THE EFFECT OF FETAL SEX WITH THE DEGREE OF ASTHMA IN PREGNANT WOMEN IN THE TRIMESTER II AND IN III

Lia Octaviana[1], Ivon Diah Wittiarika[2], Arief Bakhtiar[3]
[1]Midwifery Study Program, Faculty of Medicine, Universitas Airlangga Surabaya, lia.octaviana-2021@fk.unair.ac.id, 082233484455
[2]Midwifery Study Program, Faculty of Medicine, Universitas Airlangga Surabaya, ivon.diah@fk.unair.ac.id, 08179337032
[3]Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Airlangga Surabaya, arief-b@fk.unair.ac.id, 081553252192

ABSTRAK

Penyakit asma masih menjadi masalah kesehatan di masyarakat di hampir semua negara termasuk Indonesia.Hasil studi pendahuluan yang telah dilakukan peneliti di RS UNAIR Surabaya pada tanggal 26 Januari 2022 didapatkan jumlah ibu hamil dengan riwayat asma yang berkunjung di poli Kandungan, poli Paru, Kamar Bersalin pada bulan Januari – Maret 2021 sebanyak 10 ibu, dan diketahui terdapat ibu hamil dengan riwayat asma terkontrol dan tidak terkontrol dengan derajat asma dan usia kehamilan yang berbeda. Berdasarkan hasil tersebut diperoleh pula jenis kelamin bayi yang dilahirkan dengan perbandingan lebih banyak pada perempuan sebanyak 3,79 % dari total ibu hamil dengan riwayat asma. Tujuan penelitian ini untuk menganalisis pengaruh jenis kelamin janin dengan derajat asma ibu hamil pada trimester II dan III. Jenis penelitian analitik observasional dengan pendekatan Retrospektif. Jumlah populasi ibu hamil 264 dengan jumlah sampel ibu hamil riwayat asma sebanyak 45 ibu. Penelitian ini menggunakan instrumen observasi dan data sekunder dari rekam medis. Dilakukan pengolahan data yang kemudian dilakukan uji statistic dengan uji Fisher Exact diperoleh nilai p < 0,05. Nilai tersebut kurang dari nilai α = 1%. Dengan demikian, terdapat hubungan antara Derajat Asma Ibu dengan Jenis Kelamin Bayi yang dilahirkan. Selanjutnya dilakukan uji Koefisien Kontingensi diperoleh nilai C adalah 0,557, maka dapat disimpulkan bahwa terdapat hubungan pengaruh jenis kelamin janin dengan derajat asma ibu yang memiliki hubungan sedang atau cukup. Berdasarkan hasil analisis menggunakan uji Fisher exact diketahui bahwa jenis kelamin janin memiliki pengaruh terhadap derajat asma ibu hamil. Sebagian besar jenis kelamin janin perempuan mempengaruhi derajat asma berat, sedangkan laki-laki cenderung memiliki derajat asma intermiten.
Kata Kunci : Jenis kelamin janin, ibu hamil, derajat asma

ABSTRACT

Asthma is still a health problem in the community in almost all countries including Indonesia. The results of a preliminary study conducted by researchers at UNAIR Hospital Surabaya on January 26, 2022, the number of pregnant women with a history of asthma who visited Obstetric Poly, Pulmonary poly, maternity room in January - March 2021 as many as 10 mothers, and there are pregnant women with a history of controlled and uncontrolled asthma with different degrees of asthma and gestational age. Based on these results, it was also obtained that sex of the baby was born with more ratios in female infant as much as 3.79% of the total pregnant women with a history of asthma. The purpose of this study was to analyze the relationship of fetal sex influence with the degree of asthma of pregnant women in the second and third trimesters. A type of observational analytical research with a Retrospective approach. The total population of pregnant women is 264 with a sample of pregnant women with a history of asthma as many as 45 mothers. The research used oberservastion instruments and secondary data from medical records. Processing research results was carried out which was then carried out statistical tests with the Fisher Exact test obtained a p value of < 0.05. The value is less than the value of α = 1%. Thus, there is a relationship between the Mother's Asthma Degree and the Sex of the Baby they are giving birth to. Furthermore, the Contingency Coefficient test obtained C value of 0.557, so it can be concluded that there is a relationship between the influence of fetal sex and the degree of maternal asthma that has a moderate or sufficient relationship. Based on the results of the analysis using the Fisher exact test, it is known that the sex of the fetus has an influence on the degree of asthma of pregnant women. Most female fetal sex affects the degree of severe asthma, while male fetus tend to have intermittent asthma degrees.
***Keywords** : Fetal sex, pregnancy, degree of asthma*

