



eISSN : 2579-8324 pISSN : 2579-8413

Correspondence Address:

Editorial Room Andalas Obstetrics and Gynecology Journal, 2nd Floor Obstetrics and Gynecology Department,
M. Djamil Central General Hospital Padang, Jl. Perintis Kemerdekaan Padang, West Sumatra 25127

Website:

<http://jurnalobgin.fk.unand.ac.id/>

RESEARCH ARTICLE

The Relationship of Age with TNF- α Levels in Pregnancy and Abortion

Cici Monika^{1,*}, Gusti Revilla², Hudila Rifa Karmia³, Siti Nurhajjah², Rahmani Welan⁴

¹ Student of Faculty of Medicine, Andalas University, Padang, West Sumatra, Indonesia

² Department of Anatomy, Faculty of Medicine, Andalas University, Padang, West Sumatra, Indonesia

³ Department Obstetrics and Gynecology, Faculty of Medicine, Andalas University, Dr. M. Djamil Central General Hospital, Padang, West Sumatra, Indonesia

⁴ Department of Nutrition Sciences, Faculty of Medicine, Andalas University, Padang, West Sumatra, Indonesia

Corresponding Author: Cici Monika, cicimonika56@gmail.com

Submitted: February 15, 2024;

Accepted: January 20, 2025;

Published: February 02, 2026

DOI: <https://doi.org/10.25077/aoj.10.1.97-107.2026>

Abstract

Introduction: Tumor Necrosis Factor Alpha (TNF- α) plays a crucial role in the early control of abortion. This increase can be influenced by age. The purpose of this study was to analyze the relationship between age and TNF- α in both normal pregnancies and abortion.

Method: The type of research is analytic with a cross sectional design, collecting samples using total sampling technique, resulting in 36 patients who were subsequently assessed for TNF- α levels at the Biomedical Laboratory of Andalas University. The source of research data is secondary data. Data analysis involved the Spearman correlation test, Independent T-test, and Mann-Whitney test.

Result: The average gestational age was younger, the average maternal age was older, and the average TNF- α levels were higher in abortion compared to normal pregnancy. The BMI of all patients was normal. There is a significant difference between age in normal pregnancy and abortion ($p = 0.001$), there is no relationship between age and TNF- α levels in normal pregnancy ($p = 0.429$), there is no relationship between age and TNF- α levels in abortion ($p = 0.862$), and there is no difference in TNF- α levels between normal pregnancy and abortion ($p = 0.248$).

Conclusion: there is a significant difference between age in normal pregnancy and abortion.

Keywords: Age, TNF- α , abortion

INTRODUCTION

Abortion occurs when the fetus or young child is expelled or exits the uterus in less than 20 weeks of pregnancy or with a birth weight of less than 500 grams.⁵ Currently abortion is one of the reproductive issues that is widely discussed around the world. The abortion survey conducted by the Centers for Disease Control (CDC) to document the number and characteristics of pregnant women who experienced abortion and the number of abortion-related deaths in the United States in 2011-2020, found that a 2% increase was observed in the total abortion ratio.⁶ According to the World Health Organization (WHO) the maternal mortality rate due to abortion still reaches 15-50%. WHO estimates that there are about 4,2 million cases of abortion each year in the Southeast Asia region, with an estimated 2,3 million cases of abortion in Indonesia each year.⁷

According to information obtained from the 2018 Indonesian Demographic and Health Survey (IDHS), MMR in Indonesia recorded 140 cases (3,5%) of maternal deaths related to abortion cases from a total of 148,548 deliveries, then in 2019 showed an increase of 210 (5,8%) cases from 156,622 deliveries, and continued to increase in 2020, namely 305 (2,62%) cases from 984,432 deliveries.⁸ The MMR in West Sumatra Province over the past three years has fluctuated, namely 111 people in 2018, 116 people in 2019, and 125 people in 2020.⁹

