

# Relationship between Pre-Eclampsia, Renal Impairment and Hepatic Insufficiency among Pregnant Women in Al-Jouf Area

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**Abstract:** *Background:* Pre-eclampsia is a pregnancy-specific syndrome. It affects 3-5% of pregnant women and is characterized by oedema, high blood pressure, and proteinuria. Moreover, in women with pre-eclampsia dysfunction of many organs, such as kidney and liver, is diagnosed, while in the case of foetus growth restriction is observed. Pre-eclampsia, when left untreated, can lead to a high mortality rate. In low-income countries, this disorder is one of the main causes of maternal and child mortality. Pre-eclampsia predisposes women in later life to cardiovascular diseases. So far, in acute cases of pre-eclampsia stabilization of the mother and fetus, and finally, termination of pregnancy at a time optimal for both sides can only be considered.

*Methods:* The present work is designed to investigate the relationship between pre-eclampsia, renal and hepatic insufficiency in the Al-Jouf area through collecting information from the electronic database of maternity hospital for 100 pregnant women who suffered from pre-eclampsia compared with normal pregnancies.

*Results:* The prevalence of pre-eclampsia is more prone in eldest women (older than 35 years old) almost 45% than younger women (20-25 years old), PC to MPV ratio value showed a significant suppression in pre-eclamptic pregnancies in comparison with normal pregnant women while HbA1c % value indicated a significant increase in the pre-eclamptic cases than the healthy pregnant women. Renal indices, serum creatinine, urea, and albumin were significantly higher in the pre-eclamptic women than in women with normal pregnancies.

*Conclusion:* There is a tight relationship between hypertensive disorders during pregnancies, chronic renal disorders and hepatic insufficiency.

**Keywords:** Pre-eclampsia, Renal impairment and Hepatic disease.

## 1. INTRODUCTION

Pre-eclampsia is a serious pathological disorder characterized by elevated blood pressure after 20 weeks of pregnancy that may cause more than 60,000 deaths of pregnant women all over the world every year. It is characterized by protein in the urine, major organ impairment of the mother, either the kidney, the liver, central nervous system, the blood, or abnormal foetal growth in almost 5% of pregnancies. These complications might lead to a high fatality rate for both mother and foetus [1].

It is difficult to diagnose a case of pre-eclampsia. The maternal phenotype of pre-eclampsia is usually accompanied by endothelial cell inflammation. The more extreme beginning stage placental phenotype is related to foetal development limitation. Pregnant women may give late-beginning hypertension and proteinuria, with no presence of foetal development

limitation close to term. In acknowledgment of the multifaceted phenotype of pre-eclampsia, the American College of Obstetrics and Gynaecology refreshed its meaning of this condition in 2016 as follows: [2] Maternal circulatory pressure > 140/90 mm Hg on multiple times at any rate 4 hours separated following 20 weeks of origination in a lady with recently estimated ordinary pulse. Maternal blood pressure > 160/110 mm Hg: hypertension can be confirmed with a short interval (minutes) to facilitate timely antihypertensive therapy and one of the following:

- Proteinuria: > 300 mg in a 24 hours urine collection.
- Dipstick reading of 1+.
- Decreased platelets count.
- Kidney impairment.
- Hepatic insufficiency.
- Central nervous system or optical symptoms.

Most of the pregnant women are asymptomatic even with severe illness. Douglas and Redman

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reported that 38% of pregnant ladies didn't report an elevation of systemic blood pressure or the presence of protein in the urine [3]. Unrecognized foetal trade-off adds to the pace of foetal downfall, and 1 of every 20 stillbirths without inborn anomaly is muddled by or owing to pre-eclampsia [4]. Distortions in the development of the placental vasculature early in pregnancy may lead to under-perfusion of organs causing ischemia/hypoxia, which then leads to the release of anti-vascular agents in the illiterate blood circulation that change the maternal systemic lining function and cause high blood pressure and manifestations for other disease (blood, nervous, heart, lung, kidney, and liver diseases) [5].