INTRODUCTION

Asthma is a heterogeneous disease characterized by chronic airway inflammation. To this day, asthma remains a problem in both developing and nations [(1).] Asthma symptoms proceed from mild, which does not interfere with

[1]Alamat Korespondensi Penulis:
Lia Octaviana
Email : lia.octaviana-2021@fk.unair.ac.id

Alamat Universitas : Kampus A, Jl. Mayjen Prof. DR. Moestopo 47 Surabaya 60131

daily activities, to permanent, which does interfere with daily activities. In Indonesia, asthma is among the top ten causes of morbidity and mortality.

Survei Kesehatan Rumah Tangga (SKRT) in 1986 showed that asthma was ranked fifth among the top 10 causes of morbidity, along with chronic bronchitis and emphysema([2]. Asthma remains a public health problem In almost every country, including Indonesia. According to the most recent estimates from the World Health Organization (WHO) released in December 2016, there were 383,000 asthma-related deaths in 2015 according to The Global Asthma Report, 2018[(3)]. In 2019, WHO stated that there are approximately 235 million patients with asthma currently[(4)]. There are several factors that trigger asthma attacks[(5)]. Allergy and asthma are considered to be multifactorial diseases triggered by interactions between the environment and host genes. In general, allergic disorders are more prevalent in the north than in regions where rapid environmental changes in recent decades have led to increased outdoor and indoor pollution, climate change, and improved hygiene[(6)].

Based on the comparison of the results of Riskesdas 2007 and 2018, there are 6 provinces whose prevalence previously was below the National figure to above the National figure, which are DI Yogyakarta, East Java, Banten, South Sulawesi, Bengkulu, and Riau Islands. With details of the largest number of inpatient asthma cases in East Java (7,942 cases) and outpatient asthma cases during 2015-2017 progressively, which increased more than four times during that period[(7)]. The prevalence of asthma in pregnancy increased in the United States by around 3.7-8.4% in 1997-2001[(8)].

The impact of pregnancy on asthma varies. Changes in pulmonary function, hormonal fluctuations, and immunological aspects of the interaction between mother and fetus are predicted that they have a share in the degree of asthma in pregnant women[(9)]. Changes in placental function also have the potential to influence the degree of asthma in pregnant women with asthma[(10)]. Data shows that one-third of asthmatic patients with pregnancy experience worsening, one-third do not change, and the remainder improves[(11)]. However, The low control of asthma during pregnancy is still a major issue that can increase the risk of complications such as pre-eclampsia, IUGR, preterm birth and delivery by cesarean[(12)]. The worsening impact of postpartum mothers with a history of asthma is also at risk of increasing complications of infant abnormalities and even death[(13)].

In the research of I B Ngurah Rai obtained the prevalence of asthma exacerbations in pregnant women was 0.17%, with several triggering factors for the degree of asthma caused, such as poor asthma control during pregnancy, allergen factors and also obtained that the sex of the fetus mentioned could affect the condition of asthma during pregnancy[(14)]. The degree and exacerbation of asthma in pregnancy can increase a moderately elevated risk of complications such as low birth weight, premature babies, preeclampsia, and even death[(15)].

In Andriani Litanto's research, 2021 was known that women were more often affected by asthma and experienced worsening asthma degrees. The underlying mechanism due to gender differences in asthma prevalence refers to differences in hormones and lung capacity[(16)].

The hormone estrogen functions in the process of fetal development in utero, including maturation of the lungs, placental cells and fetal Deoxyribo Nucleic Acid (DNA). In this case it is associated with various estrogen receptors throughout the process. Estrogen receptors are found in many immune regulatory cells and influence the immunological response towards the development of allergies. This response stimulates the production of IgE levels due to allergen exposure.

