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Original Research Article

Role of Interleukins IL-2, IL-8 and IL-10 in Preeclampsia Patients at Tertiary Care Hospital from North West Rajasthan

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Abstract

Introduction: Pre-eclampsia is a multisystemic disorder of pregnancy, with the clinical diagnostic features of hypertension and proteinuria.

Aim: To study the role of interleukins IL-2, IL-8 and IL-10 in the etiology of pre-eclampsia.

Methods: This prospective hospital-based study was conducted on 60 cases including 30 patients with Pre-eclampsia and 30 healthy patients who were admitted in hospital from 1st Oct 2021 to 31 august 2022 at Department of Obstetrics and Gynaecology, Sardar Patel Medical College & AGH, Bikaner (Rajasthan).

Results: Mean age in group A was 26.23 ±3.19 year and in group B mean age was 25.53 ±3.37 year. Both groups were comparable in terms of area, education, socioeconomic status.7 (23.33%) cases in group A and in group B 4(13.33%) cases had family history of hypertension. BMI in group A was 24.44 ±2.09 kg/m2 whereas 22.98 ±1.64 kg/m2 in group B. Mean values of IL-2, IL-8, IL-10 in group A were 322.09 ± 125.36 pg/ml, 806.14 ± 450.86 pg/ml, 271.21±158.50 pg/ml whereas in group B, 312.46 ± 22.79 pg/ml, 285.38±106.43, 174.42±60.79 pg/ml respectively which were significantly different in both the groups. Mean Systolic blood pressure and uric acid were statistically significantly associated with higher level of IL-8and IL-10 ($p<0.05$).

Conclusion: Interleukins can be used as biomarkers for the prediction of pre-eclampsia in the initial stages which can add in better clinical management.

Keywords: Interleukins, pre-eclampsia.

Introduction

Pre-eclampsia is a systemic disorder unique to pregnancy occurring in 4-8% of pregnant women. It is a multi- system hypertensive disease of pregnancy with significant rates of maternal and perinatal morbidity. WHO defines pre-eclampsia as "Blood pressure of 140/90 mm Hg or greater in women with previously normal blood pressure

respectively, on two occasions at least 4 hour apart and new onset end organ damage, including proteinuria after 20 week of gestation".[1] During normal implantation, trophoblast invade the decidualized endometrium, which leads to spiral artery remodelling and obliteration of tunica media of myometrial spiral arteries, allowing increase blood flow to the placenta, all independent of maternal vasomotor changes. During the first half of human pregnancy, uteroplacental vessels undergo a series of pregnancy-specific changes including 1) apparent replacement of endothelium and smooth muscle of tunica media by invasive trophoblast, 2) loss of elasticity, 3) dilatation to wide, incontractile tubes, and 4) loss of vasomotor control.[2]

Neutrophil activation occurs in pre-eclampsia, the mechanism underlying this activation remains unknown.Cytokines could trigger neutrophil activation, expression of von willebrand factor, and cell adhesion on endothelium with resultant vascular damage. But there are conflicting reports in the literature on serum concentrations of interleukins in pre-eclampsia. Some studies show decrease in concentration of IL-10 as compared to normal pregnant women. As a result of this type of discrepancy, we decided to measure the serum concentration of interleukins in women with pre-eclampsia and to determine if they differ from those of normal age matches pregnant women.

Aim

To study the role of interleukins IL-2, IL-8 and IL-10 in the etiology of pre-eclampsia.

Methods

This prospective hospital-based study was conducted on 60 cases including 30 patients with Pre-eclampsia (group A) and 30 healthy patients (group B) who were admitted in hospital from 1st Oct 2021 to 31 august 2022 at Department of Obstetrics and Gynaecology, Sardar Patel Medical College & AGH, Bikaner (Rajasthan).

INCLUSION CRITERIA: Pregnant women whose Systolic blood pressure >140 mm Hg, Diastolic blood pressure >90 mm Hg, Proteinuria > 3 gm per 24 hour urine sample with Single viable fetus and was Normotensive before 20 week of gestation

EXCLUSION CRITERIA: Pregnancy with any infectious disease, HIV, Fever, Coagulopathies, Coronary heart disease, Lung disease, Chronic hypertension, Diabetes mellitus, Renal disease, Patient in labour, Placental abruption, twin pregnancy were excluded from the study.

Based on inclusion and exclusion criteria, patients whose blood pressure was >140/90 mm Hg and proteinuria >3gm in 24-hour urine sample were screened and selected from admitted patients after informed consent. In a clean transparent tube 4-5 ml of venous blood was drawn of patient and controls. Serum separated by centrifugation and was stored at -70 degree for further analysis of interleukins (IL-2,6,8,10) by FINE TEST kit by ELISA method at MRU at SPMC Bikaner. The method was quantitative method measures the concentration in nm/ml which was converted in pg/ml. with test values we also test 8 dilutions for each interleukin sample. Average value for IL-2 was 311.13 pg/ml, IL-8 was 542.3 pg/ml and 411.36 pg/ml for IL-10. All patients were admitted to hospital, managed according to Gestational age, to prevent maternal and fetal complications.All maternal and fetal details were recorded.