Abortion can be caused by the maternal immune system. Based on the results of previous research, the maternal immune system changes during pregnancy, causing a tolerance response to fetal tissue.¹⁰ Maternal immune responses during pregnancy increase more in antibody-mediated immunity than cell-mediated immunity. Elevated Th2-type cytokines will make pregnancy an anti-inflammatory state that will be safe for the fetus. The immune system can also cause abortion as a result of an imbalance of Th1 and Th2. When the secretion of Th1 proinflammatory cytokines such as TNF- α increases, it will cause damage to the placenta and result in abortion.¹¹

Findings from previous studies indicate that the average concentration of TNF- α in the group who experienced abortus imminent was $3,75 \pm 1,03$ ng/ml, while in normal pregnancy <12 weeks reached $3,03 \pm 0,88$ ng/ml with a p value of 0,03.¹² From the data above, it can be seen that patients with normal pregnancy have lower levels of TNF- α than patients with abortus.¹²

Increased TNF- α levels can be influenced by age.¹³ In a previous study, it was found that the sample group aged 16-17 years showed an average TNF- α concentration of 60,30 pg/ml, while the group aged 18-19 years had an average TNF- α concentration of 67,5 pg/ml.¹⁴ Age besides affecting TNF- α levels also has an impact on the occurrence of abortion because it affects a person's biological condition, physical, mental, emotional, psychological, and social readiness. Due to the lack of studies that discuss this matter, the authors are interested in conducting research related to the relationship between age and TNF- α levels in normal pregnancy and abortion.

METHOD

The type of research is analytic. The research design is cross sectional. Research conducted by previous researchers in January 2022 took place at the Biomedical Laboratory of Andalas

University for examination of TNF- α levels. The time for preparing the proposal began in December 2022-December 2023. The data source of this research is secondary data. This study has received ethical approval from the Ethics Committee of the Faculty of Medicine, Andalas University, with ethical clearance number 490/UN.16.2/KEP-FK/2023.

The inclusion criteria in this study were women with normal pregnancy of less than 12 weeks of gestation based on a clear first day of the last menstrual period (HPHT) or supported by ultrasound data, as well as women with spontaneous abortion with gestational age of less than 12 weeks based on a clear LMP or ultrasound examination. The exclusion criteria included abortion caused by congenital abnormalities identified through ultrasound examination or clear abortion outcomes, pregnant women who were taking immunosuppressant drugs, particularly TNF- α inhibitor agents such as etanercept, certolizumab, infliximab, adalimumab, and golimumab as identified from medical history, and pregnant women with obesity defined as a body mass index (BMI) ≥ 25 kg/m².

The sampling technique that will be used in this study is total sampling which is then selected according to the inclusion and exclusion criteria of the study so that the total sample is 36 patients. The independent variable in this study was maternal age and the dependent variable was TNF- α levels in normal pregnancy and abortion patients.

Univariate analysis aims to provide an overview of each variable separately so that the analysis of each variable is obtained with the results in tabular form. Bivariate analysis began with normality analysis using the Shapiro-Wilk test (data <50 samples). The statistical test used to see the relationship between age and TNF- α levels in normal pregnancy and abortion used the correlation test. If the data is normally distributed ($p \geq 0,05$) then it will continue to use the Pearson correlation test, but if the data is not normally distributed ($p < 0,05$) then a non-parametric analysis is performed namely the Spearman correlation test. The type of statistical test to see the difference in age and TNF- α levels in normal pregnancy and abortion is also carried out according to the results of the normality test if the data is normally distributed ($p \geq 0,05$) it will be continued using the T-Independent statistical test. However, if the data is not normally distributed ($p < 0,05$) then a non-parametric analysis is performed, namely Mann-Whitney.

