) is effective for irrigating thick mucus. Depending on device and volume, nasal irrigation on average is performed in 1 minute with compression pressure ≥120 mbar to reach areas of the nasal cavity.[29]

### Pharmacology Treatment

A pharmacological agent is an option when conservative therapy fails to reduce symptoms of pregnancy rhinitis.

### Decongestant

Decongestant is a vasoconstrictor agent effective to reduce nasal obstruction. Most systemic decongestant (phenylephedrine, pseudoephedrine, and phenylpropanolamine) is classified as category C by the United State Food and Drug Administration (US FDA). One study

found 206 cases of gastroschisis due to systemic decongestant during pregnancy, although there has been no study in the effectiveness of systemic decongestant for pregnancy rhinitis.3In unpregnant women, a decongestant may cause systemic side effects such as high blood pressure, palpitation, decrease appetite, tremor and sleep disturbance.[9]

Topical decongestants (oxymetazoline and phenylephrine) work rapidly to relieve nasal congestion. Pregnant women tend to overuse nasal decongestant in the long term because pregnancy rhinitis is a continuous condition. This will lead to unresolved rhinitis medicamentosa postdelivery. A topical decongestant will occupy α-adrenergic receptors more. Hence the autoregulation system will cause rebound mucosal oedema and worsen congestion.[10, 11] Benzalkonium chloride, acommon preservative in topical decongestantalso aggravate nasal congestion. Usage of topical decongestant once daily at night for more than four weeks may develop into rhinitis medicamentosa.[27]Therefore the recommended dose is a short term use of maximum 5-10 days at a lower dosage, unilateral and alternating nostril administrationin the evening.[3, 28]

**Glucocorticoids**

The intranasal steroidgives a very responsive therapeutic effect on managing all forms of rhinitis (allergicrhinitis, medicamentosa, NANIR and sinusitis). Intranasal steroid lowers the need for a systemic steroid, and it has an insignificant effect on pregnancy rhinitis. A RCT study by Ellegard et al[2]showed insignificant effects of fluticasone propionate nasal spray given eight weeks to pregnancy rhinitis, observedfrom symptoms or acoustic rhinometry data. That study also found no impact on cortisol level or fetal growth shown in the ultrasound. All currently available intranasal steroids have extremely low bioavailability,hence hardly give systemic side effects. Regardless, US FDA classifies mometasone furoate, fluticasone furoate, fluticasone propionate, and triamcinolone acetonide as category C. According to the Swedish Medical Birth Registry, there is no increment of congenital malformation incidencein rhinitis patients using budesonide inhalation in the early gestation. Hence it is classified as category B.[2, 3, 28]

Long term and repeated systemic corticosteroid usage should be avoided due to its adrenal suppression and other systemic side effects. A short-term of systemic steroid, less than two weeks, may give temporary relief. High dose corticosteroid intake gives many risks in the first trimester, for example, fetal blindness, lung oedema, uterine contraction inhibition, and fluid overload.[28] Thus, systemic corticosteroids generally should be avoided during pregnancy, except in serious threatening condition with benefit/risk ratio concerns.

**Antibiotic**

Antibiotic is not indicated in pregnancy rhinitis, although that would not be the case when bacterial sinusitis occurred. Intensive high dose of antibiotic is warranted, Beta-lactam dose should be increased by 50% because ofrenal clearance increase during pregnancy and to reach minimum inhibition concentration. Category B antibiotics, other than Beta-lactams, include penicillin, cephalosporin, aztreonam (monobactam). Imipenem is classified as category C.[3].

**Antihistamine**

Antihistamine is indicated if histamine-related symptoms are suspected, particularly effective for relieving sneezing and nasal itching.[3,5] Antihistamine has been used for a long time and known to have no adverse effect on the fetus. However, classic or 1st generation antihistamines (i.e. chlorpheniramine, triprolidine, diphenhydramine,cyproheptadine,promethazine, ketotifen) show to have side effects due to their action. Such side effects are drowsiness, dry mouth, and increase appetite.[12] Classic antihistamines are associated with oral clefts. Second and new generation antihistamines (i.e. loratadine, cetirizine, fexofenadine, desloratadine, levocetirizine) are more preferred due to lack of such side effects and no cardiac effects.This group of antihistamine is also clinically proven to have anti-inflammatory effects, aside from a known H1-histamine receptor blocker. Cetirizine and Loratadine are classified as category B.

