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ORIGINAL ARTICLE

Frequency of maternal high serum hs-C reactive protein level in pre-eclampsia patients.

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ABSTRACT… Objective: To determine the frequency of high serum high-sensitivity C-reactive protein (hs-CRP) level in pre-eclampsia women. **Study Design:** Cross-sectional study. **Setting:** Department of Obstetrics and Gynaecology, Bahawalpur Medical and Dental College, Bahawalpur. **Period:** October 2022 to February 2023. **Material & Methods:** A total of 206 women aged between 20-35 years with singleton pregnancy, gestational age >20 weeks, any parity, and pre-eclampsia were analyzed. High serum hs-CRP was defined as when serum hs-CRP was above 7.0mg/L. The patient was diagnosed with pre-eclampsia when she had systolic blood pressure ≥140mmHg, measured at two different intervals after 20 weeks of pregnancy and proteinuria (200 mg or more per 24-hour period) by laboratory test. The frequency of high hs-CRP was noted. **Results:** In a total of 206 females, the mean age was 29.69±3.12 years while 120 (58.3%) were aged between 18-30 years. The mean gestational age and parity were 27.83±2.64 weeks and 2.65±1.44 respectively. Frequency of high serum hs-CRP was noted in 135 (65.5%) females with pre-eclampsia. It was found that age (p=0.686), gestational age (0.253) and parity (p=0.927) were not having any statistically significant association with high serum hs-CRP. BMI was noted to have significant association with high serum hs-CRP (p<0.001). **Conclusion:** The frequency of high maternal hs-CRP was very high (65.5%) among females with pre-eclampsia.

Key words: Blood Pressure, Gestational Age, hs-CRP, Pre-eclampsia, Proteinuria.

INTRODUCTION

Pre-eclempsia (derived from "eklampsia", a Greek word which means sudden flashing), is a systemic syndrome which manifests hypertension, proteinuria and oedema. More often, it gets complicated with the occurrence of renal failure, pulmonary oedema and coagulopathy like symptoms, and can develop into eclampsia.[1] The literature highlights between 10-15% maternal mortality due to pre-eclampsia and eclampsia.[2] Among all pregnancies, hypertensive disorders affect around 10% of all pregnancies while pre-eclampsia is present between 3-5% of all pregnancies.[3]

The literature describes abnormal trophoblastic invasion, immunologic mal-adaptation among fetal, maternal and paternal tissues, and genetic aspects, have been among the factors behind pre-eclampsia.[4] Defective placentation creates an inflammatory change, therefore, angiogenic and metabolic factors and some other mediators of inflammation are thought to have damaging effects on endothelial cells.[5] Elevated responsiveness of the maternal circulating leukocytes contributes in the malfunctioning of endothelial cell, as have been advocated.[6] An inflammatory reaction and tissue injury are depicted by "high-sensitivity C-reactive protein (hs- CRP)", which is a sensitive prognostic marker and found elevated during pregnancy.[7,8] Human placenta is known to yield and release hs-CRP mainly into the maternal circulation.[9] The elevated levels of CRP in the amniotic fluid and fetal urine have been mentioned to elevate the chances of adverse pregnancy outcomes.[9]

Previously, rise in the maternal hs-CRP level in pre-eclamptic women has been demonstrated

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in the studies.[10-13] It has been advocated that for the assessment of severity of pre-eclampsia, maternal serum CRP level might be an effective marker.[12,13] Kashanian M et al has uncovered in their study that maternal high serum hs-CRP level was observed in 73.91% of the pre-eclampsia patients.[14] According to Nanda K et al, the frequency of maternal high serum hs-CRP in patients with pre-eclampsia was 60%.[15]

It is important to investigate the role of serum hs-CRP in pre-eclampsia through an augmented data. Therefore we planned to conduct this study. This study was though to pave the way for considering serum hs-CRP evaluation early to predict preeclampsia and manage the pregnancy accordingly. This study was done to determine the frequency of maternal high serum hs-CRP level in pre-eclampsia patients.

