

PREDICTIVE VALUE OF MATERNAL SERUM C- REACTIVE PROTEIN LEVELS WITH SEVERITY OF PREECLAMPSIA

Mahmoud Ahmed Gharib; Mostafa Shafik Mostafa; Mervat Mohammed Harira and Amany Ali Ali Attia

Obstetrics and Gynecology Department, Faculty of Medicine, Zagazig University

ABSTRACT

Background & objectives: Preeclampsia (PE) is a hypertension disorder of pregnancy that develop in 4-5% . Elevated blood pressure and proteinuria after 20 weeks of conception characterizing the disease. Its complication including a major cause of morbidity and mortality to mother and fetus. increased **C-reactive protein (CRP)** level and inflammatory cytokines in PE women have been noted.. CRP is considered a sensitive inflammatory marker in the body as its level increases in response to inflammation due to infection or tissue injury. correlated levels of CRP with severity of preeclampsia and determination of CRP levels in maternal serum in the 3rd trimester of pregnant women proved of great value in predicting preeclampsia prognosis. Authers used Proteinuria and blood pressures as parameters for severity of PE. **Aim of the work:** of this study was to investigate **C-reactive protein (CRP)** level in preeclampsia (PE) and its correlation with the severity of the disease. **Material &methodes:**This case control study included 15 women with mild PE, 15 women with severe PE, and 15 healthy pregnant women. They were selected in the third trimester of their pregnancy in Faculty of Medicine Zagazig University Hospital during the period from August 2013 to June 2014. blood pressure and level of proteinuria were used as indicators of the severity of the disease. The results were analyzed by t-test and spearman's rank correlation coefficient. **Results** of this study concerning levels of CRP revealed a highly statistically significant increase ($p < 0.001$) in serum of both mild pre-eclamptic women (group A) (median - range: 15 [7.1-30.] mg/L), and severe pre-eclamptic women (group B) (median- range : 43.1 [16.00-53.00] mg/L) when compared to their matched controls (group C) (median - range: 1.80[0.8-3.20] mg/L). There were significant correlations between serum CRP levels and Systolic blood pressure ($r = 0.643$, $p < 0.001$) and diastolic blood pressure ($r = 0.729$, $p < 0.001$) also there was a positive correlation between CRP levels and biochemical parameters as ALT ($r = 0.604$, $p < 0.001$), AST($r = 0.632$, $p < 0.001$), s.uric acid($r = 0.648$, $p < 0.001$), proteinuria(0.792, $p < 0.001$), We showed higher levels of CRP in women with PE. **Conclusion:** high serum CRP levels in patient with preeclampsia , so, correlated with disease severity.

Key words: C - reactive protein, severity of disease, preeclampsia

Correspondence author: Amany Ali Ali Attia

Tel.: +201157441222

Received: January 2016

Accepted: February 2016

INTRODUCTION

Preeclampsia (PE) is a hypertension disorder of pregnancy accompanied with endothelial cell destruction most often in primiparity .Elevated blood pressure and proteinuria after 20 weeks of conception characterizing the disease. Preeclampsia may also be accompanied by rapid weight gain , and edema. Its complication including a major cause of morbidity and mortality to mother and fetus. its cause is unknown and its pathophysiology also is not completely known. there are no completely effective treatments. the antenatal care can not balance between the mother risk to continue pregnancy and early termination with risk for the baby ^[1].

Proteinuria is considered by excretion of 300 mg/24 hours, a urine protein/ creatinine ratio of 0.3, or a qualitative 1dipstick reading. The dipstick value of 1 has many false-positive and false-negative results and is the least useful ^[1].

PE occurs in 4-5% of pregnancies worldwide and responsible for 12-18 % of pregnancy-related maternal deaths in developing countries ^[2].

Preeclampsia, is a systemic disease as many organs are involved, The disease can lead to many acute maternal complications, such as progression to eclampsia , acute renal or hepatic failure, pulmonary edema, the HELLP syndrome (hemolysis, elevated levels of liver enzymes, and low platelet count).

disseminated intravascular coagulopathy (DIC), hypertensive emergency, hypertensive encephalopathy and cortical blindness. Furthermore, there is increased risk for long-term cardiovascular disease [3].

Although PE remains a disease of theories, an improved understanding of the pathogenesis of PE has raised the possibility that the spiral arteries during the interaction between maternal and fetal sides at the time of trophoblastic invasion with decrease in remodelling causing of placental insufficiency. Causing production and release of inflammatory markers in the systemic circulation of mother which are involved in the endothelial dysfunction; the hallmark pathological finding in PE [4].

C- reactive protein found in the blood is considered as an acute-phase protein in which its level increases during inflammation, tissue damage, infection and neoplasia. [5].

Liver produces CRP in response to inflammatory cytokines, IL-6 & TNF- α stimulation.

Moreover, \uparrow concentrations of CRP and cytokines in PE women have been reported [6].

Also in PE the endothelial malfunction has been accompanied with more maternal inflammatory response to pregnancy [6].