The results of a preliminary study conducted by researchers at UNAIR Surabaya Hospital on January 26, 2022, found that the number of pregnant women with a history of asthma who visited Obstetric Poly, Pulmonary poly, maternity rooms in January - March 2021, as many as 10 mothers. There are pregnant women with a history of controlled and uncontrolled asthma with different degrees of asthma and gestational age. Based on these findings, it was also obtained that the sex of the babies born with a higher ratio in women. As many as 3.79% of the total pregnant women with a history of asthma compared to the total number of pregnant women who visited the UNAIR Surabaya Hospital, then the percentage remains the same from prior years. There is no decrease in the prevalence of pregnancy with a history of asthma in East Java with the causative factors yet unidentified for certain, one of which is the difference between the fetus' gender and the degree of the mother's asthma.

Based on the preceding description, it is crucial to prevent as early as possible the deterioration of the condition of pregnant women with a history of asthma in various ways, including knowing the triggers factors, both external and internal. Among them are fetal umbilical cord IgE and fetal sex, which can respond to the increased production of maternal cytokines that affect the tissues, thereby promoting the growth of fetal trophoblast cells. As a result, there is an imbalance between TH1 and TH2, which causes an excessive inflammatory response from the mother so that the mother's immune system decreases. With a decrease in the mother's immune system, it can exacerbate asthma exacerbations among pregnant women due to its association with sensitivity or allergic responses[17]. The purpose of this study was to analyze the influence of fetal sex influence with the degree of asthma in pregnant women in the second and third trimesters.

RESEARCH METHODS

This study employs an observational analytical study method with a retrospective approach. The sample size in this study used a total sampling of 45 pregnant women with a history of asthma based on the inclusion criteria. Data collection was carried out through analysis of medical records of samples of pregnant women, mothers giving birth from January to December 2021 with a history of asthma at UNAIR Hospital. Furthermore, data processing was carried out using bivariate analysis with fisher's exact and contingency coefficient tests.

RESULTS AND DISCUSSION

This study's data collection occurred from July 12 to September 21, 2022. Data collection in this study used secondary data, namely the outpatient medical records of pregnant women at the Obstetric Poly and Pulmonary poly and mothers who gave birth at the VK or Maternity Room of UNAIR Surabaya Hospital. This study's sample amounted to 58 pregnant

women, and there are 45 pregnant women who entered the sample unit and met the inclusion criteria, which are pregnant women in the second and third trimesters, and women giving birth without concurrent heart disease concomitant at UNAIR Surabaya Hospital. The data is to be presented in the form of general and special data. General data this data was collected to determine the fetal sex, the degree of asthma of pregnant women, the age of pregnant women, the number of pregnancies (Parity), and malnutrition in pregnant women with asthma. In contrast, the specific data consists of research variables, namely the influence of the fetal or infant gender on the degree of asthma of pregnant women.

A bivariate analysis of this research data was performed to determine the fetal sex, the degree of asthma of pregnant women, the age of pregnant women, the number of pregnancies (Parity), malnutrition, namely obesity, among pregnant women with asthma. The results of this distribution are displayed as follows:

1) The Age of Pregnant Women Data

Table 1 Age Distribution of Pregnant Women

Pregnant Women's Age (year)	Asthma Degree			
	Intermittent n(%)	Mild persistent n(%)	Moderate persistent n(%)	Severe persistent n(%)
<20	0 (0)	0 (0)	0 (0)	0 (0)
20-35	10 (22,2)	2 (4,4)	12 (26,7)	16 (35,6)
>35	0 (0)	1 (2,2)	1 (2,2)	3 (6,7)
Total	10 (22,2)	3 (6,7)	13 (28,9)	19 (42,2)

Based on Table 1, the highest age distribution is in the age range of 20-35 years in severe persistent

2) Total Parity Data

Table 2 Distribution of Total Parity

Parity	n	%
1	10	22,2%
2	13	28,9%
3	12	26,7%
> 3	10	22,2%
Total	45	100%

Based on table 2, the distribution of the highest number of pregnancies is Parity 2.

3) Pregnant Women with Malnutrition Data

Table 3 Distribution of Pregnant Women with Malnutrition

Malnutrition	n	%
No	29	64,4%
Yes	16	35,6%
Total	45	100%

4) Asthma Degree in Pregnant Women Data

Table 4 Distribution of the degree of asthma in Pregnant Women

Asthma Degree	n	%
Intermittent	10	22,2%
Mild persistent	3	6,7%
Moderate persistent	13	28,9%
Severe persistent	19	42,2%
Total	45	100%

Based on table 4, the distribution of the degree of asthma in pregnant women mostly occurs in severe persistent degrees.

