Original article

C - reactive protein levels in women with pregnancy induced hypertension

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Abstract

Objective: The main objective of this study is to determine the level of C- reactive protein in pregnancy induced hypertension (PIH) along its relation with normal pregnant mothers and also to compare it with different grades of pregnancy. C-reactive protein and inflammation are interrelated. Another objective of this study is to find out the relationship of C- reactive protein, biochemical and hematological parameter in PIH as well as its clinical correlation. ***Materials and Methods:*** The study was conducted in the department of Gynaecology and department of Pathology in Burdwan Medical College West Bengal India after taking permission from ethical committee. 50 cases of PIH mothers and age and gestational matched 50 cases of normal control pregnant mothers and 50 normal healthy non pregnant adult women were included in this present study. CRP was estimated by turbidometric method. Serum Uric acid, SGPT, Serum Creatinine were estimated by semi auto analyzer, Serum ß HCG was estimated by ELISA technique. The total leukocytes count, absolute Neutrophils count, Platelet counts were done in hematological cell counter with correlation from peripheral direct smear and manual counting. Urine protein was detected by dipstick method. ***Results:*** Serum C- reactive protein was positively correlated with severity of in PIH**.** Results shows a significantly increased C-reactive protein in PIH (Mean SD 42.02 mg/L±18 .01 mg/L, P<0.001) in comparison to normal control mother (Mean SD 4.2 ±0.93 mg/L). ***Conclusion:*** Serum C-reactive protein levels can be used as marker for early diagnosis and intervention of PIH and can be reduced maternal as well as fetal morbidity and mortality.

Key words: C - reactive protein, pregnancy induced hypertension.

Introduction

Pregnancy induced hypertension (PIH) is a pregnancy specific multi system involving syndrome characterized by newly onset of hypertension and proteinurea after twenty weeks of gestation. PIH is one of the leading causes of maternal and fetal morbidity and mortality. World wide about 50,000 mothers die due to PIH per year.

It is responsible 25%of all fetal growth retardation and 15% preterm birth in developed countries [1].Though PIH varies from region to region and from different hospitals the incidence of it in India is 8-10%[2] and maternal mortality is reported 8% amongst all maternal mortality[3].The incidences is gradually increasing over last few decades [4] . PIH is common below 25 years of age[5].

C - reactive protein (CRP) is an acute phase protein which is synthesized in hepatocytes and present in trace amount in normal healthy person and rise significantly following injury and inflammation[6]. Though the exact etiopathogenesis of PIH is not confirmed out of all etiology endothelial cell dysfunction and inflammation considered to play crucial role[7].Endothelial dysfunction is accompanied by elevated levels of markers of inflammation as CRP is one of the markers of inflammation and it has been shown that CRP is elevated in women with PIH. Recently it has been established that inflammation plays an important role due to endothelial dysfunction and generalized activation of circulating raised leucocytes and raised serum CRP. CRP is a sensitive marker of tissue damage and inflammation and can be used as potential marker for inflammatory response in PIH. The synthesis of CRP in hepatocytes increases in PIH as response to inflammatory cytokines like Il-1, IL-6, and TNF α.Serum CRP can be used as marker and intervention of PIH.

Material and method

The present study was conducted at the Department of Obstetrics& gynecology Department of Pathology, Department of Microbiology of Burdwan Medical College, Burdwan after taking approval from the ethical committee from 2007 July