RESULT

Respondent Characteristics

Table 1. Characteristics of Patient

Characteristics		Normal pregnancy (n=18)		Abortion (n=18)	
		Mean $\pm$ SD	CI 95%	Mean $\pm$ SD	CI 95%
Gestational age (weeks)		9,22 $\pm$ 1,80	8,33 - 10,12	7,61 $\pm$ 1,91	6,66 – 8,56
BMI		21,12 $\pm$ 2,05	20,19 – 22,23	21,46 $\pm$ 2,23	20,35 – 22,57

Table 1 shows that the mean gestational age in the normal pregnancy group was at 9,22

weeks and for abortion at 7,61 weeks. In respondents with normal pregnancy, the average BMI is 21 kg/m² (95% CI: 20,19-22,23), this is the same as the BMI in the abortion group, namely 21 kg/m² (95% CI: 20,35-22,57).

Table 2. Maternal Age

Maternal Age	n	Mean ± SD	CI 95%	Min	Max
Normal Pregnancy	18	27,61 ± 4,42	25,41 – 29,81	21	37
Abortion	18	33,50 ± 4,48	31,07 – 35,93	25	43
Total	36	30,56 ± 5,47	28,70 – 32,41	21	43

Based on table 2, it can be seen that the average age of mothers in normal pregnancy is 27,61 years, and in abortion, in the abortion group the average age of mothers is 33,50 years.

Table 3. Tumor Necrosis Factor Alpha (TNF-α) Levels

TNF-α Levels	n	Mean ± SD	CI 95%	Min	Max
Normal Pregnancy	18	173,73 ± 236,82	55,96 – 291,50	26,64	831,43
Abortion	18	514,02 ± 692,83	169,48 – 858,56	23,59	1854,33
Total	36	343,88 ± 538,67	161,62 – 526,14	23,59	1854,33

TNF-α levels are considered normal if they are in the range of 10-100 pg/ml, moderate if they are in the range of 100-500 pg/ml, and high if they exceed 500 pg/ml. Table 3 shows that in normal pregnancy, the lowest TNF-α level is 26,64 pg/ml and the highest is 831,43 pg/ml.

Relationship of Age with TNF-α Levels in Normal Pregnancy and Abortion

Table 4. Normality Test Results of Maternal Age and TNF-α Using Shapiro-Wilk

Variables	P-Value		Normality Test Results Normal/Abnormal
	Normal	Abortion	
TNF-α	0,00	0,00	Abnormal (<0,05)
Maternal Age	0,648	0,944	Normal (>0,05)

Based on the normality test values in table 4, the Spearman correlation test was performed to see the relationship between age and TNF-α levels in normal pregnancy and abortion. An Independent T-test was performed to determine the difference in age in normal pregnancy and abortion, and the Mann-Whitney test to determine the difference in TNF-α levels in normal pregnancy and abortion.

Relationship between Age and TNF- α Levels in Normal Pregnancy

Table 5. Relationship between Age and TNF- α Levels in Normal Pregnancy

Variables	TNF- α	
	r	P Value
Maternal Age	-0,199	0,429

Table 5 above shows that the results of the significance test using the Spearman correlation test obtained a p value of 0,429 ($p > 0,05$) which means that there is no relationship between age and TNF- α levels in normal pregnancy.

Relationship between Age and TNF- α Levels in Abortion

Table 6. Relationship between Age and TNF- α Levels in Abortion

Variables	TNF- α	
	r	P Value
Maternal Age	-0,044	0,862

Table 6 above shows that the results of the significance test using the Spearman correlation test obtained a p value of 0,862 ($p > 0,05$) which means that there is no relationship between age and TNF- α levels in abortion.

Age Differences in Normal Pregnancy and Abortion

Table 7. Independent T-test

Variables	Group				P Value
	Normal Pregnancy		Abortion		
	n	Mean ± SD	n	Mean ± SD	
Maternal Age	18	27,61 ± 4,42	18	33,50 ± 4,87	0,001

The results of table 7 above obtained a p value of 0,001, meaning that there is a significant difference between the age of the mother in normal pregnancy and abortion pregnancy.

