

# Mean Differences of TNF- $\alpha$ and PIBF Levels in < 12th Gestational Weeks Pregnant Women with Imminent Abortion

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**Abstract—Background:** The aim of the study mean difference of TNF- $\alpha$  and PIBF levels in less than 12th gestational weeks pregnant women with imminent abortion. **Methods:** The study was conducted using a cross sectional study. The study was conducted at Bhayangkara Hospital, dr Reksodiwiryo Hospital, Ibnu Sina Hospital and dr Rasidin Hospital, Padang City, West Sumatera Province, Indonesia from December 2017-December 2018. The population in this study were all patient with imminent abortion and normal pregnancy with sample size 36 people. Sampling technique with consecutive sampling. TNF-  $\alpha$  and PIBF measurement used ELISA test. Hypothesis test used independent sample T test. A two-tailed *P*-value of <0.05 was considered statistically significant. **Results:** The results of the study known mean TNF- $\alpha$  level in imminent abortion ( $3.75 \pm 1.03$  ng / ml) and at <12th gestational weeks ( $3.03 \pm 0.88$  ng / ml). The mean PIBF in imminent abortion ( $33.92 \pm 9.88$  ng / ml) and at <12th gestational weeks ( $43.41 \pm 13.52$  ng / ml). There were mean difference of TNF- $\alpha$  and PIBF levels in less than 12th gestational weeks pregnant women with imminent abortion ( $p < 0.05$ ). **Conclusion:** This analysis confirmed there were mean difference of TNF- $\alpha$  and PIBF levels in less than 12th gestational weeks pregnant women with imminent abortion.

**Index Terms—**TNF- $\alpha$ , PIBF, imminent abortion

## I. INTRODUCTION

Abortion is one of the problems in the world that affects the health, pain and death of pregnant women. Based on data from World Health Organization (WHO) states one in four pregnancies ends in abortion. The estimated incidence of abortion recorded by WHO in 2012 is 40-50 million, as is the case with 125,000 abortions per day [1].

The results of the Abortion Incidence and Service Availability study in United States in 2016 stated that the rate of abortion had declined significantly since 1990 in developed countries but this was not the case in developing countries [2].

Indonesia as one of the developing countries is noted to have an incidence of abortion of 10% -15% of six million pregnancies each year or around 600-900 thousand. Abortion if it does not end with fetal death, then this pregnancy will be at risk for the occurrence of preterm labor and low birth weight [3,4].

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The etiology of abortion is very diverse, such as genetic, anatomical, endocrine, immunological, infectious, thrombophilic and idiopathic. Some of these immunological etiologies can be caused by destructive maternal immune responses to the fetus. Immunological factors can cause abortion through autoimmune mechanisms; namely immunity to oneself and alloimmun; that is immunity to other people. Based on alloimmune theory, a pregnancy in order to succeed requires a blocking factor that can inhibit the rejection of the maternal immune system to paternal antigens [6,7].

The mechanism of action of immune abortion associated with progesterone-induced blocking factor (PIBF) has the hormone progesterone which has the role of creating an adequate immune environment during early pregnancy. PIBF is a mediator produced by lymphocytes of pregnant women who have been sensitized by progesterone. This mediator will cause tolerance to paternal antigens. Tolerance to pregnancy occurs by suppressing the production of Th-1 cytokines and triggering the activation of pro-inflammatory cytokines in this case Tumor necrosis factor alpha (TNF- $\alpha$ ) which is one of the proinflammatory cytokines that can trigger increased expression of adhesion molecules, and triggering cytotoxic activity in NK-cells associated with the occurrence of trophoblast apoptosis, an increase in TNF- $\alpha$  itself will inhibit trophoblast cell proliferation in vitro which is the cause of abortion. In addition to other pro-inflammatory cytokines other than TNF- $\alpha$ , IL-2 which are cytotoxic to pregnancy, increase protective asymmetric antibody production and by suppressing natural killer cell activity (NK), NK cell activation will trigger activation of lymphokine killer cells that causes imminent abortion [8,9].

The aim of the study mean difference of TNF- $\alpha$  and PIBF levels in less than 12th gestational weeks pregnant women with imminent abortion.

## II. MATERIALS AND METHODS

### A. Study Design and Research Sample

The study was conducted at Bhayangkara Hospital, dr Reksodiwiryo Hospital, Ibnu Sina Hospital and dr Rasidin Hospital, Padang City, West Sumatera Province, Indonesia from December 2017-December 2018. The population in this study were all patient with imminent abortion and normal pregnancy with sample size 36 people. Sampling technique with consecutive sampling.

B. Operational Definitions

The variables of this study included independent variable is TNF- $\alpha$  and PIBF levels and dependent variable are imminent abortion and normal pregnancy.

C. Data Collection Technique

This study was approved by the Ethical Committee of Medical Faculty, Universitas Andalas with registration number 472/KEP/FK/2018. The measurement of TNF- $\alpha$  and PIBF used Enzyme -Linked Immunosorbent Assays (ELISA).

