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Assessment of insulin resistance and some antioxidant markers in women with Pre-eclampsia

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Abstract
One of the main causes of maternal and perinatal death globally is hypertensive disorders of pregnancy. A pregnancy condition known as preeclampsia, with or without severe symptoms, is characterized by new-onset hypertension, typically accompanied by proteinuria, and normally develops after 20 weeks of gestation and often close to term. The aim of this research paper is to investigation of insulin resistance and some antioxidant markers in women with Pre-eclampsia (PE). This study included three groups (total n=60), fourteen pregnant women with pre-eclampsia (PE, n=40) and based on gestational age and disease severity, these chosen pre-eclamptic pregnant women were split into two groups, first age PE1 (n=20) (18-30 years), the second age PE2 (n=20) (31-41), and third group (n=20) as gestational age (17-40) without PE (CONT) as a control group. The results shown significant differences in the biochemical markers (INS, FBG, HOMA-IR, TAO-C and MDA) between pre-eclamptic women groups (PE1 and PE2) and control. The study demonstrates a strong association between insulin resistance and oxidative stress in pre-eclamptic pregnancies. These disturbances are more pronounced in older patients, suggesting that maternal age may influence the severity of PE. Early identification of metabolic and oxidative markers could aid in risk stratification and management of pre-eclampsia.

Keywords: Pre-eclampsia, insulin resistance, oxidative stress, HOMA-IR, MDA, TAO-C, pregnancy, maternal age

Introduction

A pregnancy-specific illness known as pre-eclampsia (PE) is typified by the development of proteinuria and hypertension in the second half of pregnancy. Pre-eclampsia is a major cause of maternal and fetal morbidity and mortality worldwide, occurring in around 3-5% of pregnancies [1]. The second and third trimesters of pregnancy are when PE occurs, and nulliparous women are more likely to experience it. When proteinuria is ≥0.3 g/24 hours or equal to 1+ or 100 mg/dl by dipstick response, it is accompanied by blood pressure of 140/90 mm Hg after 20 weeks of pregnancy [2]. Placental ischemia can cause increased trophoblast emigration, which can lead to endothelial cell dysfunction. Not the cause of pre-eclampsia, but a strong risk factor, inadequate placentation should be viewed as a distinct pathologic mechanism. According to this hypothesis, poor placentation is a distinct disorder that, once identified, typically but not always results in maternal syndrome [3]. This depends on the degree to which it triggers inflammatory signals, which may be influenced by fetal genes, and the type of maternal reaction to those signals, which would be influenced by maternal genes [4].

A very distinctive disease in the kidney known as glomerulo-endotheliosis, or PE, is characterized by swelling of endothelial and mesangial cells, inclusions of basement membranes, and minimal damage of renal epithelial podocytes. This is comparatively unique to PE and linked to the development of proteinuria (albumin in the case of glomerular lesion-induced proteinuria, β-microglobulin in the case of tubular lesion-induced proteinuria) [5]. Another possible explanation for the rise in urine protein excretion during pre-eclampsia is further proximal tubular function degradation beyond what is observed during a typical pregnancy. For low molecular weight proteins (such β2-microglobulin), which are freely filtered at the glomerulus and are found to be more prevalent in the urine of pre-eclamptic women than in those who are pregnant normally, this is especially noticeable [6]. The molecular weight of human insulin, a peptide hormone made up of 51 amino acids, is 5808

Da. It is created in the pancreatic islets of Langerhans. Insula, which means "island" in Latin, is where the name originates [7]. The hormone insulin plays a key role in controlling the body's metabolism of fat and carbohydrates. Insulin causes glucose from the blood to be absorbed by cells in the liver, muscle, and adipose tissue, where it is stored as glycogen [8]. An imbalance between the generation and expression of reactive oxygen species is known as oxidative stress. When tissues' normal redox state is disturbed, peroxides and free radicals are produced, which harm all of the cell's constituent parts, including proteins, lipids, and DNA. This can have harmful repercussions [9]. Redox signaling is the process by which certain reactive oxidative radicals can even function as messengers [10]."The aim of this study to Assessment of insulin resistance and some antioxidant markers in women with PE.

Materials and Methods

Study design

Between May 2023 and the end of Jan 2024, this study was carried out at Babylon Maternity and Pediatric Teaching Hospital. There were fourteen pregnant women with pre-eclampsia (PE, n=40) and based on gestational age and disease severity, these chosen pre-eclamptic pregnant women were split into two groups, first age PE1 (n=20) (18-30 years), the second age PE2 (n=20) (31-41 years), and third group (n=20) as gestational age (17-40) without PE (CONT) as a control group.

