

Original Article

# Assessing the impact of Glutathione on maternal and fetal outcome in pregnancy-induced hypertensive disorders: A case-control study.

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## Abstract

**Background:** Disorders related to hypertension in pregnancy, mainly Pre-eclampsia (PE), and Eclampsia, are the major causes of fetal and maternal morbidity and mortality. The placenta's ischemic blood supply leads to its endothelial dysfunction and reduced glutathione bioavailability involved in its pathogenesis. This study explored maternal serum Glutathione's level and changes and found out its association with fetal growth in pregnancy-induced hypertensive disorders.

**Methodology:** A Multicenter, case-control study was conducted on 240 pregnant females. The investigational group included 180 pregnant females having blood pressure above 140/90 mmHg. The Investigational group was divided into different groups, i.e. Pregnancy-induced hypertension (PIH) group, PE group, and Eclamptic group. 60 normotensive pregnant females were kept in control. The blood samples were obtained to analyze serum Glutathione (GSH) through ELIZA (enzyme-linked immunosorbent assay), while urine samples were obtained for confirmation of the PE status. Fetal well-being and signs of growth restriction were observed using ultrasound.

**Results:** A significant reduction was elucidated in serum glutathione, biparietal diameter, and femur length among all experimental groups  $p < 0.001$ . However, no significant difference was observed in the abdominal circumference  $p=0.122$  and Fetal weight  $p=0.51$ . A significantly inversely proportional relation was found between serum glutathione and gestational age, fetal weight as well as head circumference in all four groups control ( $r = -.305$   $p=0.018$ ) PIH ( $r = -.618$   $p = 0.000$ ), PE ( $r = -.707$   $p=0.000$ ) and Eclampsia ( $r = -.661$   $p=0.000$ ).

**Conclusion:** It is to conclude that the fetus's growth was markedly affected by reduced Glutathione in hypertensive disorders of pregnancy with the progression of the disease.

## Keywords

Reduced Glutathione, Fetal Growth, Pre-Eclampsia, Fetal Biometry, Biparietal Diameter, Head Circumference, Pregnancy Induced Hypertension.



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## Introduction

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Disorders related to hypertension in pregnancy are the primary cause of fetal, newborn, and maternal morbidity and mortality. Together with hemorrhage and infection, they form a deadly triad that significantly contributes to making these disorders life-threatening<sup>1</sup>, which leads to 18% maternal death globally<sup>2</sup>. Hypertension disorders in pregnancy can be classified as PIH, PE, and Eclampsia. PIH is an early onset of hypertension during pregnancy with blood pressure measurements 140 mmHg systolic over 90 mmHg diastolic<sup>3</sup>. In contrast, PE is a clinical disorder that is apparent amid the second half of pregnancy, tormenting 3–7% of pregnant females. PE is a multisystem hypertensive condition in mothers occurring after 20 weeks of gestation, and elevated BP and proteinuria usually distinguish it with wide-ranging hemolysis, raised liver proteins, decreased count of platelets, and increased levels of free adult hemoglobin, which leads to the life-debilitating condition<sup>2</sup>. PE is considered one of the driving causes of maternal mortality and dreariness<sup>3</sup>, particularly in countries with a low human development index. Pakistan is ranked as the third-highest country facing the burden of maternal, fetal, and child mortality<sup>1</sup>.

Furthermore, Eclampsia is a complication of PE that is distinctive by the occurrence of tonic-clonic seizures<sup>4</sup>. The probability of developing PE during Pregnancy among Pakistani females is high because, in Pakistan, the average maternal age is 21.1 years. Moreover, central obesity is also significantly reported in women living in Pakistan<sup>5</sup>.

Hypertension disorders in pregnancy are only symptomatically managed for its high blood pressure symptoms, and parturition is the only available cure in case of severe condition<sup>4</sup>. Thus, approximately 15% of preterm childbirths are reported as a consequence of PE. Additionally, in 25% of cases, high blood pressure during pregnancy leads to the fetus's intrauterine growth restriction and 40% fetal mortality. In pregnancies complicated by hypertensive disorders, females' body systems undergo oxidative stress to impaired trophoblastic invasion into the placental bed<sup>2</sup>.