Kumru et al., 2006 correlated CRP levels with severity of PE. He found that there is a +ve correlation between serum CRP levels & (DBP, SBP and protein excretion in urine) in PE. Proteinuria and BP were considered as indicators of PE severity [7].

Determination of serum CRP levels in the 3rd trimester of pregnancy has a great predicting value of PE prognosis. [7].

The aim of this study is to investigate CRP level in PE and its correlation with the severity of the disease and other biochemical and clinical parameters in PE.

Patient and Method

This prospective case control study comparing the level of CRP in cases with preeclampsia and normotensive pregnant ladies. This study was carried out in Faculty of Medicine Zagazig University Hospital during the period from August 2013 to June 2014.

Sample Size:

According to power 80%, 95% CI interval.

CRP mean of severe PE 34 ± 25 and CRP mean of mild PE 14.2 ± 11.6 so the calculated sample size will be 45 divided in 3 groups of patients, 15 for each group as:

a. preeclamptic patient groups (30 cases):

- (Group A) including (15) pregnant females with mild PE at the time of examination.
- (Group B) including (15) pregnant females with severe PE at the time of examination.

b. control group (group C) including (15) healthy normotensive pregnant females. All cases were in the 3rd trimester of their pregnancy.

They were selected from the outpatient clinic and inpatient of Obstetric and Gynecology department.

All participants gave their consent to participate in this study.

Patients were diagnosed according to the diagnostic criteria coated by the American College of Obstetrics and Gynecology *Committee on Obstetric Practice (2002)*:

Mild pre-eclamptic patients:

1- Blood pressure $\geq 140/90$ mmHg and $< 160/110$ mmHg for two readings 6 hours apart

2- Proteinuria ≥ 300 mg/24 hours or $\geq +1$ dipstick.

Severe pre-eclamptic patients:

1- Blood pressure $\geq 160/110$ mmHg for two readings 6 hours apart.

2- Proteinuria ≥ 5 gm/24 hours or $\geq +2$ dipstick.

3- Serum creatinine > 1.2 mg/dl unless known to be previously elevated.

4- Platelets $\leq 100,000/\text{mm}^3$.

5- Elevated liver enzymes.

6- Right quadrant or epigastric pain.

7- Occurrence of headache, cerebral or visual disturbances.

8- Intrauterine growth retardation (IUGR)

- Normal pregnancies were diagnosed on the basis of clinical and biochemical findings.

Inclusion criteria:

All patients fulfilled the following inclusion criteria:

- Age from 18:40 years
- Singleton viable pregnancy.

- Gestational age \geq 28 weeks.
 - Not in labor.
- Exclusion criteria:**
Patients with a history of
- Renal disease.
 - Diabetes Mellitus.
 - Chronic hypertension.
 - Systemic Lupus Erythematosus.
 - Systemic infection .
 - Cardiovascular disease.
 - Premature rupture of membrane (PROM).
 - Given corticosteroids at least 7 days prior to sample taking.

They were excluded during routine antenatal care, examination and laboratory investigations .

2- OPERATIONAL DESIGN:

All the patients that were included in the study were evaluated by history taken, physical examination and relevant laboratory investigations as subsequently discussed.

All Patients will undergo:

1) Full history taking to exclude the previous exclusion criteria in selected cases:

1-Personal history:

2-Present history:

3-Menstrual history:

4. Obstetrics history

5. Contraceptive history:

6-Past history:

- Hypertension or preeclampsia in previous pregnancy.
- Renal disorders.
- Diabetes mellitus.
- Systemic lupus erythematosus.
- Epilepsy.
- Operative history

7-family history:

Hypertension, preeclampsia or eclampsia.

8-previous investigations:

Through clinical examination.

General examination carried out with special emphasis on blood pressure measurement, and lower limb edema).

- Level of consciousness.
- Blood pressure measurement

During the blood pressure measurement, the patient was sitting with the arm at the heart level .To be sure of accurate readings,

suitable-size cuff of sphygmomanometer was used.

Kortkoff phase V (disappearance) was always used to measure diastolic blood pressure by auscultation.

- Pulse, temperature and respiratory rate.
- Face examination for pallor, jaundice and eye lid edema.
- Lower limb edema(type and level).
- Chest and heart examination.
- Height.
- Weight
- Body mass index (BMI) was calculated by equation (kg/m²) weight represented in kilograms divided by height measured in meters squared.

Abdominal examination:

Ultrasonography

Obstetric ultrasound for comment on single or multifetal pregnancy, fetal viability, gestational age, amniotic fluid index, placental localization, presence or absence of retro placental hematoma and its size, fetal congenital malformation and presence of IUGR or oligohydramnios.

Bed side test:

Midstream catch urinary protein by dipstick test-strip to detect the proteinuria.

3) laboratory Investigations:

- Rh type and ABO grouping.
- CBC (especially Hb. Conc. and platelet count.)
- liver function tests: serum (ALT) Alanine Aminotransferase, (AST)Aspartate Aminotransferase, level of serum albumin .
- kidney function tests (serum creatinin level, serum urea & serum uric acid).
- urine Analysis.
- detection of total protein in 24hrs urine collected sample .
- serum glucose level.
- CRP level** (Single measurement of maternal plasma C-reactive protein).