Differences in TNF- α Levels in Normal Pregnancy and Abortion

Table 8. Mann-Whitney Test

Variables	Group						P Value
	Normal Pregnancy			Abortion			
	n	Median (min-max)		n	Median (min-max)		
TNF-α	18	93,35	(26,64-831,43)	18	172,85	(23,59-1854,33)	0,248

In table 8 above, it can be seen that the results of TNF- α levels in abortion are higher at 172,85 pg/ml compared to levels in normal pregnancy which amounted to 93,35 pg/ml. The results of the significance test using Mann-Whitney obtained a p value of 0,248 which means that although

TNF- α levels in abortion are higher, there is no significant difference.

DISCUSSION

Respondent Characteristics

Table 1 shows that the mean gestational age in the normal pregnancy group was at 9,22 weeks and for abortion at 7,61 weeks. More than 80% of abortions occur at 12 weeks gestation, and at least half of these cases are caused by chromosomal abnormalities. Half of the abortions caused by cytogenic abnormalities in the first trimester manifest as autosomal trisomies. This increased incidence of trisomy correlates with increased maternal age.¹¹

In respondents with normal pregnancy, the average BMI is in the normal classification, namely 21 kg/m² (95% CI: 20,19-22,23), this is the same as the BMI in the abortion group, namely 21 kg/m² (95% CI: 20,35-22,57). This BMI is later needed to ensure that TNF- α levels in respondents are indeed influenced by age, not because of obesity (data exclusion). Several studies have been conducted to explore the correlation between BMI and the potential for spontaneous abortion. Obesity is often associated with unfavorable outcomes during pregnancy, which can include negative impacts on the embryo, endometrium, or both.¹² Nutritional deficiencies have also been identified as a risk factor for abortion. Mothers with a BMI below normal have a higher risk of spontaneous abortion compared to mothers with a normal BMI.¹³

Based on table 2, it can be seen that the average age of mothers in normal pregnancy is 27,61 years, and in abortion, in the abortion group the average age of mothers is 33,50 years. It can be concluded that the average age of mothers in abortion is older than that of normal pregnancy. This finding is in line with the Albahlol study in 2020, which states that the average age of research participants in normal pregnancy was found to be <30 years (28,51), while in the abortion group, it was more than 30 years (31,2).¹⁴ This age increases the risk of the possibility of abortion.

TNF- α levels are categorized as normal when ranging from 10 to 100 pg/ml, moderate when ranging from 100 to 500 pg/ml, and high when exceeding 500 pg/ml.¹⁵ Table 3 shows that in the normal pregnancy group, TNF- α levels varied widely, with minimum values within the normal range and maximum values reaching the high category. This indicates that elevated TNF- α levels can also be found in normal pregnancies, suggesting that TNF- α expression is influenced by multiple biological and environmental factors rather than pregnancy outcome alone.

In the abortion group, TNF- α levels also showed considerable variability, with mean values in the high category but minimum values still within the normal range. This finding demonstrates that not all abortion cases are accompanied by elevated TNF- α levels, indicating that abortion is a multifactorial condition in which inflammatory mechanisms represent only one of several contributing pathways.

From a biological perspective, TNF- α plays a pivotal role in regulating trophoblast proliferation, spiral artery remodeling, and maternal–fetal immune tolerance. Excessive TNF- α production can inhibit trophoblast invasion, impair placental vascular development, and induce

apoptosis in trophoblastic cells, thereby disrupting implantation and placentation processes and potentially leading to pregnancy loss. However, the absence of consistently elevated TNF- α levels in abortion cases observed in this study suggests that inflammatory imbalance alone may not fully explain the pathogenesis of abortion.