Amid pregnancy, the placenta serves as an interface between maternal and fetal circulation<sup>6</sup>. The condition of PE is related to the diminished trophoblastic invasion into the placental bed and the compromised remodeling of the uterine arterioles. The vessels in the placenta out-turn to have reduced Diameter<sup>2</sup> and increased resistance<sup>6</sup>. This tends to result in decreased uteroplacental perfusion and leads to placental hypoxia or ischemia. Ischemia-reperfusion injury to the placenta serves as a robust stimulant for the spawning of reactive oxygen species. This increases oxidative stress decreases the antioxidants level. As a result, due to the exceedingly reactive nature of reactive oxygen species, they cause structural and functional harm to cellular DNA, proteins, and cell membranes in females suffering from hypertensive disorders. To encounter these, several antioxidants play an essential role naturally present in the body, which is further classified as enzymatic contains Superoxide dismutase (SOD), Glutathione peroxidase (GPx), Catalase (CAT) and Thioredoxin (TRX) and non-enzymatic includes GSH, Nicotinamide adenine dinucleotide phosphate (NADPH), vitamin C and E<sup>6</sup>.

GSH is a potent antioxidant; it is a tripeptide expressed as  $\gamma$ -Lglutamyl-L-cysteinyl-glycine. The presence of the thiol group makes it an excellent non-enzymatic antioxidant. More than 99% of its concentration in cells is in a reduced state. During oxidative stress conditions, it is oxidized for reducing Hydrogen peroxides by glutathione peroxidase and is again converted to reduced form by NADPH's activity glutathione reductase. The censorious state of the cell concerns the proportions of reduced and oxidized forms of GSH.

GSH is also responsible for keeping the reduced form of Vitamin A, C, and cellular protein. It plays a crucial function in protecting cellular macromolecules from the detrimental effects of endogenous and exogenous reactive oxygen and nitrogen species. It is associated with the detoxification of free radicals and tackles oxidative stress<sup>7</sup>.

During the time between conception and birth, replication and differentiation of cells take place. Organs are functionally matured to form body systems, and speedy growth is observed. These processes are susceptible to any kind of alteration. Uteroplacental insufficiency is the foremost proclaimed theory behind the development of hypertensive disorders in pregnant females. For uninterrupted fetus growth, sufficient vascular development is required in the fetoplacental unit. Maternal high peripheral resistance and placental hypoxia are attributed to reducing fetal growth, hypoglycemia, hypothermia, perinatal acidosis, coagulopathy, and immunodeficiency<sup>6</sup>.

In obstetrical practice, fetal biometry is of great interest; it helps estimate gestational age and fetal growth assessment<sup>9</sup>. It is stated that 3 to 10% of childbirths fall in the category of restricted growth. In comparison, roughly 6 to 30% of newborn children with a restricted change in intrauterine life are reported to be from developing countries<sup>10</sup>. Restricted fetal growth four times more observed in PE concomitant with 5% reduced birth weight<sup>11</sup>.

Fetal growth restriction can be assessed by weight underneath the 10th percentile for the gestational age<sup>6,10</sup> or 2500 gm birth weight considered reduced birth weight at 37 gestational weeks or more<sup>12</sup>. The fetal biometry parameter is usually comprised of biparietal diameter, abdominal circumference, femur length, head circumference, and fetal weights; the biparietal diameter and femur length measurements are widely used in combination to assess the development of the fetus<sup>13</sup>.

Studies suggested that high-level GSH<sup>15</sup> is involved in the pathogenesis of PE and altered fetal development. In contrast, some researchers observed no difference in serum glutathione concentration in PE and normotensive females. Understanding the role of Reduced GSH concentration in PE and altered fetal growth is imperative to design suitable and legitimate preventive and therapeutic techniques. Therefore, the study endeavored to ascertain the association between maternal serum glutathione and fetal

growth rate in pregnancy-induced hypertensive disorders as it might give more clues to clinicians as to whether the pathogenesis of altered fetal growth is linked with Glutathione and may highlight the potential for antioxidant therapy to improve the pregnancy-induced hypertensive disorder complications.

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## Methodology

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### Study Design and setting

A Multicenter, convenient sample, case-control study was conducted on 240 pregnant females aged 17-38 years from July 2017 to August 2019. The research was conducted on six sites Sindh Government Lyari General Hospital, Civil Hospital, Jinnah Postgraduate Medical Center, Atia General Hospital Malir, Koochi Goath Hospital, and Liaquat National Hospital and medical college.