5) Fetal Sex Data

Table 5 Fetal Sex Distribution

The Fetal Sex	n	%
Female	30	66,7%
Male	15	33,3%
Total	45	100%

Based on table 5, the sex distribution of the fetus is mostly in the female gender.

6) Table 6 Distribution and Gender Analysis of female and male infants on the degree of asthma

Gender	Asthma Degree				Amount	P value 0.001 contingency coefficient = 0.557
	Intermittent n (%)	Mild persistent n (%)	Moderate persistent n (%)	Severe persistent n (%)		
Female	1 (3,3)	3 (10)	12 (40)	14 (46,7)	30 (100)	
Male	9 (60)	0 (0)	1 (6,7)	5 (33,3)	15 (100)	
Total	10 (22,2)	3 (6,7)	13 (28,9)	19 (42,2)	45 (100)	

Based on table 6, the female gender experienced a severe persistent asthma degree of almost 50%, while the male gender experienced an asthma degree of only 33.3%.

DISCUSSION

This study aims to analyze the effect of fetal sex with the degree of asthma in pregnant women in the second and third trimesters. Based on the results of the bivariate data test using Fisher's exact analysis, the p-value = 0.020, so it can be concluded that there is an influence between the sex of the fetus and the degree of asthma in pregnant women. Furthermore, the contingency test was carried out; it was determined that the relationship between the influence of fetal sex on the degree of asthma had a sufficient or moderate relationship.

In this study, it was discovered that female fetuses were more prevalent than male infants. The percentage of female infants born to pregnant women with asthma is more than 50% compared to the percentage of male

infants. This data was taken from the medical records of pregnant asthmatic women who delivered at Unair Hospital. The findings of this study prove that if pregnant women with asthma have a female fetus, the sex of the fetus is more at risk of deterioration asthma compared to the sex of the male fetus.

The pregnancy mechanism in asthma is caused by the hormonal state, which changes during pregnancy. Progesterone and estrogen are produced by the egg's derivatives for the first 35 days of the first trimester, after which the placenta takes over. According to the Indonesian Respirology Journal, there is a change in the levels of the hormones progesterone and estrogen and an increase in free cortisol levels; total plasma can have a significant effect. This increase in levels has a repair impact on asthma attacks during pregnancy, but some pregnant women experience resistance to stimulation or stimulation to this cortisol even though there has been an increase in serum levels 2-3 times. There is competition between glucocorticoid receptors by progesterone, deoxycorticosterone and aldosterone increases during pregnancy. An increase in asthmatic inflammation in the mother is associated, related with differences in the determination of protein or steroid transcription, lung maturation, placental cells or Deoxyribo Nucleic Acid (DNA) expression. Therefore, the hormonal changes that occur in female fetuses reduce the function of estrogen and progesterone as anti-inflammatories because a condition occurs where these receptors are no longer sensitive to cortisol[18].

In Pudyastuti research, there is an activity of the placental enzyme from pregnant women with female fetuses, which is 11β-HSD2, which decrease occurs, causing cortisol cells from the mother to relocate to the female fetus. Additionally, the deterioration of asthma symptoms is caused by the increased number of monocytes (white blood cells/ leukocytes). Changes in placental cortisol metabolism increase the mRNA ratio of Th2:Th1 cytokines and decrease the excitability of glucocorticoid and mineralocorticoid receptors. The effect will be a decrease in fetal development and suppression of the hypothalamus-pituitary-adrenal function, as indicated by a decrease in the concentration of estrogen in the umbilical cord blood of female fetuses.