**Other Methods of Management**

Nasal Continous Positive Airway Pressure (CPAP) is indicated in pregnancy rhinitis with severe

obstructive sleep apnea (OSA). In unpregnant patient, nasal CPAP is highly effective as shown by the improvement in polysomnography results. Pressure adjustment must be made in pregnant women. A study shows that nasal CPAP significantly reduces the nocturnal blood pressure in pre-eclamptic women without OSA.[3]

**Surgery**

Surgery will only be in consideration in cases with worst prognosis due to failure of conservative, pharmacological therapy, and other noninvasive measures, such as CPAP. It should be thoroughly considered that pregnancy rhinitis is a self-limiting disease in a certain period.[3]For refractory nasal obstruction due to hypertrophic turbinate, less invasive surgical measures include electrocautery, cryotherapy, laser or radiofrequency may be applied to reduce inferior turbinate volume.

## CONCLUSION

Researchers describe pregnancy rhinitis as nasal congestion that occurred in6 weeks ormore of the last final trimester of pregnancy, without a sign of respiratory infection and known allergy, which may resolve completely in 2–4 weeks postpartum. The most bothersome symptom is nasal obstruction, and other symptom includes watery rhinorrhea. Its pathomechanism remains unclear, although it is believed that estrogen, human chorionic gonadotropin hormone (HCG), human placental lactogen (HPL), and placental growth hormone (PGH) play roles. Risk factors include smoking and sensitization.

There is no drug of choice to manage pregnancy rhinitis. Women with pregnancy rhinitis should receive proper education regarding their conditions. Although most pregnancy rhinitis spontaneously resolvedafter giving birth, symptoms may significantly decrease quality of life, and medical attention is needed. Management includes conservative and pharmacology treatment, which aimed to relieve nasal congestion and other symptoms. Nonetheless, pregnancy is a specific condition that needs specific consideration. The final goal is to have an optimal outcome for both mother and baby.

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**Research Article**

# Informatic Video Increased the Number of Acceptors in Postplacental Insertion of Intrauterine Device (IUD)

## *Video Informasi Meningkatkan Jumlah Akseptor Alat Kontrasepsi Dalam Rahim (AKDR) Pascaplasenta*

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## Abstract

**Objective :** To find out the role of informatic video in obtaining consent for post placental insertion of Intrauterine Device (IUD).

**Methods :** This was a prospective randomized controlled trial. The informatic video was given to the study group compared by the level of acceptance of the respondents in the control group that was given conventional methods. This research was carried out in Pertiwi, Fatimah, and Khadijah I Mother and Child Hospital Makassar. The data were analyzed by chi-square test with significant level p<0.05.

**Results :** There was a significant correlation between informatic video groups to the consent (p=0.026) and the insertion (p=0.034) of post placental IUCD. The informatic video had the effects to increased the number of acceptors post placental IUCD with the value of significance as 0.018, therefore if the informatic video was increased, then the consent of insertion IUCD was also increased.

**Conclusions :** Informatic video had the effects of increased the number of acceptors postplacental IUCD.

**Keywords :** informatic video, postplacental insertion of Intra-Uterine Contraceptive Device (IUCD).

## *Abstrak*

***Tujuan :*** *Mengetahui hubungan antara video informasi dalam pengambilan persetujuan tindakan medis pada pemasangan AKDR pasca plasenta.*

***Metode :*** *Penelitian ini merupakan penelitian kohort dengan uji acak terkontrol prospektif. Jenis penelitian ini adalah penelitian uji kohort dimana peneliti memberikan tayangan video informasi pada kelompok penelitian serta membandingkan tingkat penerimaan pasien terhadap AKDR dengan kelompok kontrol. Penelitian ini dilaksanakan di Rumah Sakit Khusus Daerah Ibu dan Anak Pertiwi, Rumah Sakit Khusus Daerah Ibu dan Anak Fatimah, Rumah Sakit Ibu dan Anak Khadijah I Makassar. Data dianalisis dengan uji chi-square dengan kemaknaan p<0,05.*