### Study subjects

The females recruited in the study were equal to the baseline characteristics, including the gestational age of more than 22 weeks and singleton pregnancy. The Hypertensive group included 180 pregnant females having systolic blood pressure above 140 mmHg and diastolic blood pressure above 90 mmHg. This group was equally divided into three different groups i.e. Pregnancy-induced hypertensive group which recruits the patients with the onset of new hypertension Systolic and diastolic blood pressure 140/90 mmHg or more on two occasions at least 4 hours apart after 20 weeks of pregnancy, PE group recruits the patients with Systolic blood pressure of 140 mmHg or more or diastolic blood pressure of 90 mmHg or more on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure, 300 mg or more per 24 hours urine collection and Thrombocytopenia platelet count less than 100,000 and Eclamptic group which recruits preeclamptic patient with the development of seizures (tonic/clonic convulsions) as per the diagnostic criteria of PE provided by the American College of Obstetricians and Gynecologists<sup>17</sup>, In comparison, 60 subjects were enrolled in the Control group, i.e. normotensive group with no signs of proteinuria, endocrine, or renal disease.

### Maternal Parameters

Initially, the self-structured questionnaire was administered to collect the information from participants of each group. Their medical records consisted of Demographic information, present symptoms, blood pressure measurement (mmHg), Anthropometric measurements BMI (Body mass index (kg/m<sup>2</sup>), Waist circumference, Hip Circumference, and Waist to Hip Ratio), proteinuria, ultrasound findings (gestational age) and hematological findings (Hemoglobin gm/dl, platelets count (x10<sup>9</sup>/L). The 3 ml blood samples were taken from the cubital vein to analyze serum Glutathione (ng/ml). The collected blood sample was centrifuged to separate serum and keep in labeled tubes and stored at -20°C. An enzyme-linked immunosorbent assay (ELISA) method was applied by using catalogue no. E1462Hu test kit.

### Fetal Growth Parameters

Fetal well-being and signs of growth restriction were observed using ultrasound reports. The parameters used from the ultrasound reports were biparietal diameter, femur length, head circumference, abdominal circumference in centimeters, and fetal weight in grams.

### Statistical analysis

The data was analyzed using SPSS version 20.0. The findings are expressed as means along with standard deviations considered statistically

significant at p-value < 0.05. Test of significance one-way ANOVA, Pearson chi-square association test, and Spearman's Correlation test was applied among all studied groups.

### Ethical clearance

The Ethical Review Board approved the study protocol of the University of Karachi, and the study was designed under the Declaration of Helsinki. Informed consent was obtained from participants before their enrollment.

### Results

The participants' understudy were between 17-38 years of age, with the mean age of 27.66±5.32 years. The demographic and clinical characteristics of all groups under study are summarized in Table 1. Maternal age and Gestational Age were not found significant among all studied groups. In contrast, systolic blood pressure, diastolic blood pressure, and urinary protein excretion were significantly high in investigational groups than a normotensive group with p<0.05. A similar trend of having significant differences was observed in Hemoglobin level and Platelet count in all three investigational groups with p<0.01. Furthermore, the anthropometric profile analysis showed that Waist to hip ratio and BMI were significantly higher in pregnant females with hypertensive disorders considering p<0.05.

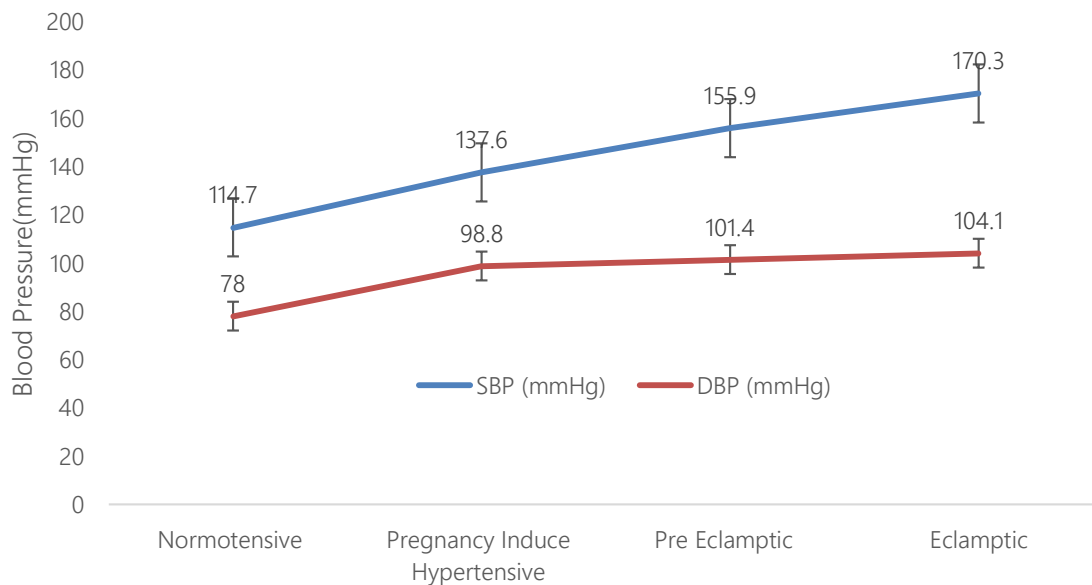
**Table 1: Demographics and clinical characteristics of Control and Investigational Groups.**