This change in the normal vascular balance towards the anti-vascular state can lead to high blood pressure, proteinuria, glomerular vascular endothelium, HELLP (haemolysis, elevated liver enzymes and low platelets) and cerebral oedema - clinical signs of pre-eclampsia. Recent discoveries of systematically organized anti-angiogenic agents provide promises for future tests to predict and diagnose pre-eclampsia as well as a treatment approach [6]. Oxidative stress may also play an important role in the pathogenesis of pre-eclampsia. The main source of reactive oxygen species (ROS) is xanthine oxidase (XO) and this enzyme occurs mainly in the liver. One hypothesis is that the increased purine degradation of chorionic hypoxia leads to an increased ROS production in the mother's liver and its release into the illiterate circulation that causes endothelial cell damage [7]. Abnormalities in the mother's immune system and decreased intestinal immune tolerance appear to play key roles in pre-eclampsia. One of the main differences in pre-eclampsia is the shift towards IFN- production. The origin of IFN has not been clearly defined and they can be natural killer cells of the uterus, chorionic dendritic cells that modulate helper T cell responses, cause changes in the synthesis or response of regulatory molecules, or changes in the regulatory function of T cells in pregnancy.

Anomalous immune responses that enhance pre-eclampsia may also be caused by a change in fetal recognition or due to an inflammatory stimuli. It has been documented that fetal cells, such as fetal red aromas, as well as the DNA of a cell-free fetus increase in the mother's blood circulation in women with pre-eclampsia. This results in the hypothesis that pre-eclampsia is a pathological process permitted by the placenta lesion such as hypoxia by increasing the fetal substances in the maternal blood circulation, which in turn leads to an immune response and

endothelial damage, and ultimately results in pre-eclampsia [8].

The National Institute for Health and Care Excellence (NICE) suggests a rundown of maternal hazard factors that can be utilized to recognize ladies who are at high hazard for pre-eclampsia in whom ibuprofen ought to be begun from 12 weeks' incubation [9]. Solid hazard factors incorporate past pre-eclampsia or hypertension in pregnancy, incessant kidney malady, interminable hypertension, diabetes (type 1 or 2) [10] immune system issues, for example, foundational lupus erythematosus or antiphospholipid condition and sub-clinical hypothyroidism or thyroid antibodies [11, 12]. To differentiate between pre-eclampsia and other causes of high blood pressure, proteinuria is the most specific diagnostic sign of preeclampsia due to temporary damage of the kidney filter leading to the spilling of protein in urine especially albumin [13]. Early control of maternal blood pressure is an important method to prevent further complications of pre-eclampsia such as cerebral stroke, convulsions (eclampsia), pulmonary oedema, bleeding due to liver damage and loss of vision. When pre-eclampsia or eclampsia damages the liver and blood cells, you can get a complication called HELLP syndrome. That stands for: haemolysis, elevated liver enzymes and low platelets count. Preeclampsia can also cause placental abruption from the uterus that can lead to stillbirth [14].

Treatment of pre-eclampsia depends on the seven-day extension of growth, if the pregnancy is at 37 weeks or later, the main successful strategy for treatment is to remove the child to treat pre-eclampsia and stay away from further complications.

If the gestation period is less than 37 weeks, however, the woman and the gynecologist may consider treatment options that give the fetus a greater chance of development, for example, corticosteroids, depending on the severity of the condition. The HR service provider may consider alternatives associated with it:

- If the level of hypertension is mellow and the maternal side effects are controlled, approach the mother to go for bed rest to diminish circulatory strain and increment blood stream to the placenta.
- Anticonvulsive treatment, for example, magnesium sulfate.
- If the level of hypertension is extreme, the mother ought to be admitted to the emergency

clinic under close observation and start the treatment by intravenous antihypertensive and anticonvulsants. Preterm conveyance might be fundamental, regardless of whether that implies likely entanglements for the baby, given the danger of serious maternal inconveniences [15-17].