Changes in this placental function are related to the invasion of placental trophoblast cells, the maturation of lung function, and fetal and maternal deoxyribo nucleic acid (DNA). During the implantation process, the placenta takes over the role of producing progesterone and estrogen. In female fetuses, there is activity of placental enzymes that have an effect on the 11beta-HSD2 receptor has decreased so that cortisol cells which should provide a repair effect on asthma attacks because of their anti-inflammatory properties; however, the opposite happened. This cortisol experiences an immune response or a negative response to an increase in cortisol which causes a decrease in the function of estrogen and progesterone. As a result of this decrease, there is also a decrease in glucocorticoid and mineralocorticoid receptor stimulation. This process causes stimulates an increase in Thelper cytokine cells in the response mechanism of changing placental function so that they respond to monocytes to produce

more and decrease maternal pulmonary function. Due to the increased number of monocytes, there is an inflammatory response in maternal serum, which can reduce the immune system of pregnant women.

According to the results of the above analysis proves that there is an effect of fetal sex on the degree of asthma in pregnant women in the second and third trimesters, in which the female gender is experiencing more severe persistent asthma worsening than the male gender during pregnancy. There is an influence difference in hormones excreted by the fetus during pregnancy that causes a distinct inflammatory response to the mother's immune system. Pregnant women carrying a female fetus have no significant improvement in the degree of asthma during pregnancy and even experience worsening. In contrast, pregnant women carrying male fetuses experience an improvement in the degree of asthma, so they are included more in the controlled asthma classification.

This is consistent with previous studies, which said there was an immunopathological relationship with allergens. According to researcher Resti et al., asthma is a prevalent disease with a rising prevalence rate. Various aspects of the innate and adaptive immune system to allergens, environmental stimuli, or viruses play a huge role in allergen sensitization, asthma symptoms and exacerbations, and response to therapy. There is a strong interaction between airway epithelial cells and the immune system in the pathogenesis of asthma. The most prevalent immunopathology in asthma is type 2 inflammation, which is characterized by airway epithelial processes involving epithelial cytokines such as IL-33. Epithelial cytokines will increase the activity of type 2 cytokines in the airway, generally produced by $CD4^+$ T cells and ILC. Local type 2 cytokine secretion will cause cascade mechanisms, including *IgE-mediated hypersensitivity*, activation of airway epithelial cells, *chemoattraction of effector cells* (mast cells, eosinophils, and basophils), and remodeling of the epithelium and subepithelial matrix[19].

In line with Litanto's research demonstrating those sex steroid hormones also influence the immune system by stimulating the activity of B cells, T cells, Mast cells, and Natural Killer cells (NK cells), influencing phagocytic cells to produce cytokines as an inflammatory response.

Sex hormones, particularly estrogen, play a role in the maturation process of the fetal lungs, creating differences between male and female fetuses. During the process of development in the womb, female fetuses have an earlier speed of lung development rate than male fetuses. This mechanism triggers ILCs to accelerate cytokine production. Early in the process of gonadal formation, Leydic cells produce the hormone testosterone. The hormone testosterone is present in female and male fetuses, but it is more abundant in male fetuses for the formation of sex, which is the testes. The androgen hormones produced are more in male fetuses than female ones. Androgen hormones are produced in the adrenal glands, which function as corticosteroids. In addition, in male fetuses, there is the hormone testosterone, which directly acts on ILC2 by inhibiting its proliferation against certain immune cells that activate

allergic asthma to become inactive[20]. Testosterone inhibits immune cells that are associated, such as inflammation and mucus production in the lungs[21].

The effect of sex hormones on asthma symptoms and their complex progress are the pathophysiology of asthma causes. Involved hormone testosterone and cytokines contribute to the equilibrium between the autoimmune and immune systems by regulatory T cells. Testosterone as an immunosuppressant and its ability to protect against the asthma-elicited inflammatory response. This protective effect comes from inhibiting androgen receptor mediators obtained from natural immunity, namely IL-2 cells which are the primary key to type 2 inflammatory responses [22].

The correlation relationship that is being shown with a positive value is a sufficient range of values. The unidirectional relationship between the two variables, which are the fetal sex and the degree of asthma in pregnant women, has a linear relationship. It can be concluded that the degree of asthma will experience worsening or improvement of exacerbations depending on the fetal sex conceived by the mother. Hence, pregnancies with a history of asthma are influenced by the immune system because, in the body, there is an occurrence of *'feto maternal tolerance*[23].