Parameters	Normotensive	PIH	PE	Eclamptic	p-value
Sample size (N)	60	60	60	60	-
Age (years)	28.57±4.8	27.98±5.63	27.82±5.52	27.30±6.5	0.542
GA (weeks)	33.18±3.7	32.36±3.05	33.06±2.7	33.11±2.02	0.402
Weight (Kg)	67.7±6.9	69.0±7.15	70.5±6.17	75.45±7.54	0.000*
Height (m)	1.62±.05	1.611±.06	1.56±.09	1.6±.08	0.001*
BMI (Kg/m <sup>2</sup> )	25.87±2.9	26.66±3.4	28.95±3.8	29.49±3.95	0.000*
WHR	0.80±0.02	0.82±0.03	0.83±0.02	0.83±0.02	0.000*
SBP (mmHg)	114.7±7.05	137.66±6.7	155.9±15.9	170.3±17.3	0.000*
DBP (mmHg)	78.0±6.8	98.8±8.02	101.4±6.6	104.1±9.5	0.000*
Proteinuria (mg/dl)	168.6±27.07	202.6±23.2	320.6±63.1	423.7±55.6	0.000*
Hemoglobin (g/dl)	10.5±0.91	11.2±0.88	12.3±0.83	12.±1.19	0.000*
Platelet count (x10 <sup>9</sup> /L)	293.38±51.1	183.7±43.2	135.57±26.4	113.13±19.5	0.000*

\* $p < 0.05$  is considered significant

GA-Gestational Age at the time of enrollment in study; BMI-Body Mass Index; SBP-Systolic Blood Pressure; DBP-Diastolic Blood Pressure; WHR-Waist to Hip Ratio; PE-Pre-eclampsia; PIH-Pregnancy-induced hypertension

Figure 1 presented the trends of Systolic blood pressure and Diastolic blood pressure changes from the normotensive group to pregnancy induce hypertensive groups that helped form the basis for the differentiation of participants in the respective four groups. Pearson chi-square association test results revealed that symptoms like Swelling (Normotensive 48%, PIH 50%, PE 76%, and Eclamptic 86%) and Headache (Normotensive 28%, PIH 33%, PE 58%, Eclamptic 78%) are significantly associated ( $p < 0.01$ ) with the progression of the disease. In contrast, visual ability changes (Normotensive 68 %, PIH 55%, PE 60%, and Eclamptic 60%) are not significantly associated ( $p = 0.511$ ).



**Figure 1: Trends of Blood Pressure changes from normotensive to Pregnancy-induced hypertensive groups.**

\*SBP-Systolic Blood Pressure ( $p$ -value  $\leq 0.001$ ) DBP-Diastolic Blood Pressure ( $p$ -value  $\leq 0.001$ )