At which blood samples were taken in early morning after fasting for 6h and before administration of magnesium sulfate. Blood samples were collected in tubes without anticoagulant after centrifugation, aliquots of plasma and serum were immediately stored at - 70°C until assayed for serum CRP level

were measured by enzyme. Immunosorbent assays (ELISA).

Follow up of patients with preeclampsia

Those patients with mild preeclampsia : out patient follow up with maternal & fetal assessment

Those patients with severe preeclampsia: follow up with Maternal evaluation and hospitalization

Termination of pregnancy:

Pregnancy is allowed to continue as long as the maternal and fetal conditions were good.

Maternal and perinatal outcome.

1- Assessment of neonatal condition:

After delivery, neonatal conditions were assessed by pediatrician .

2-Assessment of maternal condition:

Adverse maternal outcome was considered by the following criteria:

- eclampsia, ICU admission, HELLP syndrome, antepartum or postpartum haemorrhage , Hepatic failure or rupture.

Renal failure , Maternal death.

All patients were notified and consent was taken on starting the study. Collected data and results were obtained, recorded, reviewed and then data were tabulated and analyzed.

This study was reviewed and approved by Obstetric and Gynecology department, faculty of medicine, Zagazig University.

Result : Statistical analysis & presentation of the present study was conducted, using the mean, standard deviation, Chi - square, Mann Whitney, Kruskal - Wallis, spearman rank Correlation & ROC curve as all data were coded and entered to SPSS file software package Version 10.

The results were considered:

- **Significant when the error probability is less than five percent ($p < 0.05$).** (*) means significant
- **Non-significant when the error probability is more than five percent ($p > 0.05$).**
- **Highly significant when the error probability is less than zero point one percent ($p < 0.001$).** (**) means highly significant

The smaller the obtained p-value, the results more significant .

Table 1 shows that There were no statistical significant difference between all studied groups regarding maternal and gestational age ($P > 0.05$). This indicates a good matching in all studied groups. But there were statistical significant difference between all studied groups regarding BMI, SBP & DBP (p -value < 0.05) with significant increase in these levels in mild and severe groups.

Table 2 shows that there is high significant difference in CRP Level between three groups (p -value < 0.001) with marked increase in its level in severe preeclampsia more than mild , more than healthy group.

Table 3,4 show that level of CRP is different between mild & severe preeclampsia as cut off value is 15.5 mg/dl. The maternal serum CRP above 15.5 is an excellent indicator of the severity of pre-eclampsia with a sensitivity of 93.9% and specificity of 73.3%.

Table 5,6 show that there is difference in level of CRP in healthy group & preeclamptic patient (mild & severe) which showing that The maternal serum CRP at 3.15 is an excellent indicator of the of pre-eclampsia with a sensitivity of 100.0 % and specificity 93.3%.

Table 7 By applying spearman correlation test the result showed that there was statistical non significant correlation regarding CRP & Maternal age, gestational age, parity , BMI, ($P > 0.05$). But there were statistical significant +ve correlation in between CRP and SBP, DBP among the PE group ($p < 0.05$). The level of SBP, DBP were significantly elevated with increased CRP level .this means that increased CRP level is correlated with severity of preeclampsia.

Table 8 By applying spearman correlation test the result showed that there was statistical non significant -ve correlation regarding CRP and HB, platelet count and there was statistical non significant +ve correlation regarding CRP , bilirubin, s.urea and s.creatinin ($P > 0.05$). But there was significant statistical +ve correlation as regard CRP & s.uric acid SGPT, SGOT and total prt. In urine /24 hrs among the preeclamptic group ($p < 0.05$). in which there

was significant elevation in there levels by increased CRP level. this means that increased CRP level is correlated with severity of preeclampsia.

Table 9 By applying Mann whitney test the result clear that between CRP and eclampsia and c.s there was non significant statistical correlation ($P>0.05$) but their incidence increased in severe cases in which CRP level is high.

But there was statistical significant correlation between CRP and ICU, Admission and Oligohydromious ($P<0.05$) among the preeclamptic groups in which their

incidence increased in severe cases in which CRP level is high.

Table 10 By applying Mann whitney test the result showed that correlation between CRP and IUFD there was non significant statistical ($P>0.05$). But there was statistical significant correlation between CRP and NICU admission and low birth weight ($P<0.05$) among the preeclamptic groups. This means that fetal complication are more in severe cases in which CRP levels were significantly higher.