The data was entered and analysed systematically. Categorical variables were summarised as percentages and quantitative variables were summarised as mean with standard deviation (SD), or median with inter-quartile range (IQR) according to the distribution of variable. Appropriate

statistical test was used to compare the outcome between two sub-groups.

Results

In group A, majority of cases 19 (63.33%) belonged to age group 26-30 years while in group B majority of cases 14 (46.67%) belonged to 21-25 years. Mean age in group A was 26.23 ±3.19 year while in group B mean age was 25.53 ±3.37 year. (p>0.05). Both groups were comparable in terms of area, education, socioeconomic status. (table 1) 7 (23.33%) cases in group A and in group B 4(13.33%) cases had family history of hypertension.BMI in group A was 24.44 ±2.09 kg/m2 whereas 22.98 ±1.64 kg/m2 in group B. Mean values of IL-2 in group A was 322.09 ± 125.36 pg/ml whereas 312.46 ± 22.79 pg/ml in group B(p>0.05). Mean value of IL-8 in group A was 806.14±450.86 pg/ml whereas 285.38 ± 106.43 in group B(p<0.05).Mean value of IL-10 in group A was 271.21 ± 158.50 pg/ml whereas 174.42 ± 60.79 pg/ml in group B (p<0.05). (table 2)

Table 1 : Sociodemographic distribution of study population

Sociodemographic variable	Group A	Group B	P value
Age (Mean ± Sd)	26.23 ± 3.19	25.53 ± 3.37	0.412
Rural	10 (33.33)	13 (43.33)	0.980
Urban	20 (66.67)	17 (56.67)	
Primigravida	20 (66.67)	17 (56.67)	0.595
Multigravida	10 (33.33)	13 (43.33)	
Gestational age (mean)	36.1 ±1.88	38 ±1.0	0.056
BMI (Mean ± SD)	24.44±2.09	22.98± 1.64	0.139
family history of hypertension	7 (23.33)	4 (13.33)	0.495

Table 2: Clinical parameters of study population

Clinical Parameters	Group A	Group B	P value
Systolic BP(mm of Hg)	156.46 ± 9.33	123.66 ± 7.57	0.0001*
Diastolic BP (mm of Hg)	102.6 ± 6.12	79.33 ± 6.30	0.0001*
Mean platelet (lac/l)	191.36 ± 80.23	243.16 ± 114.49	0.047*
Serum creatinine (mg/ dl)	0.75 ± 0.28	0.45 ± 0.18	0.0001*
Blood urea (mg/dl)	26.72 ± 7.97	19.19 ± 4.16	0.0001*
Serum uric acid (mg/dl)	6.32 ± 1.3	4.54 ± 1.2	0.0001*
SGOT (unit/l)	43.73 ± 30.54	18.06 ± 4.26	0.0001*
SGPT (unit/l)	37.57 ± 36.87	20.90 ± 5.96	0.018*

Table 3: Distribution of subjects according to their IL-2, IL-8, IL-10

Mean	Group A	Group B	P value
IL-2 (pg/ml)	322.09 ± 125.36	312.46 ± 22.79	0.680
IL-8 (pg/ml)	806.14 ± 450.86	285.38 ± 106.43	0.0001*
IL-10 (pg/ml)	271.21 ± 158.50	174.42 ± 60.79	0.003*

Discussion

In our study, majority of cases in group A, 19 (63.33%) belonged to age group 26-30 years while in group B majority of cases 14 (46.67%) belonged to 21-25 years. Similarly

in study by Zulaihatu Sarkin-Pawa *et al* (2020)[3] Thirty-five percent of the women were between 20 and 24 years of age. In our study, mean age in group A was 26.23 ±3.19 year while in group B mean age was 25.53 ±3.37 year and this difference was found statistically insignificant (p>0.05). Similarly J Tavakkol Afshari *et al* (2005)[4] found the mean age of normotensive group was 27.2 ± 5.8 yr whereas 28.4 ± 4.9 yr in preeclampsia group. BMI in group A was 24.44 ±2.09kg/m2 whereas 22.98 ±1.64 kg/m2 in group B (p>0.05). Also Udenze I *et al* (2015)[5] found that in pre-eclampsia mean BMI was 29.12±4.69 kg/m^2 whereas 26.97±4.91 kg/m^2 in controls.

In group A majority of cases 20 (66.67%) while in group B 17 (56.67%) primigravida. More primigravidas were in group A as association of pre-eclampsia is more with primigravida. On applying chi square test, the difference was found statistically insignificant (P>0.05). Similarly Zulaihatu Sarkin-Pawa *et al* (2020)[3] found that nulliparous women constituted 65.9% of the patients.