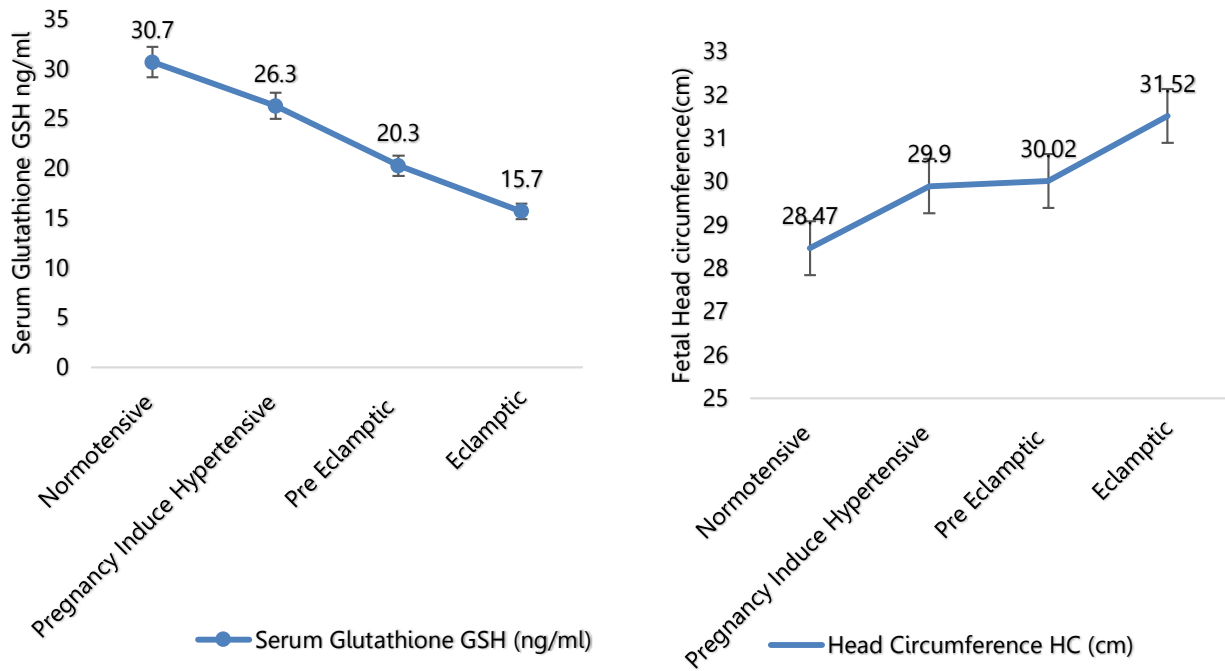
Serum Glutathione levels were significantly lower in pregnancies complicated by hypertensive disorders than the normotensive group, with the ( $p = 0.000$ ) showed in Table 2 and Figure 2. Fetal biometry measurements successfully performed in all participants include biparietal diameter showed significantly high values in Hypertensive groups ( $p = 0.000$ ), as well as Head circumference measurement, which increased substantially in investigational groups as compared to the control group with the ( $p = 0.000$ ) presented in Table 2 and Figure 3. In contrast, no significant difference was observed among studied groups in terms of the abdominal circumference ( $p = 0.122$ ) and fetal weight ( $p = 0.513$ ), as shown in Table 2.

**Table 2: Maternal Serum Glutathione and Fetal biometry in control and investigational groups.**

Parameters	Normotensive	PIH	PE	Eclampsia	p-value
	Mean $\pm$ SD				
Maternal Serum Glutathione (ng/ml)	30.7 $\pm$ 6.9	26.3 $\pm$ 4.4	20.3 $\pm$ 3.0	15.7 $\pm$ 2.3	0.000*
Biparietal Diameter (cm)	7.87 $\pm$ 0.41	7.71 $\pm$ 0.48	7.14 $\pm$ 0.75	7.1 $\pm$ 0.64	0.000*
Femur length (cm)	6.18 $\pm$ 0.9	5.97 $\pm$ 0.6	5.55 $\pm$ 0.5	5.34 $\pm$ 0.4	0.000*

Abdominal circumference (cm)	27.5±3.8	27.4±2.6	26.9±2.4	26.4±2.4	0.122
Head Circumference (cm)	28.4±2.9	29.9±2.4	30.0±2.4	31.5±2.4	0.000*
Fetal Weight (gm)	2005.7±67	1943.9±47	1917.4±45	1873.9±26	0.513