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to December 2010. The study conducted on total 150 women divided into three groups. Group A- 50 healthy non pregnant women (volunteer) mostly the staff of the Medical College. Group B- 50 healthy pregnant mothers between 28- 36 weeks of gestation (Control). Group C- 50 pregnant mothers between 28 -36 weeks of gestation who were diagnosed as PIH. Out of these 50PIH mothers 23 were diagnosed as sever PIH including 3 Eclampsia and 27 were mild PIH. Inclusive criteria's of Group A were average age group 23±3.3 yrs(22-33 yrs) ,non pregnant, non diabetics, normotensive, without any systemic infection. Not suffering from any renal, cardio vascular, dental disease, not taking corticosteroid < 7days. For Group B &C – inclusive criteria's were pregnant women between 28-36 weeks ,preferably primigravida , single ton fetus, mother with history of diabetes, renal disease, any cardiovascular illness, chronic hypertension, symptomatic infectious disease, periodontitis, obesity, Premature rupture of membrane, clinical chorioamniotis , mothers taking corticosteroid <7days ,patient in labour are not included.The mothers were diagnosed as PIH when the systolic blood pressure were persistently ≥ 140 mm of Hg and diastolic blood pressure ≥ 90mmof Hg ,on two occasion each 6 hours apart ,accompanied by proteinuria at least 1+ on dip stick testing at third trimester of gestation. Severe PIH considered having blood pressure ≥ 160/110 mm of Hg and measured on two occasions 6 hours apart with proteinuria at least 3+ on dip stick [8]Eclampsia diagnosed when the PIH mothers developed convulsion[9].We measures blood in semi fowler position before medication or clinical perturbation to avoid alteration of pressure.

Table I: Comparison of various parameters (mean ± SD) in normal pregnant mothers (control, N=50) and Pregnancy Induced Hypertensive mothers (n=50)

Parameter	Control (n=50)	PIH (n=50)	Volunteer healthy, N=50
Maternal age	22 ± 3 yrs	21.5 ± 2.6 yrs	23 ± 3.3
Gestational age	28-36 weeks	28-36 weeks	Non pregnant
Systolic B.P mm of Hg	115.6 ± 7.93	161.6 ± 18.29	1136 ± 6.44
Diastolic B.P mm of Hg	73.08 ± 6.77	102 ± 9.48	70.88 ± 4.90
C-reactive protein mg/L	4.2 ± 0.93	42.02 mg/L ± 18 .01	2.99 mg/L ± 0.81
Total leucocyte count	10.42 ± 1.94 x 10^9/L	16.17 ± 4.26 x 10^9/L	7.10 ± 1.26 x 10^9/L
Absolute Neutrophil count	7.2 ± 1.99 x 10^9/L	13.27 ± 4.47 x 10^9/L	4.23 ± 0.47 x 10^9/L
Platelet count	1.90 ± 0.20 x10^{12}/L	1.7 ± 0.37 x 10^{12}/L	1.98 ± 0.37 x 10^{12}/L
Serum Uric acid	3.70 ± 0.62 mg/dl	7.53 ± 1.30 mg/dl	3.6 ± 0.54 mg/dl
S.GPT	25.9 ± 5.8 U/l	76.54 ± 46.64 U/L	24 ± 5.8 U/L
Serum HCG	8223.40 ± 1909.64 mIU/mL	17928.35 ± 2050.02 mIU/mL	<5.0 mIU/ml
Serum HCG after delivery	3373.07 ± 382.62 mIU/mL	3452.90 ± 285.56 mIU/mL	Non pregnant

Table II: Comparison of various clinical parameters (mean ± SD in pregnant mothers (Severe PIH, N=23) pregnancy and pregnant mothers (Mild PIH n=27)

Parameter	**Severe PIH n=23**	**Mild PIH n=27**
1.mean maternal age	22.9± 2.7yrs	20.4± 2.0yrs
2.Gestational age	28-36 weeks	28-36 weeks
3.Mean Systolic B.P	176.6±15.1 mm of Hg	149±8.4 mm of Hg
4.Mean Diastolic B.P	110.3±8.3 mm of Hg	96.4±4.5 mm of Hg
5.Mean Platelet count	1.65± 0.3X10^9/l	1.95± 0.15X10^9/l
6. Mean Serum Uric acid	8.9 ± 01.34mg/dl	6.9 ± 1.40mg/dl
7.Mean Serum Creatinine	1.6± 0.3 mg/dl	1.60±0.3 mg/dl
8.Mean SGPT	104.8± 55U/L	51.3± 14.9 U/L
9.Total Leucocyte count	15.48±4.02 X10^9/L	17.43±4.28 X10^9/L
10.Absolute Neutrophil count	12.69±3.98 X10^9/L	14.25±4.83 X10^9/L
11.Serum ß HCG	17110.93± 1801.29 mIU/ml	18885± 1935.90 mIU/ml