The present study is designed to highlight the prevalence of pre-eclampsia in Al-Jouf area, Saudi Arabia regarding the age of patients, week of occurrence of hypertension during gestation period, presence of kidney impairment, and liver complications compared to normal pregnant women

### 1.1. Background and Significance

Previous studies that were conducted on preeclampsia mostly focused on the implication of health system strength [18].

Other studies focused on impact of severe pre-eclampsia on maternal and fetal outcomes in preterm deliveries [19]. Another study focused on strategy for standardization of pre-eclampsia research study design [20].

### 1.2. Gap of Literature and Description

This study is the first descriptive study to evaluate the percentage of preeclampsia in pregnant women in the Al-Jouf region by gathering information from the electronic database of the Maternity and Children's Hospital, Sakaka, Al-Jouf region, Kingdom of Saudi Arabia (KSA)

## 2. RESEARCH DESIGN AND METHOD

**Study area:** At Maternity and Children's Hospital in Sakaka, Aljouf region, Saudi Arabia.

**Sampling technique:** Taking patients history sheet from the electronic database of the hospital. Sample size: 200 patients.

**Time:** The study was conducted from February–May 2018 after getting ethical approval.

**Sample criteria:** A cross-sectional study was conducted at Maternity and Children's Hospital, Sakaka, Al-Jouf region, Kingdom of Saudi Arabia (KSA) during February–May 2018. Pregnant women with pre-eclampsia (100 cases), which is defined as “occurrence of hypertension after 20 weeks of gestation and proteinuria (presence of 300 mg or more

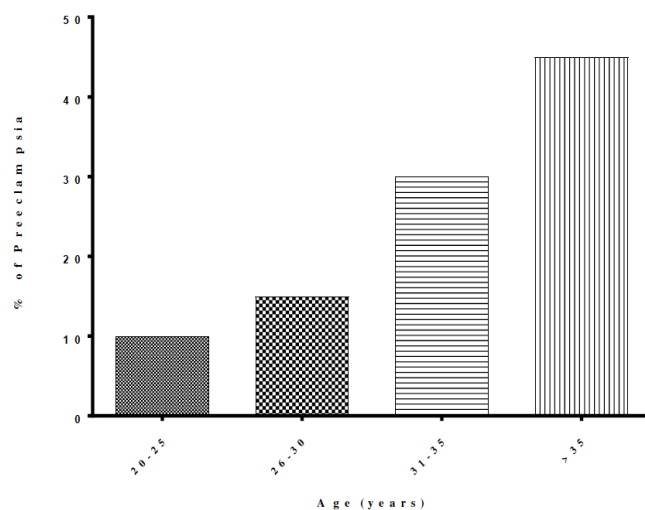
of protein in 24 h urine sample or  $\geq 2+$  on dipstick)”, was observed. Healthy pregnant women (100) were taken as controls. Women with thyroid disease, hypertension, renal disease, diabetes mellitus and liver diseases were excluded from the study groups. The medical records of both pre-eclamptic cases and normal pregnancies were reviewed for obstetrics history (age, parity and gestational age). Data were collected included glycosylated haemoglobin level (HbA1c %), white blood cell (WBC) count, haematocrit % and platelets count (PC) to mean platelets volume (MPV) ratio. Additionally, liver and kidney function tests in normal and pre-eclamptic cases were recorded.

### 2.1. Statistical Analysis

Data were statistically analysed and expressed as mean  $\pm$  standard error (SEM) using a two-way analysis of variance ANOVA followed by paired t-test for multiple comparisons by using software Prism Version 7.

## 3. RESULTS

Figure 1 showing that the prevalence of pre-eclampsia is more prone in women (older than 35 years), which was almost 45% greater than in younger women (20-25 years old). Figure 2 shows that there was no significant difference in parity between the two study groups.



