

**EFFECT OF INHIBIN A AND RELATIONSHIP WITH OF SEX HORMONES IN  
WOMEN WITH PREECLAMPSIA VESTING SABHA INFERTILITY TREATMENT  
CENTER**

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**ABSTRACT**

**Background:** Preeclampsia is a serious pregnancy complication affecting 5–8% of pregnancies and remains one of the leading causes of maternal and perinatal morbidity and mortality. Although its exact pathophysiology remains unclear, abnormal placental function and endothelial dysfunction are believed to play key roles. Inhibin A, a glycoprotein hormone produced by the placenta, has been proposed as a potential biomarker for preeclampsia. **Objective:** To evaluate the levels of Inhibin A and its relationship with sex hormones (LH, FSH, and progesterone) in women with preeclampsia. **Materials and Methods:** A case-control study was conducted at Sabha Infertility Treatment Center. It included 45 women in their third trimester: 30 with preeclampsia and 15 with normotensive pregnancies. Serum levels of Inhibin A were measured using ELISA, while LH, FSH, and progesterone were analyzed via chemiluminescence. Blood pressure and clinical data were also recorded. Data analysis was performed using SPSS v26, with significance set at  $p < 0.05$ . **Results:** Inhibin A levels were significantly higher in the preeclampsia group ( $1265.21 \pm 101.24$  ng/L) compared to the control group ( $444.38 \pm 47.03$  ng/L,  $p = 0.00$ ). No significant differences were observed in LH, FSH, or progesterone levels. Inhibin A showed a positive correlation with systolic blood pressure ( $r = 0.54$ ,  $p = 0.01$ ) and mean blood pressure ( $r = 0.35$ ,  $p = 0.03$ ), but not with diastolic pressure or sex hormones. **Conclusion:** Elevated Inhibin A may be associated with the pathophysiology and severity of preeclampsia and could serve as a potential marker for disease assessment.

**KEYWORDS:** Preeclampsia – inhibin A – pregnancy.**INTRODUCTION**

Preeclampsia is a complication that affects approximately 5 to 8% of all pregnancies, representing around 8.5 million cases worldwide each year. Unfortunately, preeclampsia remains one of the three leading causes of maternal death.<sup>[1]</sup> The majority of maternal deaths related to preeclampsia are caused by cerebral hemorrhage, resulting from poorly controlled hypertension (systolic blood pressure  $> 160$  mmHg).<sup>[2]</sup>

Other complications of preeclampsia include renal failure, pulmonary edema, liver failure or rupture, seizures (eclampsia), disseminated intravascular coagulation (DIC), retinal detachment, cortical blindness, placental abruption, and hemorrhage.<sup>[3]</sup> It is crucial to closely monitor and manage these complications to ensure the safety and well-being of both the mother and the baby.<sup>[4]</sup>

Preeclampsia is defined as the onset of hypertension (systolic blood pressure  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg) and proteinuria ( $> 0.3$

g/day) after 20 weeks of gestation in a woman who previously had normal blood pressure.<sup>[5]</sup>

Preeclampsia is responsible for 5% of stillbirths in infants without congenital abnormalities. It accounts for 8-10% of the overall preterm birth rate and contributes to 15-20% of cases of fetal growth restriction (FGR) and very low birth weight (VLBW).<sup>[6]</sup>

The precise mechanism underlying the development of preeclampsia (PE) is still not fully understood. However, it is believed to result from compromised trophoblastic invasion of the placenta, leading to subsequent endothelial dysfunction. This dysfunction is responsible for the clinical signs and symptoms observed in PE.<sup>[7]</sup>

An increasing number of biochemical agents were evaluated as markers for predicting preeclampsia. None of them has been proved to be of clinical value yet.

Hence, the identification of a reliable and early placental marker holds great potential in effectively detecting

pregnant women at a high risk of developing preeclampsia. In recent studies, inhibin A, a glycoprotein primarily produced by the syncytiotrophoblast of the human placenta during pregnancy, has been extensively evaluated for its predictive value in preeclampsia and its ability to assess the severity of the condition.<sup>[8]</sup>

## METHODS

**Study objectives** This study aims to studying the impact of inhibin A on other sex hormone (LH- FSH and progesteron) in women with preeclampsia. These evaluations can be easily conducted using the ELISA technique.

### Overall study design

This study was designed to evaluate the hormonal effects of Inhibin A and their relationship with preeclampsia of women patient in Sabha fertility center.

Ninety (30) women with age range from (21-42) year, were participants in this study female patient suffering from preeclampsia in the third trimester of pregnancy. Fifteen (15) of women had normal pregnancy and regarded as a control group in the third trimester of pregnancy.