Table III: Mean ± SD of CRP in different groups of Mothers

Parameter	Group I control (Normal pregnancy) n=50	Group II PIH n=50	Group IIA mild PIH n=27	Group II B Severe PIH n=23
	42.02mg/L ± 18.01 mg/L	4.2 ± 0.93 mg/L	33.63 ± 13.46mg/L	54.69 ± 17.71 mg/L

Table IV: Correlation of CRP with SBP, DBP, Creatinine, Platelet count, SGPT, TLC, ANC, Serum Uric acid, Serum HCG

Parameter	r	P
SBP	0.562	<0.001
DBP	0.375	<0.007
Serum creatinine	0.444	<0.001
Platelet Count	- 0.345	< 0.014
SGPT	0.348	< 0.013
TLC	0.388	<0.005
ANC	0.382	<0.006
Serum uric acid	0.193	0.176
Serum HCG (28-36 weeks)	0.485	<0.001

After diagnosing as PIH based on clinical and biochemical findings all data's including the control mothers and healthy non pregnant volunteer were tabulated in (Table-I) and were classified into mild and severe PIH (Table-II). The venous blood were collected at the side laboratory of OPD patients, and from indoor patients in supine position before administration any therapy from the antecubital vein in sterile plain and EDTA vials. A direct blood smears also drawn at the same time. Blood samples were allowed to clot at room temperature and then serum was separated by centrifugation at 2000 RPM for 7-8 minutes. Biochemical tests were done in Semi auto analyzer (Evoluio-3000,Italy) .The Platelet counts and Total leucocytes count in hematological cell counter were correlation from peripheral direct smear and manual counting. Urine protein was measured by Dip Stick, SGPT &Uric acid were estimated by semi auto analyzer. C-reactive protein estimated by turbid metric method as well as by Latex fixation slides Tests in all three groups. Serum ß HCG were estimated by ELISA. Statistical analysis was done by SPSS version 12.

Results

Comparison results showed that systolic blood pressure , diastolic blood pressure , serum uric acid, serum creatinine, serum GPT, serum ßHCG as well as total leukocyte count, absolute neutrophil count were significantly higher than control mothers (Table1). The platelet counts were reduced in PIH than control mothers. C-reactive protein was found raised in normal pregnant mothers than non pregnant healthy mother (Table1) and varies with severity (Table III). The systolic blood pressure, diastolic blood pressure ,serum uric acid, serum creatinine ,serum ßHCG ,total leucocyte count, absolute neutrophil count are positively correlated with PIH, where platelet count is negatively correlated with C-reactive protein in PIH (Table IV),(fig 1A & fig 1B). Serum CRP is significantly