Various interleukins are associated with pregnancy with pre-eclampsia like IL 2,4,6,8,10,12,18,TNF α etc. In this study we studied association of interleukins (IL-2, 8, 10) with pre-eclampsia as a predictor.

In a normal pregnancy, there is a shift in the Th1/Th2 immunebalance towards a Th2 type immune response that protects the fetus from a Th1 (cytotoxic) immune response that can harm the fetus with its products such as IL-2.[6]

In our study, Mean IL-2 in group A was 322.09 ± 125.36 pg/ml while in group B mean IL- 2 was 312.46 ± 22.79 pg/ml and this difference was found statistically insignificant (p>0.05). Similarly Samuel O. Olusi *et al* (2000)[7] the plasma concentration of IL-2 was slightly higher in normal pregnant women (76.3±13.7 pg/mL) than in pre-eclampsia (57.8±10.8 pg/mL), the difference was not statistically significant (*P*=0.3).

IL-8 cytokine is considered to be pro-inflammatory cytokine and would therefore be expected to be increased in pre-eclampsia.

In our study, mean IL-8 in group A was 806.14 ± 450.86 pg/ml while in group B mean IL-8 was 285.38±106.43 pg/ml and this difference was found statistically significant(p<0.05). On contrary Beatrice Mosimann *et al* (2013)[8] found that the proportions of women with detectable concentrations of IL-8 were significantly lower in those with PE than in the controls (IL-8:13/39(3.27pg/ml, range 0.61–6.08)) vs 83/117 (3.50 pg/ml, range 0.33–60.24)), P < 0.0001). Also Yvonne Jonsson (2006)[9] found that Pre-eclamptic women had significantly increased levels of circulating IL-8 (p=0.003) compared to women with normal pregnancies.

The anti-inflammatory cytokines (IL-10) are crucial for the functioning of T helper cell 2 (Th2) and regulatory T cells (Treg)[10] for the successful progression of pregnancy. Any modulation in their level may affect the functioning of several immunological and apoptotic pathways leading to pregnancy-associated syndromes like pre-eclampsia.[11]

In our study, mean IL-10 in group A was 271.21 ± 158.50 pg/ml while in group B mean IL-10 was 174.42 ± 60.79 pg/ml and this difference was found statistically significant (p<0.05). On contrary Meryl C Nath *et al* (2020) found that at the time of active disease, women with preeclampsia (n=1599) had significantly lower IL-10 levels compared with normotensive controls (n=1998; standardised mean differences, -0.79 [95% CI, -1.22 to -0.35]; P=0.0004).[12]

The variability in the differences in IL-10 results in the pre-eclampsia and

normotensive groups obtained in some previous good studies explained that it was likely to be influenced by the research design used, including ethnic or differences in respondents, the method which is used to detect IL-10, and the gestational age at which the sample was obtained. In addition, the short half-life of IL-10 can also contribute to variable research results.[13]

In our study, high level of IL-2 had statistically insignificant association with Systolic Blood pressure, uric acid, BMI and Diastolic blood pressure.In our study, high level of IL-8 and IL-10 was significantly associated with high Systolic Blood pressure, and uric acid and whereas not significantly associated with Diastolic blood pressure and BMI. In our study IL-8, IL-10 level had positive correlation with high systolic blood pressure and Uric acid however no positive correlation was found with diastolic blood pressure and BMI.

Similarly P Žák *et al* (2019)[14] observed in 40 women found a significant positive correlation between IL-10 levels and systolic blood pressure (SBP) and diastolic blood pressure in the second trimester ($p<0.001$) and the third trimester ($p<0.001$).

Also Riza Madazli *et al* (2003)[15] found that the plasma levels of IL-10 significantly increased with the increments in diastolic blood pressure.

To the best of our knowledge this is the first study of its type to demonstrate a correlation between plasma IL-2, IL-8 and IL-10 levels with blood pressure and uric acid levels as a marker of endothelial cell damage. Plasma levels of IL-8 and IL-10 significantly increased with the increments in blood pressure and uric acid.This indicates a correlation between the severity of the disease process and the levels of these cytokines.

Conclusion

Our study shows that pre-eclampsia is significantly associated with higher level of IL-8 and IL-10 ($p<0.05$). Our study shows interleukins can be used as biomarkers for the prediction and better clinical management of pre-eclampsia in the initial stages.Integrative studies revealing the molecular mechanism responsible for cellular communication between interleukins and signalling pathways are important to determine their exact effect on inflammation process. The new therapeutic strategies targeting the pool of these pro- and anti-inflammatory interleukins may be designed for the treatment of this disorder. Since all the interleukin function in a spatiotemporal manner, a large cohort study including several immune system interleukins may be warranted for better understanding of the immunological etiology and pathophysiology of pre-eclampsia.

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