Determination of Fasting Blood glucose (FBG) and fasting Insulin (INS) Levels

Fasting Blood glucose (FBG) (mg/dl) was assessed by spectrophotometric method. The enzyme-linked immunosorbent assay (ELISA) was used to quantify the amount of insulin. ELISA is a sandwich-based solid phase enzyme-linked immunosorbent test. A monoclonal antibody that targets a specific antigenic location on the insulin molecule is applied to the microtiter wells. The enzyme conjugate, which is an anti-insulin antibody coupled with biotin, is incubated in an aliquot of patient sample that contains endogenous insulin. The unbound conjugate is removed by washing after incubation. The biotin-anti-insulin antibody binds to the streptavidin peroxidase enzyme complex during the second incubation stage. The quantity of insulin in the sample is directly correlated with the amount of bound HRP complex. The amount of insulin present in the patient sample is directly correlated with the color intensity that develops after the substrate solution is introduced. The standard curve of insulin determination was plotted in Figure (1).

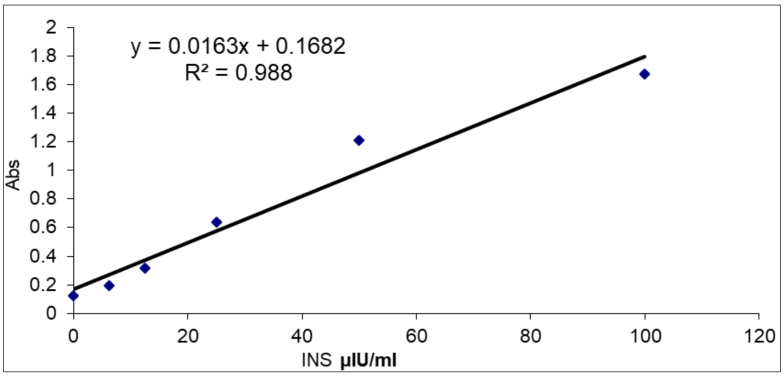

Fig 1: The standard curve for determination of INS concentration

Maternal fasting insulin and plasma glucose levels were used to calculate insulin resistance. The surrogate indices of homeostasis model assessment of insulin resistance (HOMA-IR) was used to calculate insulin resistance. The indirect indices' equation is as follows:

HOMA = [glucose (in mmol/L) × insulin (in µ IU/mL)] / 22.5.

Determination of Serum total antioxidant capacity (TAO-C) and Malondialdehyde (MDA)

Serum total antioxidant capacity (TAO-C) and Malondialdehyde (MDA) were estimated by specific procedures depending on kits protocols and measurements created by spectrophotometer.

Results

Table 1 displays the participants' characteristics. It contains information from the control groups as well as pre-eclamptic individuals. The number of patients, clinical and biochemical characteristics' mean ± SD, range, and P-values.

Table 1: The anthropometric and clinical characteristics of different groups.

Parameters	PE1 N=20 Mean+SD	PE2 N=20 Mean+SD	CONT N=20 Mean+SD
Age (Years) Range	26.2±4.9 17-30	37.3±4.9 31-40	26.2±8.4 19-36
BMI (Kg/m^2) Range	34.4±4.0 27.7-39.1	33.5±4.5 27-46.7	23.5±5.8 24.4-45.6
Gestational age (Weeks) Range	23.2±2.4 21-29.5	32.3±4.2 27-38.5	34.4±3.5 18-39.5
BP (mmHg) Range	140.7±7.1 141-167	146±5.0 143-159	128±3.3 110-130

Table 2 displays the biochemical parameretrs (INS, FBG, HOMA-IR). It contains information from the control groups as well as pre-eclamptic women groups (PE1 and PE2).

Table 2: The biochemical parameretrs results

Parameters	PE1 N=20 Mean±SD	PE2 N=20 Mean±SD	CONT N=20 Mean±SD	P-value
FBS (mmol/l)	7.2±0.7	9.4±1.3	4.9.0±0.7	<0.05
INS (μIU/ml)	13.9±4.2	18. 9±5.3	5. 66±3.8	<0.05
HOMA-IR	4.1±0.09	5.1±1.89	1.3±1.6	<0.05
TAO-C (mmol/l)	1.58±0.8	1.79±0.7	3.08±0.89	<0.05
MDA (μmol/l)	7.2±2.4	9.5±2.5	2.5±1.6	<0.05

Figure 2 displays the boxplot of antioxidant (TAO-C) and lipid peroxidation (MDA) parameters. It contains information from the control groups as well as pre-eclamptic women groups (PE1 and PE2).