\*Significant p≤0.05; PE-Pre-Eclampsia; PIH-Pregnancy-Induced Hypertension



**Figure 2: Level of serum Glutathione in all four groups. Figure 3: Fetal Head circumference in all four groups**

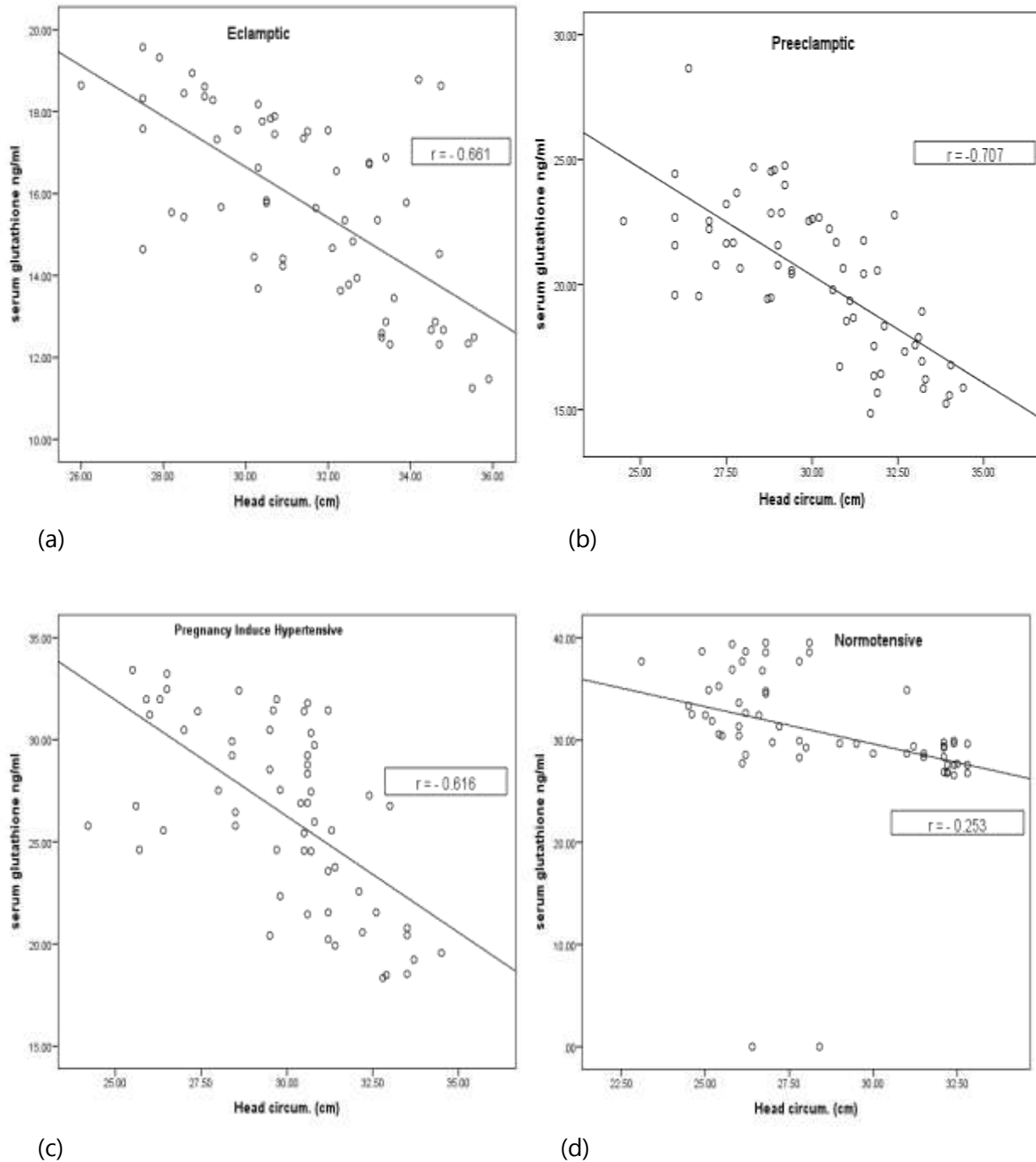
Spearman's correlation showed an enormously significant negative correlation of serum Glutathione and Fetal Biometry parameters includes Head circumference (presented in Figure 4) and abdominal circumference. The relation found between the gestational age and serum glutathione in investigational groups females that are mentioned in Table 3 was found to be inversely proportional, indicating the increase in severity of the problem with the rise of pregnancy duration. However, BMI and systolic and diastolic blood pressure also showed an inverse correlation with Serum Glutathione in all three-pregnancy-induced hypertensive groups compared to the normotensive group findings mentioned in Table 3.