MATERIAL & METHODS

This cross-sectional study was performed at "The Department of Obstetrics and Gynaecology, Bahawalpur Medical and Dental College", Bahawalpur from October 2022 to February 2023. A sample size of 206 was calculated by using $n= z^2pq/d^2$, where expected proportion (maternal high serum hs-c reactive protein level) p= 73.9%,[14] q= 1-p and d= 6% at 95% confidence level and 5% margin of error.

Inclusion criteria were the women aged between 20-35 years with singleton pregnancy, gestational age >20 weeks, any parity, and pre-eclampsia. Exclusion criteria were the patients with history of hypertension, diabetes and renal disease. Women with body mass index (BMI) ≥35 kg/m^2 were also excluded. High serum hs-CRP was defined as when serum hs-CRP laboratory test (latex agglutination test) of patient resulted in > 7.0mg/L. The patient was diagnosed with pre-eclampsia when she had systolic blood pressure ≥140mmHg, measured at two different intervals after 20 weeks of pregnancy and proteinuria (200 mg or more per 24-hour period) by laboratory test. Singleton pregnancy and gestational age were confirmed on the basis of obstetrical ultrasonography. The patients were briefed about the objectives of the study and were ensured about their provided information to be kept confidential. It was also conveyed to them that no risks were associated with this study. Informed and written consent was acquired from each patient. Approval from "Institutional Ethical Committee" was also obtained (IEC/22/12).

At the time of enrollment, socio-demographic characteristics (name, age, parity, BMI,) were noted. After an overnight fast, venous blood sample was drawn by using a sterile needle and syringe and sent to institutional laboratory to assess the level of hs-CRP. This test was performed by a senior pathologist having minimum of 5 year experience. The frequency of maternal high serum hs-CRP was noted. A special proforma was designed to record study information.

Data was analyzed by "Statistical Package for Social Sciences (SPSS)", version 26.0. Qualitative variables like age groups, parity and high serum hs-CRP level were shown as frequency and percentages. Quantitative data were presented as mean and standard deviation (SD). Effect modifiers were controlled by stratified tables and post-stratification chi-square test was employed taking $p<0.05$ as significant.

RESULTS

In a total of 206 females, the mean age was 29.69±3.12 years (ranging between 22-35 years) while 120 (58.3%) were aged between 18-30 years. The mean gestational age and parity were 27.83±2.64 weeks and 2.65±1.44 respectively.

Characteristics		Number (%)
Age (years)	18-30	120 (58.3%)
	31-35	86 (41.7%)
Gestational age (weeks)	≤32	188 (91.3%)
	>32	18 (8.7%)
Parity	≤1	63 (30.6%)
	>1	143 (69.4%)
Body mass index (kg/m^2)	<25	93 (45.1%)
	≥25	113 (54.9%)

Table-I. Characteristics of females with pre-eclampsia (n=206)

Frequency of high serum hs-CRP was noted in 135 (65.5%) females with pre-eclampsia as shown in Figure-1.

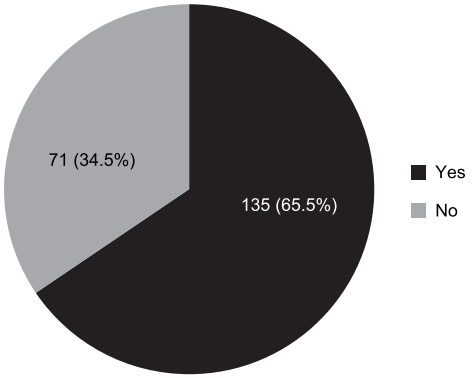

Figure-1. Frequency of high serum high-sensitivity C-Reactive Protein (n=206)

It was found that age (p=0.686), gestational age (0.253) and parity (p=0.927) were not having any statistically significant association with high serum hs-CRP. BMI was noted to have significant association with high serum hs-CRP (p<0.001). Stratification of high serum hs-CRP with respect to study variables is shown in Table-II.