Table(1):Demographic data of studying groups

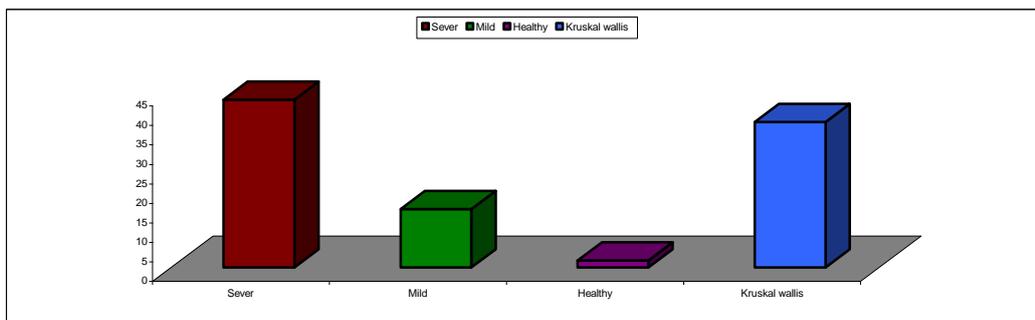
	Severe	Mild	Healthy	F	P value
	$\bar{x} \pm SD$	$\bar{x} \pm SD$	$\bar{X} \pm SD$		
Maternal age	23.460 \pm 3.70	25.160 \pm 5.075	25.260 \pm 5.630	2.005	> 0.05
Gestational age	33.40 \pm 3.60	33.60 \pm 4.18	36.00 \pm 3.18	2.317	> 0.05
BMI	30.25 \pm 3.86 (a,b)	27.06 \pm 2.28 (a)	25.40 \pm 1.72	11.82	< 0.001 (**)
SBP	177.33 \pm 17.09 (a,b)	149.33 \pm 9.61 (a)	116.00 \pm 12.98	76.67	< 0.001 (**)
DBP	115.33 \pm 6.39 (a,b)	95.33 \pm 5.16 (a)	72.00 \pm 7.74	165.8	< 0.001 (**)

(a) severe or mild significant differ from healthy.

(b) severe significant differ from mild.

Table(2) : Comparison between Healthy, mild and severe preeclamptic groups as regard CRP level :

CRP Mg/dl	Severe	Mild	Healthy	Kruskal wallis	P value
Median	43.10	15.00	1.8		
Range	16.00-53.00	7.1-30	0.8-3.2	37.35	< 0.001 (**)



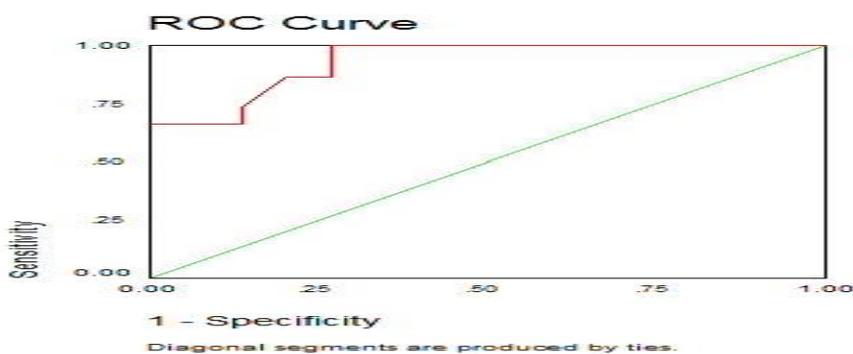
Figure(1): Comparison between Healthy, mild and severe preeclamptic groups as regard CRP level

Table (3,4) : show Validity of CRP as predictor of severity of preeclampsia &The accuracy between mild and severe in CRP:

Cut off value	Severe 15 case	Mild 15 case	Total 30 case
CRP>15.5	14	4	18
CRP≤15.5	1	11	12
Total	15	15	30

Sensitivity	Specificity	PPV	NPV	Kappa	P value
93.9	73.3	77.8	91.7	0.667	< 0.001 **

AUC (95% CI) : 0.93 (0.85- 1.01)



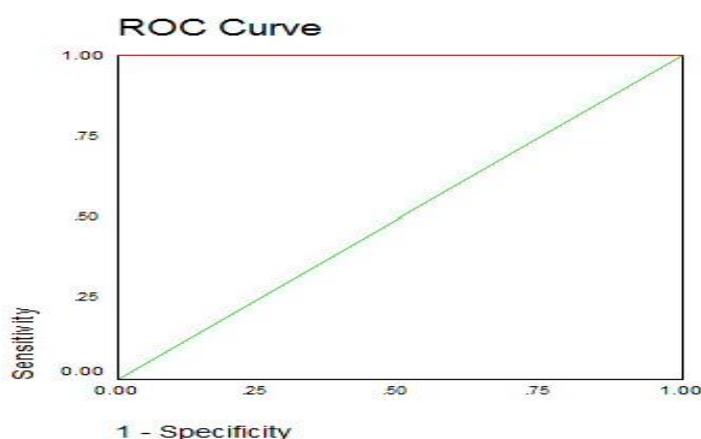
Figure(2) :Show Validity of CRP as predictor of severity of preeclampsia &The accuracy between mild and severe in CRP.