***Hasil :*** *Terdapat hubungan yang bermakna antara pemberian video informasi terhadap persetujuan (p=0,026) dan pemasangan (p=0,034) AKDR pascaplasenta. Video informasi memiliki pengaruh dalam meningkatkan jumlah akseptor AKDR pascaplasenta dengan nilai signifikansi sebesar 0,018, sehingga jika bantuan video informasi meningkat maka keputusan dalam pemasangan AKDR juga meningkat.*

***Kesimpulan :*** *Video informasi memiliki pengaruh dalam meningkatkan jumlah akseptor AKDR pascaplasenta.*

***Kata kunci :*** *AKDR pascaplasenta, video informasi.*

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## INTRODUCTION

Family Planning (KB) is an effort to regulate pregnancy, birth, distance and ideal age for childbirth, through promotion, protection and assistance in accordance with reproductive rights to create quality families.[1] In an effort to improve maternal health, the main goal of family planning programs is for unmet need groups, and postpartum mothers are a very important target. Therefore, postpartum contraception is a strategic effort in Reducing Maternal Mortality Rate (MMR), as well as Infant Mortality Rate (IMR) where the number of births in Indonesia is very large, estimated at around 4,500,000 annually and 760,000 (17%) in including an unwanted or unplanned birth (KTD).[2,3]

Intrauterine Device (IUD) is contraception that is often recommended for postpartum mothers as a type of contraception because it is more effective than other types of contraception in terms of the effect on lactation or effectiveness in preventing pregnancy.[4,5] In mothers who have limited access to medical services, during labour is an opportunity to get contraceptive services, especially IUD insertion. Compared with sterilization, the use of IUD is more straightforward, a low cost relatively and high reversibility rate.[5]

Based on data of the Indonesian Demographic and Health Survey (SDKI), IUD contraception tended to decrease from 8.1% to 4.9%.1 In South Sulawesi, the insertion of IUD contraception in postpartum is around 3,158 women or 6,77% of all new patients who received postpartum contraception. This number has not met the national target.[4]

Many factors cause low interest in using IUD. Among them are various kinds of myths in society regarding IUD insertion such as can cause infertility, abortion, discomfort in intercourse, cancer, IUD can move, IUD can come out, and IUD can injure the husband's penis.[6] The lack of society understanding of the IUD has caused reluctance to use the IUD.[6-8] A new method is needed to introducing the IUD to society through an easier-to-understand method by using information videos.

Informed consent to medical care service requires an explanation of the right information including a clear description about the installation technique, advantages and side effects of IUD.[9] Video has been claimed as one of the more successful media in capturing patient attention compared to other methods in delivering information.[10] We aim the role of informatic video in obtaining consent for post placental insertion of IUD in several maternal and child hospitals in Makassar.

## METHODS

This was a prospective randomized controlled trial. Subjects were pregnant women who performed antenatal care (ANC) in the third trimester at Pertiwi, Fatimah, and Khadijah I Mother and Child Hospital Makassar from May to September 2018. The total samples were 200 patients, divided into two group: 100 study group with informatics video and counselling, and 100 control group with conventional counselling only. Of the total samples, 85 patients agreed on the study group and 71 patients in the control group. The research team gave the information to the subject, then asked to fill out a questionnaire regarding the factors that influence the decision to use a postplacental IUD. Subjects who said they were willing to use a post placental IUD were asked to sign a written informed consent.

The inclusion criteria were pregnant women in the third trimester who performed antenatal care (ANC) and will give birth in Mother and Child Hospital, ready to use IUD, and fill out inform consent. The exclusion criteria were pregnant women with postpartum complication (postpartum bleeding, infection, rest placenta) and had the risk of postpartum infection.

Data were analyzed by continuity correction and chi-square test to see the relationship between the independent variables on the dependent variable and linear regression test to see variables that influence the decision to use IUD contraception. Data were processed with the help of Statistical Product and Service Solutions (SPSS) for Windows version 23.0.

Before this research was conducted, the researchers requested ethical clearance from the commission of ethical biomedical research at the Faculty of Medicine, Universitas Hasanuddin Makassar, with number: 297 / 114.8.4.5.31 / PP36-KOMETIK / 2018.

## RESULTS

We included 200 subjects, 44 of them were excluded due to their refusal to participate. Then 156 subjects were randomized. We analysed 85 subjects in the study group and 71 subjects in the control group. Characteristics of the subjects are presented in table 1.