The thing to note is that we do not rule out relievers or asthma medications that are used to suppress asthma exacerbations. Severe asthma requires therapy, namely high doses of ICS, to prevent uncontrolled asthma or asthma that is still "uncontrolled"[24]. Although the mother was initially given asthma medication such as ICS (*inhaled corticosteroids*) or oral medication, pregnant women with female fetus sex were not known to experience improvement during pregnancy until approach delivery. Even when approaching the final trimester, the mother experiences a severe degree of asthma and must be done in delivering maternity aid by cesarean section.

There is possible that the results of the analysis of the effect of asthma degree on the fetal sex with a moderate or sufficient correlation because some mothers with male gender experienced intermittent degrees and some mothers were asthma diagnosed controlled with ICS or oral asthma medication. Meanwhile, in the female gender, the condition worsened; although they had been given a reliever medication, it only slightly repaired the exacerbation.

This study is consistent with the research of I.B. Ngurah Rai (2009), which indicates that there is a suspicion that the fetal sex can influence the condition of asthma during pregnancy. The fetal sex conceived by the mother influences the degree of asthma and asthma exacerbations during pregnancy. According to the findings of this study, women who conceived a fetus with a female gender raised the prevalence of the degree of asthma experiencing a worsening of severe persistent. On the contrary, in pregnant women carrying a male fetus, the prevalence rate of asthma is low and asthma improves. Research conducted by Jacquelline shows things related to the sex of the male fetus. Testosterone inhibits immune-related cells such as inflammation and mucus production in the lungs so allergic asthma becomes inactive.

Research by Beecroft et al. with a prospective blind trial examining 34 pregnant women with moderate and severe asthma who

received regular asthma therapy discovered that pregnant women with female fetuses significantly complained of symptoms of shortness of breath, awakening at night, worsening of cough symptoms compared to pregnant women with male fetuses which reported more experienced improvement in asthma symptoms.

Based on the results of the data analysis, it was found that the degree of asthma in pregnant women was more severe with severe persistence. Severe persistent symptoms are characterized by frequent exacerbations and interfere with activities, and will get worse at the end of the trimester of pregnancy. The worsening degree of persistent severe asthma is often experienced by pregnant women who are carrying a female fetus. As for the use of pain relievers, it only slightly improves the exacerbations. If this persists in the third trimester even before delivery, the delivery process can be done perabdominally or caesarean section. In pregnant women with a moderate degree of persistent asthma, which is characterized by symptoms of exacerbations that interfere with activities and have received daily relievers, the delivery process can be performed vaginally without comorbidities. This is evidenced by the fact from the delivery of pregnant women with moderate degrees of persistent asthma that there are vaginal deliveries in hospitals by obstetricians.

This study's results align with the Indonesian Respirology Journal that asthma attacks occur in more than 50% of the extremely severe asthma group and only 12% of mild asthma during pregnancy. Asthma attacks of the severe persistent classification can be caused due to uncontrolled asthma. This asthma attack can cause sustained shortness of breath during pregnancy and can occur complications for the mother and her fetus.

In research, it was found that there was a relationship between the degree of asthma attacks and changes in asthma's course during pregnancy. According to the Indonesian Respirology Journal that asthma attacks occur in more than 50% of the extremely severe asthma group and only 12% of mild asthma during pregnancy. Asthma attacks of the severe persistent classification can be caused due to uncontrolled asthma. This asthma attack can cause sustained shortness of breath during pregnancy and can occur complications for the mother and her fetus. However, this also necessitates a differential diagnosis to determine whether this tightness is caused by asthma during pregnancy or other consequences, such as COPD, chronic heart disease, gastroesophageal reflux disease, interstitial lung disease, anemia, pulmonary edema, vocal cord dysfunction, pulmonary embolism, pneumothorax, panic or anxiety, and thyrotoxicosis.

The risk that can occur in severe asthma is that it worsens the outcome of pregnancy, for example the occurrence of abortion or miscarriage problems, premature birth, low birth weight (LBW) fetuses, neonates with hypoxia or oxygen deprivation, and even mortality[25]. The occurrence of potential hypoxia in relation to Low Birth Weight infants, the incidence of preeclampsia, congenital abnormalities, spontaneous abortion and placenta previa[26]. The impact of worsening postpartum mothers with a history of asthma is also at risk for babies who were born. There is an increase in complications of infant abnormalities and even mortality .