D. Data Analysis

The quantitative variables were recorded as Mean $\pm$ SD, median and percentage. Test the normality of data by shapiro wilk test and hypothesis test used independent sample T test. A two-tailed P-value of <0.05 was considered statistically Data were analyzed using the SPSS version 21.0.

III. RESULTS

Characteristics of respondents (Table 1).

**Table 1:** Characteristics of respondents

Characteristics	Imminens Abortion (Mean $\pm$ SD)	< 12th gestational weeks pregnant women (Mean $\pm$ SD)	p value
Age (years)	26.94 $\pm$ 6.76	28.83 $\pm$ 6.08	0.384
Parity	9.61 $\pm$ 2.20	9.39 $\pm$ 1.42	0.382

Table 1 showed there were not mean difference of age and parity between imminens abortion and < 12th gestational weeks pregnant women (p>0.05).

**Table 2:** Mean difference of TNF- $\alpha$  and PIBF levels in <12th gestational weeks pregnant women with imminent abortion

Variables	Imminens Abortion (Mean $\pm$ SD)	< 12th gestational weeks pregnant women (Mean $\pm$ SD)	p value
TNF- $\alpha$ (ng/ml)	3.75 $\pm$ 1.03	3.03 $\pm$ 0.88	0.032
PIBF (ng/ml)	33.92 $\pm$ 9.88	43.41 $\pm$ 13.52	0.002

Table 2 showed mean TNF- $\alpha$  level in imminent abortion (3.75  $\pm$  1.03 ng / ml) and at <12th gestational weeks (3.03  $\pm$  0.88 ng / ml). The mean PIBF in imminent abortion (33.92  $\pm$  9.88 ng / ml) and at at <12th gestational weeks (43.41  $\pm$  13.52 ng / ml). There were mean difference of TNF- $\alpha$  and PIBF levels in less than 12th gestational weeks pregnant women with imminent abortion (p<0.05).

IV. DISCUSSION

This analysis confirmed there were mean difference of TNF- $\alpha$  and PIBF levels in less than 12th gestational weeks pregnant women with imminent abortion.

Previous study known there was relationship between levels of TNF- $\alpha$  and PIBF in abortion, where there was an inverse relationship that is an increase in TNF- $\alpha$  levels and a decrease in PIBF which triggers iminence abortion. Another study who stated that TNF- $\alpha$  levels in imminent abortion (3.83 $\pm$ 1.00 pg/ml) were higher than those of normal pregnant women (2.72 $\pm$ 0.42 pg/ml). Other than that it was found that the mean TNF- $\alpha$  level in women with imminent abortion who became abortion was 2.694 $\pm$ 1.1237 pg/ml and the mean TNF- $\alpha$  level in women with imminent abortion who continued their pregnancy was 1.649 $\pm$ 0.5848 pg/ml. The mean serum TNF- $\alpha$  in the imminent abortion patients with prognostic abortion has significantly higher levels than patients with good prognostics [10-12].

Hudic et al. in his study involving 20 normal pregnant women and 30 women with imminent abortion at 6-24 weeks' gestation, it was found that PIBF levels in the serum of women with imminent abortion (214.4 $\pm$ 120.6 ng/ml) lower than normal pregnant women (357.0 $\pm$ 159.9 ng/ml). Apart from that PIBF levels in urine, results were also obtained (19.5 $\pm$  12.9 ng/ml in imminent abortion; 45.3 $\pm$ 33.7 ng/ ml in normal pregnancies [10].

The mechanism of action of immune abortion associated with progesterone-induced blocking factor (PIBF) has the hormone progesterone which has the role of creating an adequate immune environment during early pregnancy. PIBF is a mediator produced by lymphocytes of pregnant women who have been sensitized by progesterone. This mediator will cause tolerance to paternal antigens. Tolerance to pregnancy occurs by suppressing the production of Th-1 cytokines and triggering the activation of pro-inflammatory cytokines in this case Tumor necrosis factor alpha (TNF- $\alpha$ ) which is one of the proinflammatory cytokines that can trigger increased expression of adhesion molecules, and triggering cytotoxic activity in NK-cells associated with the occurrence of trophoblast apoptosis, an increase in TNF- $\alpha$  itself will inhibit trophoblast cell proliferation in vitro which is the cause of abortion. In addition to other pro-inflammatory cytokines other than TNF-a, IL-2 which are cytotoxic to pregnancy, increase protective asymmetric antibody production and by suppressing natural killer cell activity (NK), NK cell activation will trigger activation of lymphokine killer cells that causes imminent abortion [8,9,13-15].

The study of mean differences in levels of TNF- $\alpha$  and progesterone-induced blocking factor (PIBF) serum at normal gestational age of less than 12 weeks with iminence abortion can provide benefits as a way to determine the etiology of immunological side abortion.

V. CONCLUSION

The conclusion of this study confirmed there were mean difference of TNF- $\alpha$  and PIBF levels in less than 12th gestational weeks pregnant women with imminent abortion.

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