The variability of TNF- α levels observed in both normal pregnancy and abortion may be explained by the influence of other factors, including genetic predisposition, metabolic conditions, infections, stress, hormonal regulation, and environmental exposures. Although obesity and immunosuppressant drug use were controlled in this study, other potential confounding factors were not assessed, which may have affected TNF- α expression and contributed to the observed results. Furthermore, several non-inflammatory risk factors have been reported to contribute to abortion, such as advanced maternal age, extremes of reproductive age, nutritional status, parity, interpregnancy interval, previous history of abortion, psychosocial stress, and lifestyle factors. Therefore, the findings of this study support the concept that abortion results from a complex interaction between immunological, biological, and socio-demographic factors rather than a single biomarker.

Overall, these results highlight the heterogeneous role of TNF- α in early pregnancy and abortion. While TNF- α may contribute to the inflammatory environment associated with pregnancy loss, its role appears to be context-dependent and influenced by multiple interacting factors. Future studies with larger sample sizes and comprehensive assessment of immunological, hormonal, and genetic parameters are required to better elucidate the role of TNF- α in early pregnancy outcomes.¹⁶

Relationship of Age with TNF- α Levels in Normal Pregnancy and Abortion

Based on the normality test values in table 4, the Spearman correlation test was performed to see the relationship between age and TNF- α levels in normal pregnancy and abortion. An Independent T-test was performed to determine the difference in age in normal pregnancy and abortion, and the Mann-Whitney test to determine the difference in TNF- α levels in normal pregnancy and abortion.

Relationship between Age and TNF- α Levels in Normal Pregnancy

Table 5 above shows that the results of the significance test using the Spearman correlation test obtained a p value of 0,429 ($p > 0,05$) which means that there is no relationship between age and TNF- α levels in normal pregnancy. This can happen because age is not the only thing that can affect TNF- α levels. TNF- α can be caused by other factors such as drugs, obesity, genes, infections in pregnant women, diabetes mellitus, vascular disorders such as atherosclerosis, stress, and exposure to pollution. In this study, samples taking drugs that can affect TNF- α levels and obese patients were excluded from the study, but other factors such as genes, maternal diseases, stress, and exposure to air pollution were not further analyzed.

From previous studies, there are differences in research results, such as that conducted by Gupta in 2003, where a significant correlation was found between age and TNF- α levels.¹⁷ In Gupta's

study, the samples used were people aged 66-88 years as many as 10 samples. In this study, no significant correlation was detected between age and TNF- α levels, which could be due to the young age of the sample, which is under 60 years old.

Relationship between Age and TNF- α Levels in Abortion

Table 6 above shows that the results of the significance test using the Spearman correlation test obtained a p value of 0,862 ($p > 0,05$) which means that there is no relationship between age and TNF- α levels in abortion. This contradicts the findings of Bruunsgaard's research in 2000 which found TNF- α levels to have a significant relationship with age. The study was conducted on a sample aged 81 years as an elderly group. Bruunsgaard's study was conducted on atherosclerosis patients, which means that other things affect TNF- α levels, namely vascular factors.¹⁸

Age Differences in Normal Pregnancy and Abortion

The results of table 7 above obtained a p value of 0,001, meaning that there is a significant difference between the age of the mother in normal pregnancy and abortion pregnancy. This study follows Purwaningrum's research in 2017 which obtained a p value of 0,014 ($p < 0,05$), meaning that there is a significant relationship between maternal age and the incidence of abortion.¹⁶ This proves that age is an important risk factor for abortion. Mothers who become pregnant at a high risk age of <20 years or >35 years are more likely to have an abortion than those aged 20-35 years. This is related to pregnancy at the age of <20 years biologically, where the reproductive organs are not yet fully functional and are not ready to receive the results of conception. In addition, the strength of the perineal muscles and abdominal muscles has not yet worked optimally.¹⁶ On the other hand, in pregnancies aged ≥ 35 years, the body experiences a decrease in function. Increased maternal age contributes to inadequate progesterone production, causing a lack of progesterone production by the corpus luteum to support the implantation process.¹⁶