**Table 3: Correlation of Serum Glutathione with other study variables.**

Variables	Control		PIH		PE		Eclampsia	
	R	p-value	R	p-value	R	p-value	R	p-value
GA (weeks)	-0.183	0.163	-0.664	0.000*	-0.784	0.000*	-0.701	0.000*
BMI (kg/m <sup>2</sup> )	-0.433	0.001*	-0.523	0.000*	-0.286	0.027	-0.166	0.204
SBP	-0.189	0.14	-0.44	0.000*	-0.85	0.000*	-0.83	0.000*
DBP	-0.173	0.18	-0.65	0.000*	-0.78	0.000*	-0.82	0.000*
Proteinuria (mg/dl)	-0.23	0.06	-0.743	0.000*	-0.877	0.000*	-0.819	0.000*
BPD	0.08	0.54	0.062	0.63	-0.003	0.98	-0.73	0.000*
FL	-0.17	0.19	-0.62	0.000*	-0.75	0.000*	-0.681	0.000*
HC (cm)	-0.305	0.018*	-0.618	0.000*	-0.707	0.000*	-0.661	0.000*

AC (cm)	-0.253	0.051	-0.616	0.000*	-0.707	0.000*	-0.661	0.000*
Fetal Weight (gm)	-0.181	0.166	-0.697	0.000*	-0.791	0.000*	-0.748	0.000*

\*Significant  $p \leq 0.05$ ; GA-Gestational Age at the time of enrollment in study; BMI-Body Mass Index; SBP-Systolic Blood Pressure; DBP-Diastolic Blood Pressure; HC-Head Circumference; AC-Abdominal Circumference; FL-Femur Length; BPD-Biparietal Diameter; PE-Pre-eclampsia; PIH-Pregnancy-induced hypertension



**Figure 4 (a-d): Scatter plot demonstrating the negative correlation between Serum Glutathione and fetal Head circumference in all study groups.**

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## Discussion

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Oxidative imbalance in pregnancy-induced hypertensive females is characterized by a significantly decreased level of Serum Glutathione with the severity of the disease, which consequently negatively impacts maternal health and fetal growth. Several studies have reported that the Oxidative imbalance induces substantial variance in the production of reactive oxygen species and the naturally occurring antioxidants<sup>6,15,18</sup> in the Placental tissues due to impaired remodeling of spiral arteries, which are vulnerable to hypoxia and reperfusion injury, due to which the production of oxidative substances largely amplifies. Several antioxidants play an essential role in countering this imbalance, which is further classified as enzymatic includes SOD, GPx, CAT, and TRX and non-enzymatic includes Reduced Glutathione, NADPH, NADH, vitamin C and E<sup>6,10,18</sup>.

Glutathione is a tripeptide expressed as  $\gamma$ -L-glutamyl-L-cysteinyl-glycine. The presence of the thiol group makes Glutathione an excellent non-enzymatic antioxidant. More than 99% of its concentration in cells is in a reduced state. During oxidative stress conditions, Glutathione is oxidized for reducing Hydrogen peroxides by glutathione peroxidase and is again converted to reduced form by NADPH's activity glutathione reductase. GSH is also responsible for keeping the reduced form of Vitamin A, C, and cellular protein<sup>7</sup>.

It has been speculated through some earlier findings that the diminished amount of Glutathione during Preeclampsia can be taken in the account through the explanation that in the circumstances when oxidative stress severity is exceptionally high, the antioxidants are either directly damaged or harmed through an alteration in their gene expression leading to significant disfigurement of proteins<sup>19</sup>. The apoptosis and protein misfolding occurring at the placental interface due to lower Glutathione levels may also contribute to confinement in the fetal growth in PE females<sup>7</sup>. Our study results presented a significantly decreased level of GSH in pregnancies complicated by hypertension compared to the normotensive

pregnancy group, which Ultimately compromised the ability of GSH to neutralize the reactive oxygen species and leads to the pathogenesis of PE<sup>20</sup>.

Reduction in GSH is more explored with trimester wise comparison in PE and normotensive pregnant females after obtaining maternal erythrocyte and cord samples<sup>2</sup>. Multiple recent studies supported our research findings, either they performed in plasma or erythrocyte; both samples showed decreased GSH level in pregnancy-induced hypertensive groups compared to the normotensive group<sup>14,20</sup>. However, some researchers came up with different results and observed no difference in the level of GSH in a PE and standard group in the same direction, no significant difference in the level of GSH in erythrocyte sample of severe and mild PE female than normal pregnant female<sup>16,21</sup>. Previously a substantially high level of GSH in placental and decidual tissues found in the PE group than normotensive<sup>15</sup>.

In obstetrical practice, Fetal biometry is of great interest; it helps estimate gestational age and fetal growth assessment<sup>9</sup>. The decrease level of GSH impairs the normal evaluation of gestational age. In later stages of pregnancy, reduce the level of Glutathione detect growth aberration and hurtful neonatal outcome<sup>22</sup>.