At time of admission a complete clinical history was taken from each woman including maternal age, parity, gestational age, smoking, past medical history and family history of hypertensive disease In this study, pregnant women with chronic diseases such as diabetes, hypertension, or any history of cancer were excluded.

Examination was done to the patient including checking BP, measured in sitting position with suitable arm cuff with patient at rest using mercury sphygmomanometer using Korotokoff sound. The patient were considered preeclamptic when systolic and diastolic blood pressure were  $\geq 140/90$  mmHg two consecutive reading 4-6 hours apart (the first and fifth korotekoff sounds were used in the determination of systolic and diastolic blood

pressure), and  $\geq 1+$  albumin (30 mg/dl) on dipstick by qualitative estimation a random cleancatch urine sample (this is usually correlates with a urinalysis report of 300mg or more of protein in a timed 24-hour urine collection).

### Serum samples

Approximately 5 ml of venous whole blood samples were drawn. The blood samples were collected in anticoagulant-free tubes for 30 minutes. company at a speed of 3000 revolutions per minute to obtain serum , The serum was then separated and divided into Eppendorf tubes and These samples were stored in a freezer with a temperature of -20 degrees The solutions were stored in a refrigerator with a temperature range of (2-8) degrees until the tests were conducted hormonal analysis (inhibin A)- by ELISA (enzyme linked immune sorbent assay) and sent for liver function test, renal function test complete blood picture and inhibin A measurement. LH -FSH and Progesteron This test was performed on the fully-auto chemiluminescence (CLIA) analyzer Maglumi 800.

### Statistical Analysis

The data were statistically processed using SPSS software version 26, where the arithmetic mean, standard deviation, and percentages were calculated. An independent sample t-test was used to identify the differences between two groups Pearson Correlation was used to identify the relationships between the study variables, and a significance level of  $P < 0.05$  was adopted to indicate statistical significance. The results were presented using Microsoft Excel 2019.

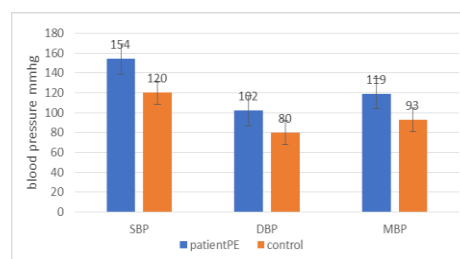
## RESULTS

(Table1) showed that the biomarker data (inhibin) significantly increased ( $p < 0.05$ ) in preeclampsia group compared to the control group. On the other hand, there were no statistically significant differences ( $p > 0.05$ ) in the other biomarkers (FSH, LH, Progesterone).

**Table 1: Comparison between preeclampsia and control group in different Biochemical parameters.**

Biochemical parameters	PE N= (30) M $\pm$ SE	Control N= (15) M $\pm$ SE	P value
Inhibin A ng/l	1265.21 $\pm$ 101.24	444.38 $\pm$ 47.03	0.00***
FSH mlu/ml	0.96 $\pm$ 0.026	0.99 $\pm$ 0.00	0.25
LH mlu/ml	0.97 $\pm$ 0.013	0.99 $\pm$ 0.00	0.12
Progesterone ng/ml	65.09 $\pm$ 3.14	63.38 $\pm$ 2.49	0.98

According to the results, there was a significant increase ( $p < 0.05$ ) in systolic( SBP) and diastolic blood pressure (DBP) levels, as well as mean blood pressure (MBP), in the preeclampsia group compared with control group as shown in (fig.1).



**Fig. 1: The comparison between preeclampsia group and control in the systolic blood pressure (SBP),**

### diastolic blood pressure (DBP), and mean blood pressure (MBP).

The findings in the table(2) of this study indicate no statistically significant correlation between Inhibin A and LH, FSH, or Progesterone. However, the negative correlation coefficients with LH and FSH ( $r = -0.29$ ).

**Table 2: Shows that the correlation between inhibin A hormone and another biochemical parameter.**

Biochemical Parameter	Inhibin A	
	p-value	r- value
LH	0.14	-0.29
FSH	0.09	-0.29
Progesteron	0.83	0.04

The results in table (3) indicate that Inhibin A is positively and significantly correlated with both systolic blood pressure (SBP) and mean blood pressure (MBP), whereas no significant association was observed with diastolic blood pressure (DBP). This pattern may suggest a potential role for Inhibin A in influencing the mechanisms that regulate blood pressure. The correlation coefficient with SBP ( $r = 0.54$ ) indicates a moderate positive relationship, implying that higher levels of Inhibin A may be associated with elevated systolic pressure.