In previous studies, it was known that the complications and impact caused by asthma in pregnancy were quite significant. In a descriptive cohort study, data were obtained from 1603 pregnant women, of which 2.6% had a suspected history of asthma, one of whom was diagnosed with cardiovascular disease, six others were found to have respiratory complaints other than asthma, and some had abortions at 9 weeks of gestation (Fazel et al., 2018). In total, it is known that 2.1% were diagnosed with asthma with a classification of 38.2% intermittent asthma, 29.4% mild asthma, 23.5% moderate asthma and 8.8% severe asthma.

Pregnant women with uncontrolled asthma at a gestational age ranging from 37-42 weeks can have IUGR (intra-uterine growth retardation) fetuses and low oxygen saturation supply. The presence of respiratory symptoms and wheezing experienced by the mother during her pregnancy may be a factor in exacerbating asthma. If this worsening continues, it can result in infant death[(27)].

Inferred from the preceding discussion, the degree of asthma in pregnant women is influenced by the sex of the fetus. However, there are still deficiencies in the translation of the study's findings, particularly the absence of specific data acquired, so that the influence of fetal sex on the degree of asthma is insufficient. In addition, the only data obtained are secondary data from medical records, necessitating the need for actual evidence and additional supporting data.

Therefore, it is expected that future research will provide an accurate explanation of the relationship between the fetal sex and the degree of asthma in pregnant women, including the hormones that influence it and the inflammatory response elicited, so that preventive measures can be obtained in handling it.

CONCLUSIONS AND RECOMMENDATIONS

Conclusions

Based on the results of the data analysis and discussion regarding the Effect of Fetal Sex with the Degree of Asthma in Pregnant Women during the second and third Trimesters, it can be concluded as follows:

1) Fetal sex has an influence on the degree of asthma in pregnant women with a moderate or sufficient correlation.

2) Most of the sex of the female fetus influences the degree of severe asthma in pregnant women. Meanwhile, pregnant women with male fetuses tend to have intermittent asthma degrees.

Recommendations

It is hoped that further research will be conducted on the high correlation between the two variables. In addition, it is hoped to be able to undertake research on other factors that can influence the degree of asthma in pregnant women, as well as the relationship of fetal hormonal or genetic factors that can trigger an inflammatory response to asthma exacerbations in pregnant women.

REFERENCES

1. Agustina W. Respon imun pada penderita asma selama kehamilan. 2015;3(2):39–46.

2. Putra DP, Bakhtiar A, Amin M. Correlation between coenzyme q10

level long-term steroid inhalation in patients with bronchial asthma. Indian J Forensic Med Toxicol. 2020;14(2):2342–7.

3. Boulet L-P, Reddel HK, Bateman E, Pedersen S, Fitzgerald JM, O'byrne PM. GINA 2019 main report June 2019 wms - Global Initiative for Asthma - GINA [Internet]. Global Intiative for Asthma. 2019 [cited 2021 Dec 1]. Available from: https://ginasthma.org/GINA-2019-main-report-June-2019-wms/

4. Kemenkes RI. Hasil Riset Kesehatan Dasar Tahun 2018. Kementrian Kesehat RI. 2018;53(9):1689–99.

5. Rosalina FA. Digital Repository Universitas Jember - Faktor Predisposisi dan Pencetus Serangan Asma Broncial. Epidemiol Biostat Popul Dep Public Heal Fac Jember Univ [Internet]. 2015;69. Available from: http://repository.unej.ac.id/bitstream/handle/123456789/65672/Ainul Latifah-101810401034.pdf?sequence=1

6. Miftahussurur M, Nusi IA, Graham DY, Yamaoka Y. Helicobacter, hygiene, atopy, and asthma. Front Microbiol. 2017;8(JUN).

7. Pusat Data dan Informasi Kementrian Kesehatan RI. Infodatin-Penderita Asma di Indonesia. Kementeri Kesehat Republik Indones. 2019;

8. Kemenkes RI. Keputusan_Menteri_Kesehatan_RI_Tentang_Pedoman_Pengendalian_Asma 1.pdf. 2018. p. 34.

9. Tantri IN, Saturti TIA. Serangan asma akut derajat sedang pada kehamilan. 2016;1–30.

10. Blais L, Kettani F-Z, Forget A, Beauchesne M-F, Lemière C. Asthma exacerbations during the first trimester of pregnancy and congenital malformations: revisiting the association in a large representative cohort. 2015 [cited 2015 Apr 17]; Available from: http://thorax.bmj.com/

11. SUBIJANTO AA. Genetic diversity of HLA-DR and varion of asthma susceptibility; an overview of Asthma in Pregnancy. Biodiversitas J Biol Divers. 2008;9(3):237–43.