**Figure 1:** The percentage of preeclampsia occurrence at different ages.

There was no significant difference in WBC and haematocrit (HCT%) between the two groups but it was found that PC to MPV ratio value was significantly lower in the cases compared with the controls, and the HbA1c % value was significantly higher in the

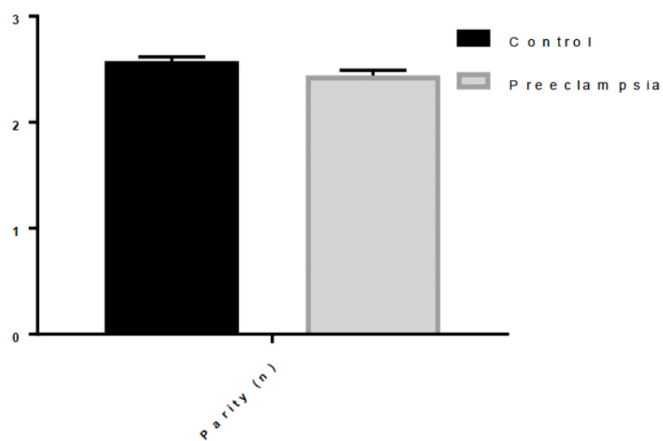


Figure 2: Parity in both preeclamptic pregnant cases and controls.

preeclamptic cases than the controls (Table 1, Figure 3).

Table 1: Median (Interquartile Range) of Haematological Values in Preeclamptic and Control Women

Variable	Cases	Controls
HbA1c %	6.86 ± 0.195	4.77 ± 0.24*
WBCs x10 <sup>3</sup> /μL	8.11 ± 0.064	7.85 ± 0.05
Hematocrit %	34.31 ± 0.306	33.4 ± 0.547
PC / MPV	21.16 ± 0.475	27.13 ± 0.574*

Table 2 and Figure 4 shows the significant increase in serum activities of liver enzymes, AST and ALT in preeclamptic cases mounted to 105.8% and 268.4%, respectively, compared to the control group.

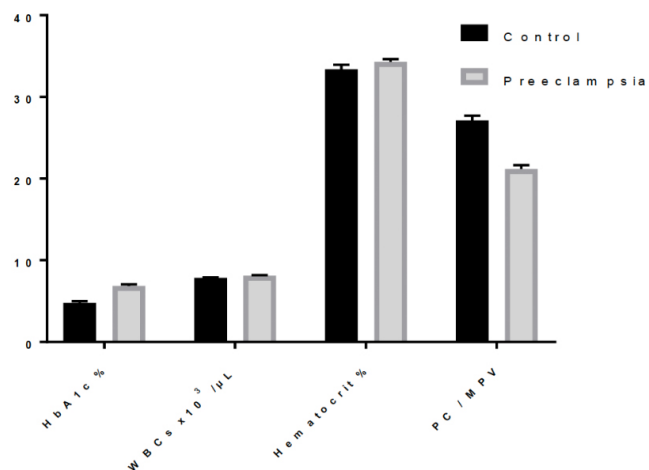


Figure 3: Median (interquartile range) of haematological values in preeclamptic and control women.

The renal indices, serum creatinine, urea and albumin were significantly higher in the preeclamptic

women than the normal pregnant ones (Table 3, Figure 5).

Table 2: Average Values of Liver Function Tests, AST and ALT, in Normotensives and Pre-Eclamptic

Variable	Cases	Controls
AST (U/L)	38.5 ± 4.039	18.7 ± 1.85*
ALT (U/L)	47.9 ± 3.954	13.0 ± 1.783*

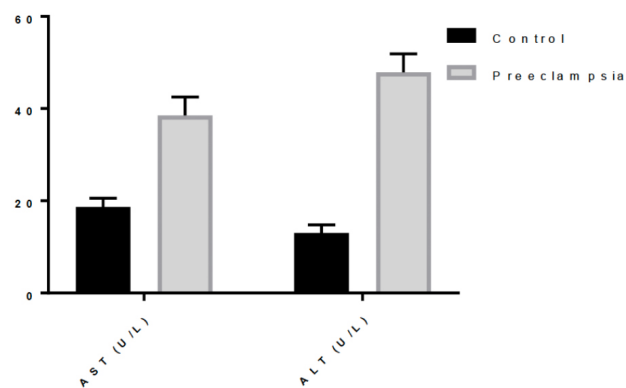


Figure 4: Average values of liver function tests, AST and ALT, in normotensives and pre-eclamptic.