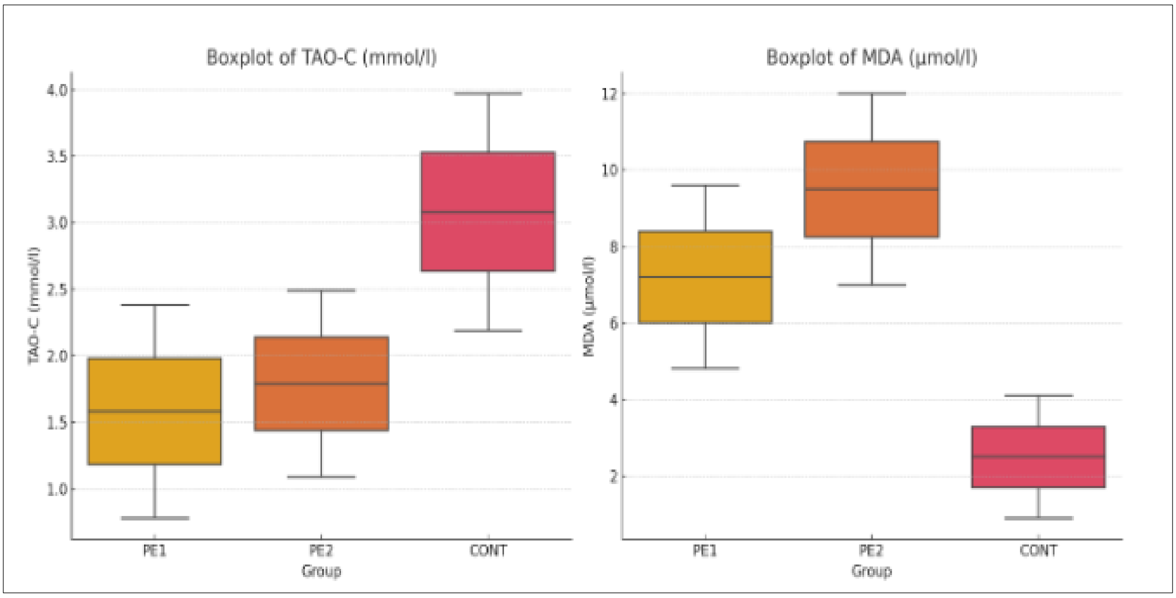

Fig 2: TAO-C and MDA levels in study groups

Figure 3 shown the ROC curve for insulin (INS) levels used to distinguish between pre-eclamptic (PE1 + PE2) and control (CONT) groups.

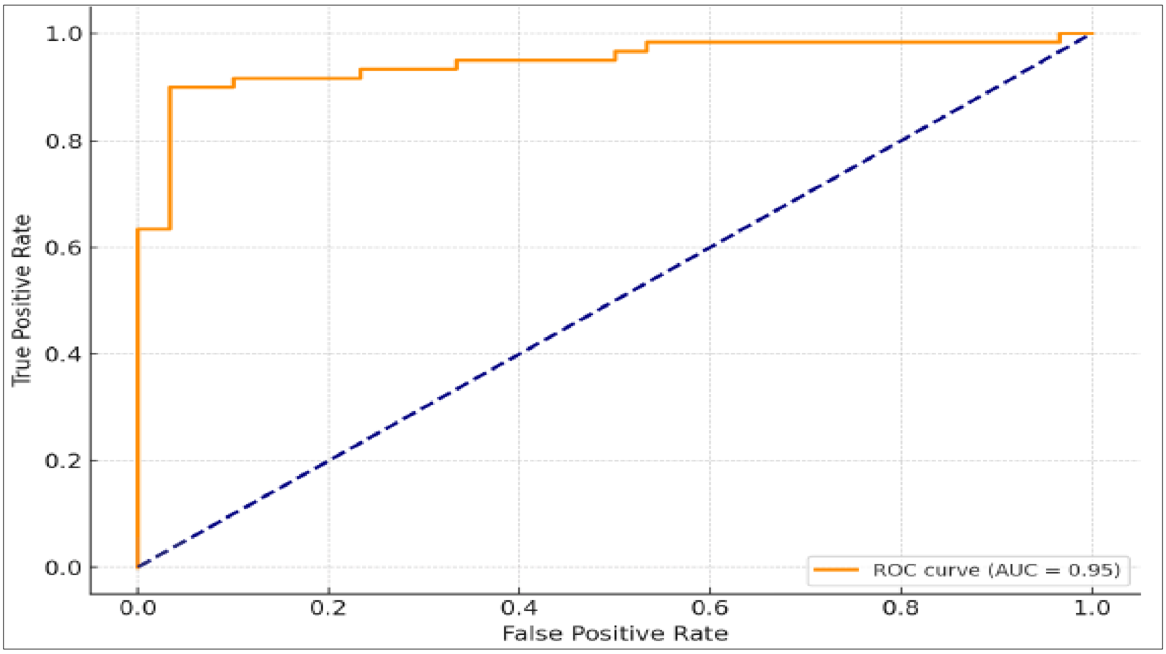

Fig 3: ROC curve for INS to predict pre-eclampsia patients

Discussion

Insulin resistance and oxidative stress play integral roles in the pathophysiology of pre-eclampsia Authors: Mireille G. Silva Indesta A. D.A. Rwaished *et al*. There was a considerably higher degree of insulin and HOMA-IR in women with PE compared to control women, especially in older age (PE2) women, suggesting that they have significantly higher levels of fasting glucose in PE.