Another study conducted by Asnur in 2022 found that there was a significant correlation between maternal age and the incidence of abortion at Dr. M. Djamil Padang Hospital in 2018-2020 with a p value of 0,012.¹⁹ In this study it was found that age significantly affects biological conditions, such as ovarian sensitivity to gonadotropins, ovum quality, and an increased risk of chromosomal abnormalities. Age also affects the function of the placenta and hormones in the body.¹⁹

Not in line with the study conducted by Qubro in 2018, this study showing that the results of the analysis of maternal age and the incidence of abortion at Abdul Moeloek Hospital Bandar Lampung had a p value of 0,128 ($p > 0,05$). This means that there is no significant relationship between the age of the mother during pregnancy and the incidence of abortion.²⁰ In contrast, Yange's research in 2015 found that there was no significant correlation between age and abortion indicated by a p value of 0,997 ($p > 0,05$).²¹ The cause is the limited number of samples investigated, so the results obtained may be by the percentage but do not show a significant relationship when tested statistically.²¹

Differences in TNF- α Levels in Normal Pregnancy and Abortion

In table 8 above, it can be seen that the results of TNF- α levels in abortion are higher at

172,85 pg/ml compared to levels in normal pregnancy which amounted to 93,35 pg/ml. The results of the significance test using Mann-Whitney obtained a p value of 0,248 which means that although TNF- α levels in abortion are higher, there is no significant difference. This is in accordance with a study conducted by Kuar in 2011, namely, there is no significant relationship between TNF- α with normal pregnancy and abortion.²²

This study is in line with a study conducted by Bombell in 2008 which noted that there was no significant correlation between TNF- α and the occurrence of abortion.²³ The same study was also conducted by Progoshin in 2004 with the result that there was no correlation between the level of TNF- α in the control group, namely normal pregnancy, and the level of TNF- α in the group that experienced abortion.²⁴ This study is in line with research by Babbage, et al., in 2001 which found that there was no correlation between TNF- α and the occurrence of abortion.²⁵

This study was by Pietrowski, et al., in 2004 who researched the TNF- α -308 and -863 genes and found that TNF- α polymorphisms were not associated with the incidence of recurrent abortion in Caucasian women.²⁶ The study was also in accordance with Baxter, et al., in 2002 who found that there was no significant correlation between TNF- α levels and the incidence of recurrent abortion.²⁷

In contrast to the results of a study conducted by Putra in 2018, the average TNF- α level in abortion cases ($767,57 \pm 347,94$ pg/mL) was shown to be higher than normal pregnancy ($446,32 \pm 365,51$ pg/mL), with a p value of 0,006 ($p < 0,05$). Suganda's research in 2019 also showed that there was indeed a correlation between TNF- α levels and the occurrence of abortion because TNF- α has a role in inhibiting trophoblast development, inhibiting the invasion of the spiral artery into the decidua, and damaging blood vessels in the decidua, this causes disturbances in the implantation process and contributes to the occurrence of abortion.¹³ In Adhi's research in 2014, it was also found that the average serum TNF- α concentration in the abortion group ($3,83 \pm 1,52$ ng/ml) and the normal pregnancy group ($2,76 \pm 1,49$ ng/ml) had a p value of 0,032 ($p < 0,05$). This finding indicates a significant correlation between TNF- α levels and the incidence of abortion.²⁸ These findings are consistent with previous studies showing that pregnancy outcomes are influenced not only by immunological mechanisms but also by maternal and obstetric factors, supporting the multifactorial nature of abortion.²⁹

CONCLUSION

This study found that maternal age was significantly higher in women experiencing abortion compared to those with normal pregnancy. However, no significant correlation was observed between maternal age and TNF- α levels in either normal pregnancy or abortion. In addition, there was no significant difference in TNF- α levels between the two groups. These findings indicate that maternal age is an important factor associated with abortion, but its effect does not appear to be mediated through TNF- α levels. Therefore, TNF- α alone may not adequately explain the occurrence of abortion, suggesting that other biological and non-biological factors may contribute to early pregnancy loss.