**Table 1.** Characteristics of the Subjects

| Characteristics | Study group (n = 85, %) | Control group (n = 71, %) | *P-value* |
|---|---|---|---|
| **Age (years)** | | | |
| <20 | 6 (7.1) | 5 (7) | 0.999 |
| 20-35 | 62 (72.9) | 52 (73.2) | |
| >35 | 17 (20) | 14 (19.7) | |
| **Parity** | | | |
| Primipara | 28 (32.9) | 25 (35.2) | 0.924 |
| Multipara | 47 (55.3) | 37 (52.1) | |
| Grande Multipara | 10 (11.8) | 9 (12.7) | |
| **Education** | | | |
| High | 50 (58.8) | 53 (74.6) | 0.056 |
| Low | 35 (41.2) | 18 (25.4) | |
| **Health Worker support** | | | |
| Supportive | 79 (92.9) | 63 (88.7) | 0.526 |
| Unsupportive | 6 (7.1) | 8 (11.3) | |
| **Husband Support** | | | |
| Supportive | 68 (80) | 56 (78.9) | 1.000 |
| Unsupportive | 17 (20) | 15 (21.1) | |
| **History of Contraception** | | | |
| No | 32 (37.6) | 39 (54.9) | 0.118 |
| Pill | 11 (20.8) | 2 (6.2) | |
| Injection 4 weeks | 2 (3.8) | 5 (15.6) | |
| Injection 12 weeks | 18 (34) | 13 (40,6) | |
| Implant | 15 (25) | 10 (31.2) | |
| AKDR | 7 (13.2) | 2 (6.2) | |

Based on the table above, each group showed the majority of patients in the age group 20-35 years, multipara, higher education, health worker support and husband support. The results of statistical tests show that age, parity, education, health worker support, husband support, and history of contraception are found to be p value> 0.05 at a significance level of 95%, meaning that the above variables do not have a correlation with the patient's decision to obtain an information video.

**Table 2.** Correlation of the Decisions of Patients who Obtained Informatics Video

| Variable | Study | Control | Total | *P-value* |
|---|---|---|---|---|
| | **Consent (n = 200, %)** | | | |
| Yes | 85 (85) | 71 (71) | 156 (78) | |
| No | 15 (15) | 29 (29) | 44 (22) | 0.026 |
| Total | 100 | 10 | 200 | |
| | **Insertion (n = 156)** | | | |
| Yes | 79 (92.9) | 57 (80.3) | 136 (87.2) | |
| No | 6 (7.1) | 14 (19.7) | 20 (12.8) | 0.034 |
| Total | 85 | 71 | 156 | |

Base on continuity correction test, the two variables show the value of p-value obtained is <0.05 at a significance level of 95%, so that patients who agree, have a correlation with the patient's decision to obtain informatic video, as well as the IUD insertion. Patients who have agreed to the IUD insertion have a correlation with the patient's decision to obtain an informatic video (Table 2).

**Table 3.** Significant Test of the Effect of Informatic Video on Postplacental Insertion of IUD

| Model | Unstandardized Coefficients | | Standardized Coefficients | t | Sig |
|---|---|---|---|---|---|
| | β | Std. Error | β | | |
| (Constant) | 1.138 | 0.139 | | 8.206 | 0.000 |
| Insertion | 0.281 | 0.118 | 0.189 | 2.383 | 0.018 |

Table 3. shows the significance of informatic video on post placental insertion of IUD. The results show a significance of 0.018. A significance level of 0.018 <0.05; this means that informatic video assistance is significant or influences the patient's decision to IUD insertion. The coefficient value of 0.018 is positive so that if the informatic video assistance increases, the patient's decision to IUD insertion will also increase.