**Table (3): Shows that the correlation between inhibin A hormone and blood pressure parameters.**

Anthropometric parameter	Inhibin A	
	p-value	r- value
SBP	0.01	0.54
DBP	0.49	0.13
MBP	0.03	0.35

## DISCUSSION

Preeclampsia is a syndrome with multiple causes, characterized by high blood pressure and proteinuria in pregnant individuals after 20 weeks of gestation. In preeclampsia, there is an increase in the concentrations of certain protein markers in the maternal circulation. These protein markers serve as indicators or biomarkers of the condition such as inhibin A.<sup>[9]</sup>

Inhibin A play vital roles in establishing and maintaining a healthy pregnancy. They are primarily produced by the placenta, decidua, and fetal membranes, and their levels in maternal serum and other biological fluids change throughout gestation.<sup>[10]</sup> Inhibin A also shows promise as a clinical tool for diagnosing and monitoring gestational pathologies such as threatened abortion and hypertensive disorders.<sup>[11]</sup> Dysregulation of inhibin signaling has been implicated in the development of several reproductive disorders, highlighting their potential as biomarkers and therapeutic targets for pregnancy-related complications.<sup>[12]</sup>

The results of this study showed an increase in the average levels of inhibin A in women with preeclampsia

compared to the control group. The reason for the highest levels of serum inhibinA in the PE group may be the presence of more pronounced placental ischemia. In preeclampsia, the placenta is exposed to oxidative stress due to disruptions in the delivery of oxygen, leading to an imbalance in oxygen supply, these findings align with a study conducted by Williamson, et al., They found significantly higher concentrations of Inhibin A hormone in the PE group compared to the control group.<sup>[13]</sup> In another study conducted by Akolekar et al, samples of Serum Inhibin A were taken from the uterine artery. The levels were then compared among patients with preeclampsia, gestational hypertension, and healthy women. It was found that Serum Inhibin A levels were significantly increased in PE followed by gestational hypertension and lowest in control group.<sup>[14]</sup> Our study also revealed no statistically significant differences in the remaining hormones included in the study, namely FSH (follicle-stimulating hormone), LH (luteinizing hormone), and progesterone, which is consistent with studies conducted by Hertig et al. and U. Pecks et al., they were found no difference in the levels of progesterone between preeclamptic and normotensive pregnancies.<sup>[15][16]</sup> The results of this study contradict the study conducted by Wan et al., which showed that the levels of estrogen and progesterone in the serum of women with preeclampsia were significantly higher compared to the control group.<sup>[17]</sup> These studies suggest that placental dysfunction may be one of the main causes of reduced production of sex hormones by the placenta in cases of preeclampsia.

In this study the mean systolic and diastolic blood pressure were calculated in all two groups to evaluate the severity of the disease and symptoms. It is evident that the mean blood pressure was lowest in the control group compared to the subjects in the PE groups. The increased blood pressure in the PE groups is attributed to the initial stage of trophoblast invasion being patchy, and the spiral arteries retaining their muscular wall.<sup>[18]</sup>

Based on the study conducted by Li et al, no significant differences were observed in the levels of FSH hormone and the expression of FSH mRNA and protein in the placenta between normal pregnancy and pre-eclampsia, which suggesting that locally produced FSH at the maternal-fetal interface may exert its physiological effects through paracrine way<sup>[19]</sup> These results align with our current study.

Zeeman et al. conducted a study to assess the use of third-trimester inhibin A levels as an additional tool to evaluate the severity of pregnancy-induced hypertension in women being evaluated for preeclampsia. The study found that inhibin A levels were significantly associated with the severity of hypertensive disorders of pregnancy. Additionally, the levels of inhibin A were significantly higher in women with both mild and severe cases of preeclampsia.<sup>[20]</sup> Preeclampsia is a global burden with 10 million incidences annually and 210 daily deaths

worldwide. Diagnosis is mainly based on the features following full presentation. The main focus of preeclampsia (PE) and its symptoms is hypertension, specifically an increase in blood pressure. Diastolic pressure, which is related to arteriolar spasm, can cause permanent damage to blood circulation and has a significant impact. Systolic pressure values can affect the autonomic nervous system, external sensation reactions, and mental perception.

## CONCLUSIONS

- The results of this study concluded that there are significant differences in anthropometric measurements and biochemical measurements between the preeclampsia group and the healthy pregnant group.
- The higher the blood pressure, the higher the level of inhibin A hormone.

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