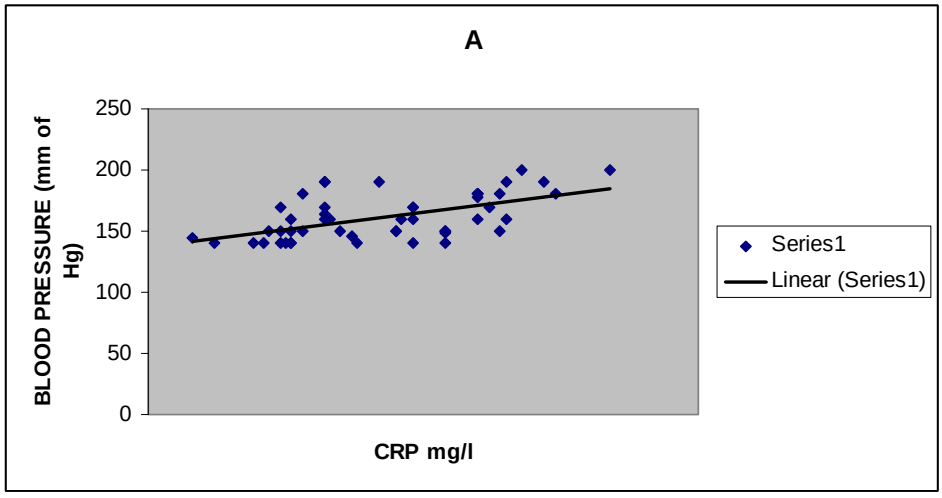

Figure 1A: showing positive correlation between the serum concentration of c-reactive protein and systolic blood pressure.

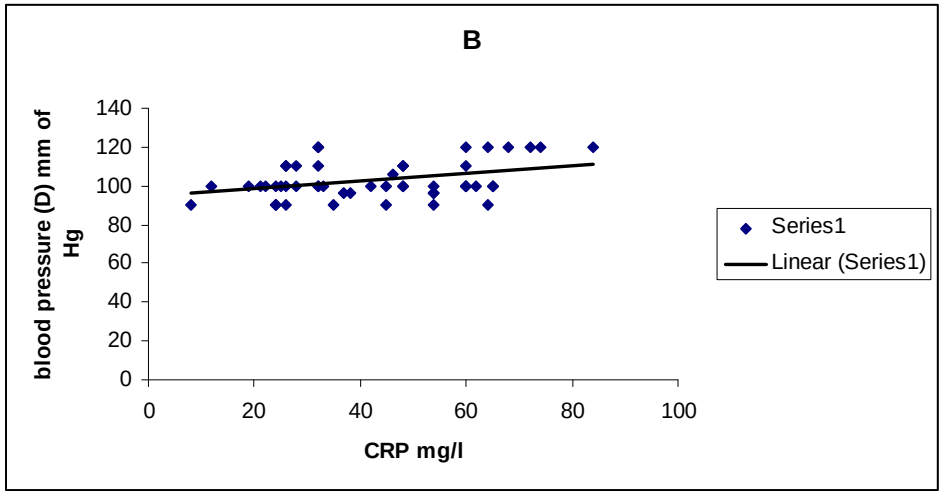

Figure 1B: showing positive correlation between the serum concentration of c-reactive protein and diastolic blood pressure.

high and directly related with PIH(42.02 mg/L±18 .01 mg/L p=<0,0001) than normal non women (2.99±0.81mg/L)and normal pregnant mother (4.2 ±0.93 mg/L).

Discussion

The pathogenesis of PIH remains uncertain in spite of many research efforts .Many theories have been implicated in the genesis of PIH. Endothelial cell dysfunction and inflammation are considered to have a major role in the etiopathogenesis of PIH. Systemic inflammation might contribute to the pathogenesis of PIH[10] .Inflammation leads to endothelial dysfunction, predisposing women to develop PIH. [11]. CRP is elevating marker in PIH [12] .PIH is associated with increased CRP levels however, there are few studies concerning correlation of CRP levels due to severity of PIH.. In the present study it is found that significant rise of serum C-reactive protein in mild and severe PIH (including eclampsia).It was found in the study that CRP is positively correlated with diastolic blood pressure, systolic blood pressure, Serum Uric Acid ,Serum Creatinine, Total leukocyte count, Absolute Neutrophil Count, SGPT, ßHCG, and is negatively correlated with Platelet. This study assumes that serum CRP is a positive finding in PIH and also proves that inflammation plays an important role in the pathogenesis of PIH.

Conclusion

Simple determination of serum CRP (even by latex fixation slide test which needs no special instruments and can be done at PHC level) along with clinical features helps the diagnosis of PIH and its severity for management by which ultimately reduces the grave complication of PIH by referring the mother to referral hospital in right time to get a healthy baby with healthy mother.

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