## DISCUSSION

In this study, most maternal age of patients was low-risk age group, around 20-35 years old. This is in accordance with the demographic conditions of the Indonesian population where the structure of the population of Indonesia includes the structure of the youngest population with the most reproductive age, as well as in Makassar, South Sulawesi.[11]

Most of the patients are multiparous; this is in accordance with the purpose of the IUD, namely to make the distance of pregnancy so that for women of childbearing and multiparous age what is needed is a long-term contraceptive method.[12] IUD acceptors are women who do not want to get pregnant and their motivation

to install contraception is still high, especially in multiparous women.[13]

The results of our study found no significant association with education, parity and age on the level of decision to use IUD. The high level of education may not necessarily affect the level of decision in accepting IUD insertion. This can occur due to the influence of the quality of the counsellor in providing education to IUD acceptors. In accordance with a systematic review study, it was reported that there were differences in the success rates of IUD reception between public hospitals and clinics or home visits.[14]

Based on the results of our study, it was found that the husband's support was one of the factors that correlated the level of decision making for IUD insertion. The same results with the study that there is a relationship between the husband's support for the level of IUD insertion decisions. The purpose of using contraception is the goal of reproductive health which is a common goal of the family, especially the husband. Determining the desired number of children, when to postpone, place or end a pregnancy is a big decision and is the result of discussion between the wife, husband and family. Mothers supported by their husbands will find it easier to family planning programs and to make repeat visits or consult if there are things that are needed.[15,16]

The results of our study also found that the support of health workers had a correlation with the level of decision for IUD insertion. In accordance with the research conducted, where the relationship between the attitudes of officers and the use of IUD contraceptive services was reported. There was a significant correlation between staff support and the level of IUD insertion. Health workers are one of the reinforcing factors in IUD insertion. [15,16] Our study result can be explained that the support and attitudes of officers greatly influence the knowledge of IUD acceptors.

Previous KB usage history shows that experience has a strong influence on the selection of family planning methods, this is consistent with research that contraceptive methods have a strong relationship with the methods used previously, even 91% of women in Indonesia still choose the same contraceptive method after one year later.[17]

**Comparison of Postplacenta IUD Consent and Insertion**

In this study, 44 patients refused to use the postplacental IUD, 15 patients in the video group and 29 patients in the conventional group. Reasons for refusing also varied, from the video group found six patients wanted to use another method of contraception, four patients because the IUD could interfere with intercourse, two patients because the husband did not agree, and three patients were still hesitant to use contraception. While from 29 patients in the conventional group, 15 patients also chose to use another method of contraception, eight patients because the husband did not support, four patients were still hesitant to use contraception, and two patients because they interfered with intercourse. The existence of myths is one of the bases of rejection of post placental IUD insertion, this is determined by the attitude of the patient who has an influence in determining the IUD consent and insertion.[16]

In this study also prioritizes the autonomy rights of the respondents as patients, this is consistent with research that the most important principle of counselling is the autonomy of clients and their own decision making which aims to protect clients and medical personnel.

The results of this study found that the informatic video had a significant association with the level of consent for post placental IUD insertion.[18] Our results show that of 200 samples which were divided into video groups and conventional groups, the rejection of post placental IUD insertion was higher in the conventional group (29%) refused to use the IUD and showed significant results in terms of consent ($p=0.026$). Knowledge has a correlation with the installation of IUD, so it is logical that all sources that are the place to obtain this knowledge will also affect the level of IUD insertion.[19] A person's knowledge is usually obtained from various sources, such as mass media, electronic media, manuals, health workers, etc. Based on research, correct socialization can avoid the occurrence of misunderstandings and mistakes so that a method of providing adequate information media is needed in providing understanding to the public. In addition, there was also a multimedia theory called the multimedia principle proposed which

states that "humans learn more than words and images compared to just words".[20]

In this study it was found that the use of informatic video gave a significant result of 0.018 greater than the conventional method, this is consistent that using video is very clearly acceptable to patients, because video provides an ideal solution regarding doubts that experienced by patients with consistency, structured, clear, and easily understood to facilitate and increase the active role of patients in making decisions.[10]

The strength of this study that this is a cohort study that patients followed starting from counselling, consent to post placental IUD insertion. All the factors that can influence the results of this study indicate a homogeneity so that confounding factors can be controlled.

The disadvantage of this study is that the informatic video displayed is only a procedure for post placental IUD insertion while overall counselling still uses the conventional method. This study was also limited in providing counselling only in the third trimester. In addition, counselling cannot be monitored one by one in the decision-making process. In this study, it does not aim to determine the best counselling procedure but to be the basis for developing an instrument to help effective counselling, so further research is still needed.

## CONCLUSIONS

Informatic video with conventional counselling had the effects to increased the number of acceptors post placental IUCD. The more modalities used to provide information, the better the perceptions that can improve the decision making of post placental IUD insertion.

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