Table (5,6): Show Validity of CRP as an indicator of preeclampsia & The cut off between patient and healthy in CRP:

Cut off value	Preeclamptic groups 30 case	Healthy group 15 case	Total 45 case
CRP>3.15	30	1	18
CRP≤3.15	0	14	12
Total	30	15	45

Sensitivity	Specificity	PPV	NPV	Kappa	P value
100.0	93.3	96.8	100.0	0.94	< 0.001 **

AUC (95% CI) : 1.0 (1.0- 1.0)



Figure(3): Show Validity of CRP as an indicator of preeclampsia & The accuracy between patient and healthy in CRP

Table(7): Spearman rank Correlation between CRP and clinical parameters in the preeclamptic group (30 case).

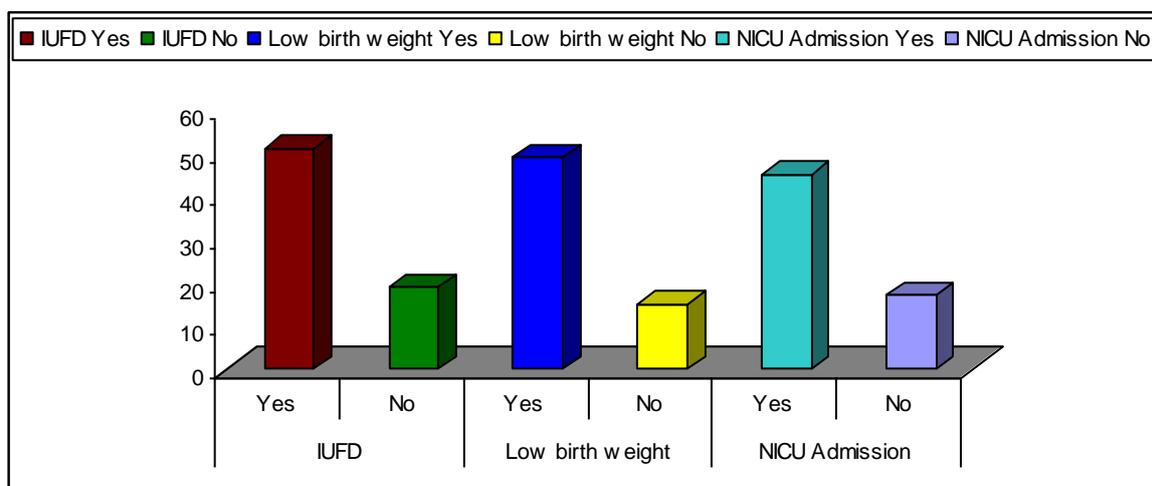
Correlation in patients group	CRP	
	R	P value
Maternal age	-0.009	> 0.05
Gestational age	-0.27	> 0.05
BMI	0.204	> 0.05
Parity	0.041	> 0.05
Systolic BP	0.643	< 0.001 (**)
Diastolic BP	0.729	< 0.001 (**)

Table(8): Spearman rank Correlation between CRP and biochemical parameters in the preeclamptic group (30 case).

Correlation in patients group	CRP	
	R	P value
HB(g/dl)	-0.158	>0.05
Platelet count(n/mm ²)	-0.321	>0.05
S.uric acid	0.684	< 0.001 (**)
Bilirubin	0.343	>0.05
SGPT(IU/L)	0.604	< 0.001 (**)
SGOT(IU/L)	0.632	< 0.001 (**)
S.urea(mg/dl)	0.084	>0.05
S.creatinin(mg/dl)	0.083	>0.05
Total prt. In urin/24hrs	0.792	< 0.001 (**)

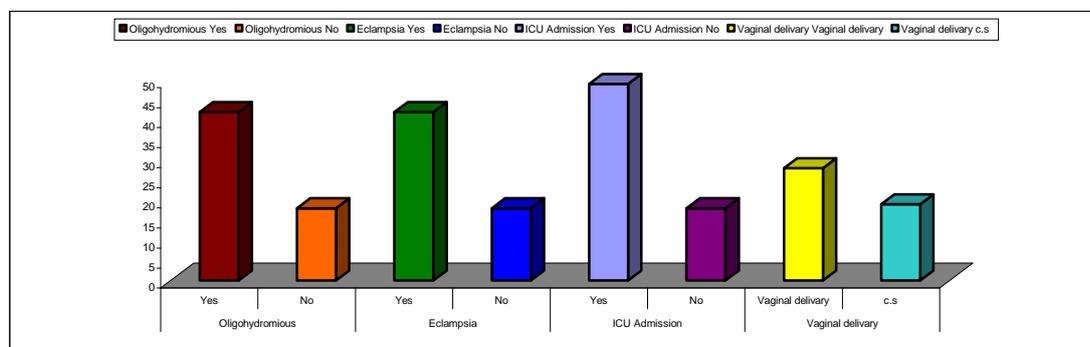
Table (9) :Spearman rank Correlation between CRP and maternal out come in preeclamptic groups (30 case).