Table 3: Average Values of Serum Creatinine, Urea and Albumin in Normotensives and Pre-Eclamptic

Variable	Cases	Controls
Urea (mg/ dL)	28.7 ± 1.075	20.49 ± 0.884*
Creatinine (mg/ dL)	0.717 ± 0.025	0.537 ± 0.017*
Albumin (g/dL)	2.81 ± 0.082	3.34 ± 0.098*

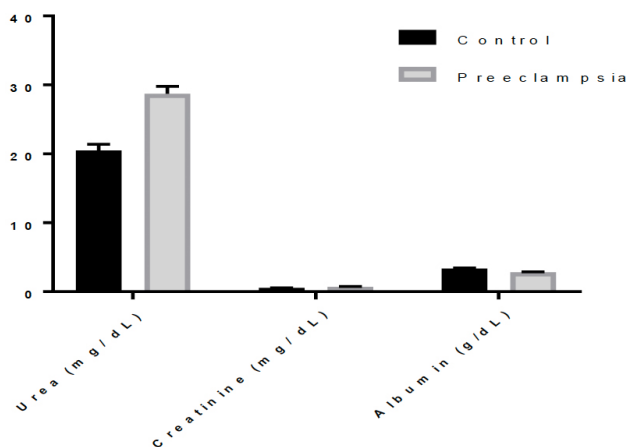


Figure 5: Average values of serum creatinine, urea and albumin in normotensives and pre-eclamptic.

#### 4. DISCUSSION

The renal function indicators, serum creatinine, urea and egg whites were essentially higher in the pre-

eclamptic women than the typical pregnant ladies that can be clarified as renal limit encounters physiological alterations in pregnancy. Sound pregnant ladies showed broad glomerular hyperfiltration by 40 to 60% in the second 50% of pregnancies [21]. This hyperfiltration appears to result essentially from a decline in the oncotic pressure [22].

Besides, an increased rate of renal plasma flow (ERPF) is found during pregnancy, (~80% by 12 weeks' development) [22]. On the other hand, during preeclampsia these utilitarian changes in renal haemodynamic are one of a kind. The GFR in ladies with preeclampsia is basically lower when differentiated and sound gravid control subjects (91 mL/min/1.73 m<sup>2</sup> versus 149 mL/min/1.73 m<sup>2</sup>).

This lessening in the GFR during preeclampsia agrees with conventional histopathological changes in the kidney, called glomerular endotheliosis, which is depicted by fibrin proclamation, endothelial extending, and loss of hairlike space [23].

Disregarding the way that these renal histological changes have been considered pathognomonic for preeclampsia, this may not be the circumstance. A couple of social affairs have performed antenatal renal biopsies in the run of the mill pregnant ladies and ladies with gestational hypertension. For instance, Strevens *et al.* shown that five of twelve ordinary pregnant women had, however, astoundingly smooth verification of glomerular endotheliosis [24].

Pre-eclampsia is the most widely recognized glomerular ailment worldwide and stays a main source of newborn children and maternal mortality. Regardless of the way that the particular pathogenesis of this state of hypertension and proteinuria is so far divided, a solid line of evidence has recognized a lopsidedness of proangiogenic and against angiogenic proteins as a key factor in the headway of pre-eclampsia [25,26]. In addition, more thought has been starting lately directed to the renin-angiotensin-aldosterone system (RAAS), to give an understanding of the hypertension of pre-eclampsia [27]. The turmoil of the RAAS and the unevenness among angiogenic and threatening to angiogenic factors, which may be both fundamental to preeclampsia and incessant kidney sickness (CKD), may explain why a past loaded up with preeclampsia slants ladies to make CKD.