The current study meticulously presents fetal biometry assessment, which shadowed this geographical region's criteria, especially for the normotensive group<sup>13,23</sup>, also highlighted the significant differences in fetal biometry parameter measurements in pregnancy induce hypertensive groups. We determined statistically significantly reduced femur length and biparietal diameter in pregnant females of all three hypertensive groups; similar results of a retrospective study speculated that 52.5% of pregnant females were PE and possessed poor biparietal diameter growth and its association with an adverse neural developmental outcome in the fetus<sup>24</sup>. However, reduction in abdominal circumference and fetal weight was also reported in the present study hypertensive group, highlighting the influence of oxidative stress on



impaired fetal growth<sup>25</sup>. A similar result of reduced birth weight among preterm PE, term PE than normal pregnant females with increased oxidative stress was also interpreted<sup>26</sup>. Whereas fetal Head Circumference remained significantly increased in pregnancy-induced hypertensive groups; interestingly similar trend elucidated by Eviston et al. of an increased rate of fetal head growth in a PE group at term gestation with reduced birth weight<sup>27</sup> this uniqueness in our result can be determined by more exposure of fetus at term with neurotrophins and brain derived neurotrophic factor which are vital elements for brain growth<sup>28</sup>. Still, limited studies provided their increased level in PE females<sup>29,30</sup>, while the reduced head circumference is also observed<sup>31</sup>.

Moreover, in this study, a significant negative association of maternal GSH with systolic and diastolic blood pressure, proteinuria, and gestational age was observed. In contrast, the moderate negative association was confirmed with BMI in all three investigational groups indicating the increase in severity of the problem with the progression of pregnancy; similar findings were demonstrated in a recent study with a reduction in fetal growth<sup>32</sup> in addition to this significant inverse correlation of maternal GSH with fetal growth assessment parameters like Head circumference, abdominal circumference and fetal weight was also evidenced in all three-pregnancy induced hypertensive groups as compared to the normotensive group.

To the best of our knowledge, in the context of the association of serum glutathione with fetal growth, an assessment was not directly reported in previous studies. As we suggested, Bakheit et al. proposed a significant negative association between Serum GSH and diastolic blood pressure in PE females<sup>33</sup>. However, Glutathione, among other antioxidants, was found to be reduced in PE females. Still, no correlation was seen<sup>22</sup>, as well as another study also presenting the same trend between antioxidant level and systolic blood pressure in PE females<sup>34</sup>. Disparity with the previous finding's moderate positive correlation of GSH with blood pressure in PE females have also

been established<sup>15</sup>, which was further strengthened by reporting a positive correlation of serum glutathione with maternal features (weight and BMI) and neonatal features (birth weight and head circumference)<sup>35</sup>.

It can be speculated that the restriction of fetal growth in pregnancy-induced hypertensive disorders is described as a result of decreased Glutathione levels. In PE, a reduced level of GSH is inefficient to compensate for the stress caused by the reactive oxygen species and leads to ischemia-reperfusion injury. The ischemia-reperfusion causes oxidative mutilation of DNA and results in the restriction of the fetus's growth in females with PE<sup>6</sup>, which the leaving effects like increased head circumference while marginal decreased in Abdominal girth and femur length. Besides, disruption of homeostatic conditions, such as hypoxia actuated oxidative stress, has also been illustrated to lead to an increment in luminal misfolded proteins resulting in apoptosis of the cells. It is believed that apoptosis and protein misfolding occurring at the placental interface due to lower levels of Glutathione may also contribute to confinement in the fetal growth in PE females<sup>18</sup>.

The major strength of this research is the large sample size of the investigational group. It allowed a realistic view of serum glutathione value in PE females and precisely assessed its assumed relationship with PE and fetal growth. Our study's limitation includes a cross-sectional study design and not having the exactly matched gestational week among studied groups for more appropriate fetal growth assessment.

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## Conclusion

The present research concluded that the maternal serum Glutathione is strongly inversely correlated with gestational age, systolic blood pressure, diastolic blood pressure proteinuria, fetal head circumference, and fetal weight; furthermore, serum glutathione is significantly reduced in pregnancies complicated by hypertension with the severity of disease which consequently produces a negative impact on maternal health and fetal

growth. GSH level assessment's ultimate goal is to predict information concerning a mother and a fetus to verify how closely GSH influences the fetus.

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### Conflicts of Interest

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None.

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None.

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