Correlation in patients group	Number	CRP		Mann_ whitney test	P value
		MEDIAN	RANGE		
oligohydramnios.					
Yes	4	42	29-53	2.201	<0.05*
No	26	18	7.1-53		
Eclampsia					
Yes	3	42	29-53	1.92	>0.05
No	27	18	7.1-30		
ICU Admission					
Yes	3	49	29-53	2.35	<0.05*
No	27	18	7.1-30		
Vaginal delivery					
c.s	13	28	9.5-43	0.629	>0.05
	17	19	7.1-53		

**Figure(4):** Spearman rank Correlation between CRP and maternal out come in preeclamptic groups (30 case).

Table(10): Prearman rank Correlation between CRP and Fetal out come in preeclamptic groups (30 case).

	Number	CRP		Mann_ whitney test	P value
		MEDIAN	RANGE		
IUFD					
Yes	1	51	7.1-53	1.33	>0.05
No	29	19			
Low birth weight					
Yes	4	49	16-53	2.25	<0.05 *
No	25	15	7.1-30		
NICU Admission					
Yes	5	45	29-53	2.258	<0.05 *
No	24	17	7.1-30		



Figure(5):Prearman rank Correlation between CRP and Fetal out come in preeclamptic groups .

DISCUSSION

Pre-eclampsia, is a complication of pregnancy of the 2nd half at which hypertension and proteinuria considered characteristics of disease, and is one of the leading risks to intra uterine fetal morbidity & death.^{[8].}

Although pre-eclampsia remains a disease of theories, an improved understanding of the pathogenesis of pre-eclampsia has raised the possibility that spiral arteries remodelling deficiency occurs in maternal and fetal sides interaction during invasion of trophoblasts has been considered as an aetiology of insufficient placenta. This would lead to the release of factors of inflammation in the systemic circulation of mother which are involved in the endothelial dysfunction; the hallmark pathological finding in pre-eclampsia^{[9].}

an acute-phase protein is C- reactive protein that can be found in the circulation with its level increase as an inflammatory response to, tissue damage, infection and neoplasia.^{[10].}

High CRP levels were associated with severe preeclampsia . CRP was in +ve relation with the severity of disease in preeclampsia which was significant. These findings suggested that elevated CRP may occur due to dysfunction endothelial cell in PE and could be a risk marker in this disease.^{[11].}

In the light of the previous postulation, the study **aim** was to assess serum **CRP** in group of pregnant females with pre-eclampsia to evaluate their clinical utility in diagnosis and estimation of disease severity to prove that CRP may be used as a marker and predictor of severity of preeclampsia.

Results of this study concerning levels of CRP revealed a highly significant statistical increase ($p < 0.001$) in serum of both mild and severe pre-eclamptic women when compared to their matched controls). . These results are in agreement with the previous reports of **Lau DC, et al., Yusuf Ustun et al., Selahattin Kumru et al.**,^[8,11,12] who had recorded an elevation of plasma CRP among pre-eclamptic women when compared to their matched controls and positive significant correlation inbetween CRP levels and pre-eclampsia severity. these results support the hypothesis that systemic inflammation is involved in the pathogenesis of preeclampsia. the prognosis of the disease could be predicted by evaluating the serum CRP levels when severe preeclampsia is diagnosed.

Also in agreement with **Zaima Ali et al.**,^[14] who found that there were high levels of CRP, an inflammatory marker, in third trimester in the preeclamptic pregnant women.

On the opposite side, these results are disagreeing with studies which done by **Savidou MD et al., Makrina, D. et al., Stefanovic M et al.**,^[15, 16,17] who did not find a significant role of CRP in pregnancies complicated by preeclampsia as compared to normotensive pregnant women. Differences in sample size, timing of sample collection and CRP detection technique followed by these studies may be the cause of these results.

In addition, in this study another characteristic receiver operator curve(ROC) analysis was applied to assess the diagnostic performance of CRP in discriminating different studied groups , according to the (ROC) curve for serum CRP and preeclampsia. The best cutoff value between mild and severe preeclamptic group is (15.5 mg/L) which gives sensitivity of (93.9%) and specificity of (73.3%) negative predictive value(NPV) 91.7 %, positive predictive value(PPV) 77.8 %, and area under the curve (AUC) of 95%.

. The best cutoff value between patient and control group is (3.15 mg/L) which gives sensitivity of (100%) and specificity of 93.3% (NPP 100 %),(PPV 96.8 %), and (AUC of 95%)and This result disagree with that of

Ustun y, et al.,^[18] who found that, according to ROC curve, the best cut off value of serum CRP between mild and severe preeclamptic group was (11.5 mg/L) which was given sensitivity of (94%) and specificity of (92%).

Also **Kashanian, M et al.**,^[19] stated that measurement of maternal serum CRP with value of 6 mg/L can predict preeclampsia with sensitivity of 78.1%, specificity of 72.1%, (PPV of 25%), and (NPP of 96.5%) and diagnostic accuracy of 72.8%.

Also, In this study we found in preeclamptic women , a statistically significant positive correlation between serum levels of CRP and SBP ($r = 0.643$, $p < 0.001$) and DBP ($r = 0.729$, $p < 0.001$) also there was a +ve correlation between CRP levels and laboratory investigation as ALT ($r = 0.604$, $p < 0.001$), AST($r = 0.632$, $p < 0.001$),, s.uric acid($r = 0.648$, $p < 0.001$), proteinuria($r = 0.792$, $p < 0.001$),.