In the pathogenesis of pre-eclampsia, the placenta is the central organ since the departure of the placenta invalidates the contamination [28]. Fanatical appraisal

reveals a couple of varieties from the ordinary including infarcts, arthrosis, apoplexy and interminable aggravation [29]. During conventional placentation, the undeveloped organism inferred cytotrophoblast cells assault the maternal winding veins. As a significant part of this methodology, the cytotrophoblasts get an endothelial phenotype [30]. In pre-eclampsia, the attack of the cytotrophoblasts into the winding veins is deficient; they are just present in the shallow layers of the decidua. The strange placentation is thought to prompt an arrival of emitted factors that enter the mother's dissemination, coming full circle in the clinical signs and manifestations of pre-eclampsia. The arrangement of hypofiltration during preeclampsia isn't clarified; both (renal) haemodynamic parts and auxiliary changes to essential renal changes are proposed [31]. Recently, podocyte modifications and podocyturia have been recorded during preeclampsia [31]. Proteinuria in patients with preeclampsia may not only be mediated by endothelial changes as portrayed traditionally rather it can also occur by aggravations of podocyte science including weakened perseverance, improved apoptosis and down-rule of nephron and other key proteins of cut stomach [32]. This investigation additionally demonstrates the huge increment in serum exercises of liver proteins, AST and ALT in preeclamptic cases mounted to 105.8% and 268.4%, respectively, as compared to the control bunch that can be clarified as preeclampsia-induced liver illness is a turmoil remarkable to pregnancy and is every now and again found in the third trimester of pregnancy. Serious preeclampsia is characterized by outrageous height in foundational circulatory strain and proof of organ bargain. HELLP condition is a particular liver-related issue of pregnancy that was first portrayed by Weinstein in 1982 as a group of stars of clinical and lab variations from the norm in pregnant ladies in their third trimester [33].

Almost 70% of cases occur between weeks 27 and 37, with 20% happening inside 48 hours of conveyance. Highlights of preeclampsia happen in most of patients giving HELLP disorder. 10% to 20% of patients with extreme preeclampsia will create HELLP. Liver contribution in preeclampsia isn't normal, in any case, but if present it means extreme malady. A few quality variations, for example, glucocorticoid receptor quality (GCCR), toll-like receptor 4 quality (TLR4), vascular endothelial development factor quality, FAS quality, bunch of separation 95 (CD95), and the coagulation factor V Leiden change are related with expanded danger of HELLP in contrast to solid ladies. Insufficient vascular placental attack has been the main

speculation in the aetiology of preeclampsia-eclampsia and HELLP disorder. Thrombotic microangiopathy prompts microangiopathic haemolytic frailty and liver harm in patients with HELLP. HELLP disorder has likewise been accounted for in a couple of cases that are related to abandons in  $\beta$ -oxidation of unsaturated fats [34].

## 5. CONCLUSION

Preeclampsia is a multisystem vascular turmoil of pregnancy that remains a main source of maternal and fetal horribleness and mortality. Preeclampsia stays an underrecognized chance factor for future cardiovascular and kidney illness in ladies and speaks to the conjunction of previous vascular hazard factors with endothelial injury of placental blood vessels. Preeclampsia stays a significant issue worldwide for mothers and children. Not withstanding concentrated examination, we have not had the option to improve the administration or early acknowledgment of preeclampsia. In any event, some portion of this is a result of the inability to normalize the way to deal with this unpredictable condition.

This investigation presumed that pregnant ladies with preeclampsia are progressively inclined to renal weakness, proteinuria, greasy liver, apoplexy, and raised liver compounds than ordinary pregnant ladies.

## CONFLICTS OF INTEREST

There is no Conflicts of Interest regarding this work.

## ETHICS APPROVAL

All the procedures were approved by the local committee of bioethics in Aljouf University in compliance with ethical standards. Data collected will be kept hidden and locked where others have no access to it.

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