REFERENCES

1. Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, et al. *Obstetri Williams*. 24th ed. Yeomans ERJ, editor. Jakarta: EGC; 2014. p. 4–21.
2. Walensky RP, Bunnell R, Layden J, Kent CK, Gottardy AJ, Leahy MA, et al. Abortion surveillance—United States 2020. *MMWR Surveill Summ*. 2022;71(10):1–29. doi:10.15585/mmwr.ss7110a1.
3. Sari RDP, Rahmanisa S, Citra E. Hubungan beban kerja mental terhadap kejadian abortus pada pekerja buruh pabrik di PT. Great Giant Pineapple. JK UNILA. 2019;3(1):117–22.
4. Farawansya K, Lestari PD, Riski M. Faktor-faktor yang berhubungan dengan kejadian abortus di Rumah Sakit Muhammadiyah Palembang tahun 2020. *JIUBJ*. 2022;22(1):621–28.
5. Dinas Kesehatan Provinsi Sumatra Barat. Laporan Akuntabilitas Kinerja Instansi Pemerintah (LAKIP) SATKER 03. Padang; 2020.
6. Prawirohardjo S. *Ilmu kebidanan*. 4th ed. Saifuddin AB, editor. Jakarta: Bina Pustaka Sarwono Prawirohardjo; 2010. p. 97–221.
7. Balasundaram P, Farhana A. *Immunology at the maternal-fetal interface*. Treasure Island (FL): StatPearls Publishing; 2022.
8. Supit IA, Pangemanan DHC, Marunduh SR. Profil Tumor Necrosis Factor (TNF- α) berdasarkan Indeks Massa Tubuh (IMT) pada mahasiswa Fakultas Kedokteran Unsrat angkatan 2014. *eBiomedik*. 2015;3(2):640–3.
9. Suganda Y. Perbedaan kadar Tumor Necrosis Factor Alpha (TNF- α) dan Progesterone-Induced Blocking Factor (PIBF) serum pada usia kehamilan kurang 12 minggu dengan abortus iminens [Tesis]. Universitas Andalas: Padang, Indonesia; 2019.
10. Almujaheed A, Muhammad S, Asterina. Relationship between risk factors and the incidence of gestational trophoblastic neoplasia at RSUP Dr. M. Djamil Padang year 2019–2021. *Andalas Obstetrics and Gynecology Journal*. 2024;8(2):746–53. doi:10.25077/aoj.8.2.746-753.2024.
11. Fitriyanti R. Faktor-faktor yang berhubungan dengan kejadian abortus di RSUD KRT Setjonegoro Wonosobo Tahun 2020 [Skripsi]. Poltekkes Kemenkes Semarang: Semarang, Indonesia; 2021.
12. Hadi R, Akbar IB, Budiman B. Hubungan indeks massa tubuh terhadap kejadian abortus spontan di RSUP Dr. Hasan Sadikin Bandung pada tahun 2017–2018. *Prosiding Pendidikan Dokter*. 2020;6(1):330–4.
13. Helgstrand S, Andersen AMN. Maternal underweight and the risk of spontaneous abortion. *Acta Obstet Gynecol Scand*. 2005;84(12):1197–201. doi:10.1111/j.0001-6349.2005.00833.x.
14. Albahlol IA, Almaeen AH, Alduraywish AA, Dar UF, El-Metwally TH. Vitamin D status and pregnancy complications: serum 1,25-dihydroxyvitamin D and its ratio to 25-hydroxyvitamin D are superior biomarkers than 25-hydroxyvitamin D. *Int J Med Sci*. 2020;17(18):3039–48. doi:10.7150/ijms.48963.
15. Hidayat A, Kartika AI, Fitria MS. Perbandingan kadar Tumor Necrosis Factor Alpha (TNF- α) pada tukang parkir 1–3 tahun dan >3 tahun dengan metode ELISA. *JAMBS*. 2021;8(2):71–6.
16. Purwaningrum ED, Fibriana AI. Faktor risiko kejadian abortus spontan. *HIGEIA*. 2017;1(3):84–94.
17. Gupta S, Chiplunkar S, Kim C, Yel L, Gollapudi S. Effect of age on molecular signaling of TNF- α -induced apoptosis in human lymphocytes. *Mech Ageing Dev*. 2003;124(4):503–9.

doi:10.1016/S0047-6374(03)00029-5.