Preeclampsia is a pregnancy-associated systemic illness that is marked by hypertension, proteinuria, and edema, and it has an impact on the maternal vascular unit. The increase in vascular resistance and endothelial dysfunction is linked to the clinical aspects observed in affected women [12]. The cause of preeclampsia is multifactorial; two of included possible causes are immunological derangements, (immune response of mother against paternal immune antigens in placenta) genetic components, Increased insulin resistance and further oxidative stress followed by endothelial dysfunction [13].

Metabolic disturbances in women with preeclampsia resemble those in non-pregnant patients with coronary heart disease, suggesting common pathophysiological mechanisms. These metabolic changes manifest as hypertriglyceridemia, hyperleptinemia, oxidative stress, insulin resistance, and systemic chronic inflammation [14, 15]. Moreover, systemic inflammation, as reflected by elevated C-reactive protein (CRP) levels as well as major alterations in lipidas and lipoproteins levels are linked to an increased risk of preeclampsia [16]. The expression of some biochemical factors of preeclampsia resembles those appearing in insulin resistance syndrome (1) which directs the thought to a potential association between insulin resistance and preeclampsia [17].

Insulin resistance is a major metabolic abnormality during preeclamptic pregnancies, and several studies have demonstrated that preeclampsia is marked by a state of augmented insulin resistance [18]. This metabolic derangement is detectable prior to the clinical onset of preeclampsia and has been demonstrated as elevated fasting insulin and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) values in the first trimester in women who go on to develop preeclampsia [19]. Insulin resistance during pregnancy may persist throughout the entire gestation period, and multiple studies have documented significantly elevated levels of insulin as well as HOMA-IR in women with preeclampsia as compared to normotensive pregnant women [20].

Furthermore, elevated MDA and decreased TAO-C levels in these patients indicate a definite status of oxidative imbalance. As implied by the extent of these changes in the PE2 cohort, maternal age appears to smooth over metabolic and oxidative deficits characteristic of pre-eclamptic pregnancies. This study showed that women with PE (especially in the older age group PE2) had significant changes in insulin resistance and oxidative stress biochemical parameters. These findings add to the growing evidence that PE is associated with metabolic morbidities and oxidative imbalance. Compared to normotensive controls, pre-eclamptic women showed significantly elevations in fasting blood glucose (FBG), insulin (INS), and HOMA-IR index indicative of insulin resistance. These effects were stronger in the PE2 group, suggesting an incremental decline in metabolic function with age. Other recent studies have also reported similar results, showing that insulin resistance may precede and promote the development of PE by influencing perfusion and by damaging the endothelium (21). Oxidative stress is known to be a major pathological mechanism in PE. The present study also demonstrated significantly decreased total antioxidant capacity (TAO-C) and increased malondialdehyde (MDA) concentrations in the PE groups, particularly the PE2 group. This imbalance indicate an enhanced lipid peroxidation process, further supporting the role of oxidative stress in the pathophysiology of PE. The current study provides some additional support for these findings, as multiple studies have shown elevated levels of reactive oxygen species (ROS) with depleted antioxidant defenses in women with PE [22]. Herein the analysis of ROC curve to assess the diagnosis of insulin (INS) level based on the differentiation of pre-eclamptic women (PE1 + PE2) with control (CONT) groups is hereby presented. The different age-related distinctions within groups PE1 and PE2 should also be noted. Women with PE2 had inferior oxidative and metabolic parameters, implying a potential role of maternal age in the severity of PE, with accumulated oxidative stress and insulin resistance. This is in line with recent studies demonstrating that advanced maternal age is correlated with more advanced disease of PE, and adverse perinatal outcomes [23]. These findings overall support the hypothesis that PE is a multifactorial disease characterized by metabolic and oxidative dysfunction. The monitoring of these biomarkers may have predictive and therapeutic significance, especially in high-risk pregnancies.

Conclusion

The results highlight the significance of early screening for insulin resistance and oxidative stress in pregnant women at risk of PE. Fattening metabolic health and antioxidant capacity interventions are potentially promising approaches to prevention and management. This may give rise to causality and further direct targeted therapeutic strategies to alleviate the burden of pre-eclampsia. The ROC analysis demonstrates that each marker, but particularly insulin levels, are potentially useful predictive biomarkers for pre-eclampsia. This lends support to the notion that insulin resistance is not simply associated with, but may be predictive of, pre-eclampsia. However, reporting the exact area under the curve (AUC), sensitivity, specificity, and optimal cutoff from the ROC analysis would strengthen this study.

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