These result in agreement with **Mirzaie F et al.**,^[20] who determined serum CRP level in PE, and its correlation with the disease severity and with laboratory and clinical findings. In this cross-sectional study that include 43 pregnant female with mild PE, 43 pregnant female with severe PE, and 43 healthy pregnant female. They were selected in the 3rd trimester of their pregnancy. Mean diastolic pressure and level of proteinuria were used as indicators of the preeclampsia severity .

And in agreement with **Anil, B et al.**,^[21] who recorded a statistically positive significant correlation between CRP levels and (SBP,DBP) which shows that the elevation of CRP level is proportional to severity of preeclampsia and supported his results by the concept that systemic inflammation is a hallmark in the preeclampsia pathogenesis and serum CRP level may be the marker to predict severity of disease.

But these finding disagree with **Nanda, K et al.**,^[22] who said: Although maternal levels of CRP are elevated in overt preeclampsia, there is still a debate about its usefulness as a predictive marker for preeclampsia .

In this study, the correlation between CRP and complicated pregnancy outcome it was found that increased serum levels of CRP are associated with low fetal birth weight ($P < 0.05$), and there was statistical significant +ve correlation between them, that means -ve correlation between serum CRP levels and of the newborns weight in preeclamptic groups also there was significant statistical +ve relation between CRP and NICU admission ($P < 0.05$) among the preeclamptic group. .but there was statistical significant +ve correlation between level of CRP and maternal ICU Admission and Oligohydramious ($P < 0.05$) among the preeclamptic group.

These results are in agreement with the studies done by **Naicker T et al., Guven MA et al., Gandevani SB et al., Zaima Ali et al.,** [23-26] who reported higher levels of CRP in preeclampsia and found -ve relationship between CRP and birth weight of fetus especially in severe preeclampsia.

This study not agree with the study done by **Archana et al.,** [27] who evaluate the relationship between CRP and bad fetal outcomes like fetal distress, LBW, IUGR and IUFD however they found that there is no significant relationship inbetween bad fetal outcome and CRP except for distress, and IUFD which were significant ($p < 0.05$).

In this study as regard demographic data, there were no statistical significant difference between all studied groups regarding maternal age and gestational age ($P > 0.05$). This indicates a good matching in all studied groups

CONCLUSION AND RECOMMENDATIONS

It was found that there were +ve relation between level serum CRP and biochemical and clinical parameter in preeclampsia which proved to be of great value that plasma levels of CRP correlated +ve with the degree of preeclampsia severity .

Determination of plasma CRP level in 3rd trimester of pregnant women was of great significant value in prediction of of preeclampsia prognosis and outcome.

Therefore, it can be concluded that serum levels of CRP may be used as an indicator for severity of preeclampsia.

REFERENCES

1. **Goyal R, Yellon SM, Longo LD, Mata-Greenwood E:** Placental gene expression in a rat "model" of placental insufficiency. *Placenta*, **2010** ;31:568–575
2. **Mohamed, A.M.; Kishk, N.A.; Shokeir, N.F. :** Role of antenatal care in toxemia of pregnancy in alexandria. *J Egypt Public Health Assoc* **2009** ;81: 1-28.
3. **Silasi M, Cohen B, Karumanchi AS, Rana S. :Abnormal placen-tation, angiogenic factors, and the pathogenesis of preeclampsia** *Obstet Gynecol Clin North Am*, **2010**;**37**:239 –253
4. **Wathén, K. A.:** Pre-eclampsia: The role of soluble VEGF receptor-1 and related anti-angiogenic factors beyond. University of Helsinki, Finland. Thesis for doctoral degree , **2011** ; (7):14-29.
5. **Windgassen, E. B.; Funtowicz, L.; Lunsford, T. N.; Harris, L. A., and Mulvagh, S. L. :** C-reactive protein and high-sensitivity C-reactive protein: an update for clinicians. *Postgraduate Medicine* ,**2011**; 123(1): 114-119.
6. **Braekke K, Holthe MR, Harsem NK, Fagerhol MK, :** Calprotectin, a marker of inflammation, is elevated in the maternal but not in the fetal circulation in preeclampsia. *Am J Obstet Gynecol*, **2005** ; 193 (1): 227-233.
7. **Kumru S, Godekmerdan A, Kutlu S,:** Correlation of maternal serum high-sensitive C-reactive protein levels with biochemical and clinical parameters in preeclampsia. *Eur J Obstet Gynecol Reprod Biol* **2006** ; 124(2): 164-167.
8. **Lau DC, Dhillon B, Yan H, Szmitko PE, Verma S. "Adipokines: molecular links between obesity and atherosclerosis".** *Am. J. Physiol. Heart Circ. Physiol.*,**2005** ; 288 (5): H2031–2041.
9. **Wathén, K. A.:** Pre-eclampsia: The role of soluble VEGF receptor-1 and related anti-angiogenic factors beyond. University of Helsinki, Finland. Thesis for doctoral degree. **2011**; (7):14-29.
10. **Windgassen, E. B.; Funtowicz, L.; Lunsford, T. N.; Harris, L. A., and Mulvagh, S. L.:** C-reactive protein and high-sensitivity C-reactive protein: an update for clinicians. *Postgraduate Medicine* ,**2011**; 123(1): 114-119.
11. **Yusuf Ustun , Yapral Engin –Ustun , Mansur Kamaci,** Association of fibrinogen and Creactive preotein with severity of preeclampsia, *Eur J Obstet Gynecol Reprod Biol*, **2005**; 121: 154-158.