18. Bruunsgaard H, Skinhøj P, Pedersen AN, Schroll M, Pedersen BK. Ageing, Tumour Necrosis Factor-Alpha (TNF- α) and atherosclerosis. *Clin Exp Immunol*. 2000;121(2):255–60. doi:10.1046/j.1365-2249.2000.01298.x.
19. Qubro DZ, Sari RDP, Soleha TU. Hubungan antara usia dan paritas ibu dengan kejadian abortus di Rumah Sakit Abdul Moeloek Bandar Lampung. *Majority*. 2018;7(3):128–31.
20. Yange G. Hubungan abortus inkomplit dengan faktor risiko pada ibu hamil di Rumah Sakit Pindad Bandung periode 2013–2014 [Skripsi]. Universitas Kristen Maranatha: Bandung, Indonesia; 2015.
21. Kaur A, Kaur A. Recurrent pregnancy loss: TNF- α and IL-10 polymorphisms. *J Hum Reprod Sci*. 2011;4(2):91–4. doi:10.4103/0974-1208.86091.
22. Bombell S, McGuire W. Cytokine polymorphisms in women with recurrent pregnancy loss: meta-analysis. *Aust N Z J Obstet Gynaecol*. 2008;48(2):147–54. doi:10.1111/j.1479-828X.2008.00850.x.
23. Prigoshin N, Tambutti M, Larriba J, Gogorza S, Testa R. Cytokine gene polymorphisms in recurrent pregnancy loss of unknown cause. *Am J Reprod Immunol*. 2004;52(1):36–41. doi:10.1111/j.1600-0897.2004.00179.x.
24. Babbage SJ, Arkwright PD, Vince GS, Perrey C, Pravica V, Quenby S, et al. Cytokine promoter gene polymorphisms and idiopathic recurrent pregnancy loss. *J Reprod Immunol*. 2001;51(1):21–7. doi:10.1016/S0165-0378(01)00078-2.
25. Pietrowski D, Bettendorf H, Keck C, Bürkle B, Unfried G, Riener EK, et al. Lack of association of TNF- α gene polymorphisms and recurrent pregnancy loss in Caucasian women. *J Reprod Immunol*. 2004;61(1):51–8. doi:10.1016/j.jri.2003.09.004.
26. Baxter N, Sumiya M, Cheng S, Erlich H, Regan L, Simons A, et al. Recurrent miscarriage and variant alleles of mannose binding lectin, tumor necrosis factor and lymphotoxin α genes. *Clin Exp Immunol*. 2002;126(3):529–34. doi:10.1046/j.1365-2249.2001.01661.x.
27. Putra RS. Perbedaan kadar Human Leukosit Antigen-G (HLA-G) dan Tumor Nekrosis Faktor- α (TNF- α) pada abortus spontan dan kehamilan normal [Tesis]. Universitas Andalas: Padang, Indonesia; 2018.
28. Adhi KC. Kadar Human Leukocyte Antigen-G (HLA-G) dan Tumor Necrosis Factor Alpha (TNF- α) serum ibu pada abortus dan kehamilan normal [Tesis]. Universitas Sebelas Maret: Surakarta, Indonesia; 2014.
29. Syukri MH, Desmawati D. Demographic and obstetric determinants of cesarean section in RSUP Dr. M. Djamil Padang in 2019. *Andalas Obstetrics and Gynecology Journal*. 2023;7(2):405–10. doi:10.25077/aoj.7.2.405-410.2023.