12. Zairina E, Abramson MJ, McDonald CF, Li J, Dharmasiri T, Stewart K, et al. Telehealth to improve asthma control in pregnancy: A randomized controlled trial. Respirol ,Faculty Pharmacy, Airlangga Univ. 2016;21(5):867–74.

13. Enninga EAL, Nevala WK, Creedon DJ, Markovic SN, Holtan SG. Fetal Sex-Based Differences in Maternal Hormones, Angiogenic Factors, and Immune Mediators During Pregnancy and the Postpartum Period. Am J Reprod Immunol. 2015 Mar 1;73(3):251–62.

14. Ngurah Rai I. Prevalensi Asma Eksaserbasi Pada Ibu Hamil Dan Pengaruhnya Terhadap Janin Dan Ibu Di Rsup Sanglah Denpasar. J Intern Med. 2009;10(3).

15. Breton M-C, Beauchesne M-F, Lemiè C, Rey E´, Forget A, Blais L. Risk of perinatal mortality associated with asthma during pregnancy. Thorax [Internet]. 2009 [cited 2021 Dec 1];64:101–6. Available from: http://thorax.bmj.com/http://thorax.bmj.com/http://thorax.bmj.com/

16. Litanto A. Kekambuhan asma pada perempuan dan berbagai faktor yang memengaruhinya. 2021;4(2):79–86.

17. Bidaki R, Karimi M, Mojibyan M, Hadi Nodoshan H, Zare A, Rafiee P, et al. Maternal stress in pregnancy based on Holmes-Rahe questionnaire and umbilical cord IgE. Can J Med. 2011;2(3):76.

18. Pudyastuti, Sri dan TD. Asma Pada Kehamilan: Mekanisme dan Implikasi Klini. J Respirologi Indones. 2020;40(4):251–61.

19. Yudhawati R, Krisdanti DPA. Imunopatogenesis Asma. J Respirasi Fak Kedokt Univ Airlangga. 2019;3(1):26.

20. Laffont S, Blanquart E, Savignac M, Cénac C, Laverny G, Metzger D, et al. Androgen signaling negatively controls group 2 innate lymphoid cells. J Exp Med. 2017;214(6):1581–92.

21. Cephus JY, Stier MT, Fuseini H, Yung JA, Toki S, Bloodworth MH, et al. Testosterone Attenuates Group 2 Innate Lymphoid Cell-Mediated Airway

Inflammation. Cell Rep [Internet]. 2017;21(9):2487–99. Available from: https://doi.org/10.1016/j.celrep.2017.10.110

22. Koper I, Hufnagl K, Ehmann R. Gender aspects and influence of hormones on bronchial asthma – Secondary publication and update. World Allergy Organ J. 2017 Jan 1;10(1):46.

23. Maselli DJ, Adams SG, Peters JI, Levine SM. Management of asthma during pregnancy. Ther Adv Respir Dis. 2013;7(2):87–100.

24. Wang H, Li N, Huang H. Asthma in Pregnancy: Pathophysiology, Diagnosis, Whole-Course Management, and Medication Safety. Vol. 2020, Canadian Respiratory Journal. 2020.

25. Shedd GC, Hays CN. The Pregnant Patient With Asthma: Assessment and Management. J Nurse Pract [Internet]. 2016;12(1):1–6. Available from: http://dx.doi.org/10.1016/j.nurpra.2015.10.019

26. Tata LJ, Lewis SA, McKeever TM, Smith CJP, Doyle P, Smeeth L, et al. Effect of maternal asthma, exacerbations and asthma medication use on congenital malformations in offspring: A UK population-based study. Thorax. 2008;63(11):981–7.

27. Abdullah K, Zhu J, Gershon A, Dell S, To T. Effect of asthma exacerbation during pregnancy in women with asthma: A population-based cohort study. Eur Respir J [Internet]. 2020;55(2). Available from: http://dx.doi.org/10.1183/13993003.01335-2019