Characteristics		High Serum hs-CRP		P-Value
		Yes (n=135)	No (n=71)	
Age (years)	18-30	80 (59.3%)	40 (56.3%)	0.686
	31-35	55 (40.7%)	31 (43.7%)	
Gestational age (weeks)	≤32	121 (89.6%)	67 (94.4%)	0.253
	>32	14 (10.4%)	4 (5.6%)	
Parity	≤1	41 (30.4%)	22 (31.0%)	0.927
	>1	94 (69.6%)	49 (69.0%)	
Body mass index (kg/m^2)	<25	89 (65.9%)	4 (5.6%)	<0.001
	≥25	46 (34.1%)	67 (94.4%)	

Table-II. Stratification of high serum hs-CRP with respect to study variables (N=206)

DISCUSSION

Pre-eclampsia is a multi-factorial entity involving multiple organs, usually occurring after 20th week of gestation in a previously non-hypertensive women.[16] The recent decades have shown advancements regarding role of hs-CRP for the diagnosis of sub-clinical infections or underlying inflammatory disorders. Some researchers have highlighted the possible linkage between high hs-CRP and preeclampsia.[17] As, majority of the women face pregnancy related complications in the latter half of the pregnancy, it is of utmost importance if prediction of most occurring complications is done well before the time of occurrence. Recent literature highlight that hs-CRP is a better predictor of inflammation than traditional CRP.[18]

We noted that serum hs-CRP levels were high in 65.5% pre-eclampsia women. A study done by Aruna P et al from India noted that serum hs-CRP level was 8.07±2.09 mg/dl versus 1.71±0.85 among pre-eclampsia and normal pregnant females (p<0.001).[19] Ayatollahi H et al from Iran found that higher levels of hs-CRP among pregnant females with pre-eclampsia when compared to those with normal pregnancy.[20] The authors also highlighted the importance of hs-CRP in predicting the severity of pre-eclampsia (p<0.05).[20] A study by Teran E et al from UK shared that CRP was significantly high among pregnant females with pre-eclampsia when compared to those with normal pregnant (4.11±0.37 mg/dl vs. 2.49±0.26 mg/dl, p=0.001).[21] A study done by Harmin S et al from Bangladesh found that there was a strong association between CRP and pre-eclampsia[22] Their findings shared that CRP was raised in 68% of pregnant women with pre-eclampsia which is very close to what we noted in the present study (65.5%). A study done by Hvilsom et al found that high levels of CRP were significantly associated with nearly 2-fold rise in the chances of preterm birth.[23] Some other researchers have also observed that high serum CRP levels are linked with intrauterine growth retardation.[24] As vast majority of pre-eclampsia women have high levels of hs-CRP, these women should be monitored for the severity of pre-eclampsia and related outcomes.

Our study showed that 65.5% of pregnant women with pre-eclampsia were having high levels of serum hs-CRP which is considered to be an important inflammatory marker. Considering

the fact that hs-CRP is a simple and affordable investigation, this should be done among all pregnant women with pre-eclampsia. Future studies should be planned to evaluate the outcome of females with high levels of hs-CRP to measure its impact on the maternal and fetal outcomes.

There were few limitations of this study. The present study was a single center study with a cross-sectional design; further studies with prospective designs involving multiple centers need to be planned.

CONCLUSION

The frequency of high maternal hs-CRP was very high (65.5%) among females with pre-eclampsia.

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2	Sana Javed	Methodology, Discussion.	
3	Bushra Mehmod	Data collection, Literature Review.	
4	Bazgha Sahar	Proof reading, Literature Review.	
5	Shehla Tabassum	Study concept, Data analysis, Proof reading.	
6	Abeera Malik	Critical Revisions, Data Interpretation.	