12. **Selahattin Kumru, Ahmet Godekmerdan, Selim Kutlu, Zeynep Ozcan,** Correlation of maternal serum high-sensitive C-reactive protein levels with biochemical and clinical parameters in preeclampsia, *Eur J Obstet Gynecol Reprod Biol*, **2006** ; 124: 164-167.
13. **Hwang HS, Kwon JY, Kim MA. :** Maternal serum HSCRP in normal pregnancy in pre-eclampsia. *Int J Gynaecol & Obst*; 98:105-109.
14. **Zaima Ali , Faraz Ahmed Bokhari , Saima Zaki, Uzma Zargham et al.,** Correlation of CRP Levels in Third Trimester with Fetal Birth Weight in Preeclamptic and Normotensive Pregnant Women *Journal of the College of Physicians and Surgeons Pakistan* , **2015** ; Vol. 25 (2): 111-114
15. **Savvidou MD, Lees CC, Parra M, :** Levels of C-reactive protein in pregnant women who subsequently develop pre-eclampsia. *BJOG. Mar . 2002*; 109(3):297-301.
16. **Makrina, D.; Christoph, C.; Mauro, P.; Aroon, D. and Kypros H. :** Levels of C-reactive protein in pregnant women who subsequently develop preeclampsia, *BJOG: An International Journal of Obstetrics and Gynaecology*, **2002**; 109(3): 297-301.
17. **Stefanovic M, Vukomanovic P, Milosavljevic M, Kutlesic R, et al.;** Insulin resistance and C-reactive protein in preeclampsia. *Bosn J Basic Med Sci*, **2009** ; 9:235-238.
18. **Ustun y, Engin-ustun Y, Kamaci M :** Association of fibrinogen and C-reactive protein with severity of preeclampsia. *Eur J Obstet Gynecol Reprod Biol* **2005**; 121(2): 154-158.
19. **Kashanian, M.; Aghbali, F. and Mahali, N. :** Evaluation of the diagnostic value of the first-trimester maternal serum high-sensitivity C-reactive protein level for prediction of pre-eclampsia. *Journal of Obstetrics and Gynaecology Research*, **2013**; 39(12): 1549-1554.
20. **Mirzaie F, Rahimi-Shorbaf F and Kazeronie AH :** Association of maternal serum C-reactive protein levels with severity of preeclampsia. *Acta Medica Iranica*.**2009**; 47(4): 293-296.
21. **Anil, B.; Jayashree, V.G.; Dhiraj, J.T.; Nitin, N.;** Serum hs-CRP and uric acid as indicator of severity in pre-eclampsia. *International Journal of Pharma and Bio-Sciences*.**2011**; 2(3): 17-23.
22. **Nanda, K.; Sadanand, G. and Muralidhara, K. C. S. :** C- reactive protein as a predictive factor of pre-eclampsia. *Int J Biol Med Res*. **2012**; 3(1): 1307-1310.
23. **Naicker T, Khedun SM, Moodley J, :** Quantitative analysis of trophoblast invasion in preeclampsia. *Acta Obstet Gynecol Scand* ,**2003**; 82(8): 722-729.
24. **Guven MA, Coskun A, Ertas IE, Aral M, :** Association of maternal serum CRP, IL-6, TNF-a, homocysteine, folic acid and vitamin B12 levels with the severity of preeclampsia and fetal birth weight. *Hypertens Pregnancy* .**2009** ; 28:190-200.
25. **Gandevani SB, Banaem LM, Mohamadi B, Moghadam NA :** Association of high-sensitivity C-reactive protein serum levels in early pregnancy with the severity of preeclampsia and fetal birth weight. *J Perinat Med* **2012**; 1:1-5.
26. **Zaima Ali , Faraz Ahmed Bokhari , Saima Zaki, Uzma Zargham :** Correlation of CRP Levels in Third Trimester with Fetal Birth Weight in Preeclamptic and Normotensive Pregnant Women *Journal of the College of Physicians and Surgeons Pakistan* , **2015**; Vol. 25 (2): 111-114
27. **Archana J Dhok, Sangeeta Daf*, Kanchan Mohod , Satish Kumar :** Role of Early Second Trimester High Sensitivity C-Reactive Protein for Prediction of Adverse Pregnancy Outcome **2011**;Vol. 13

Corresponding author: Email; dr_amanyali @ yahoo.com Tel; 01157441222, 0506110061