Correlation between maternal serum C-reactive protein concentrations and the degree of pre-eclampsia.

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Abstract

Introduction: Hypertensive disorders complicating pregnancy are common& form one of the deadly triadalong with hemorrhage and infection that contribute greatly to maternal morbidity & mortality. This disorder complicates about 5-7% of pregnancy worldwide.

Aim of this study was to measure the levels of maternal serum C-reactive protein in pre-eclamptic and eclamptic patients at 28, 32 and 36 weeks of gestation and to find out any possible correlation between these levels and the severity of pre-eclampsia and eclampsia compared with normal values of control group

Methods: The study will be conducted on eighty primigravida at 28, 32, and 36 weeks of gestation attending El-Shatby maternity university hospital. They will be classified equally into the following groups: Group 1: (20 cases) Twenty normal pregnant women their blood pressure recorded as SBP 130 mmHg or less and DBP is 80 mmHg or less. These patients had no proteinuria, taken as a control group .Group 2: (20 cases) Twenty cases with mild pre-eclampsia, their blood pressure recorded as systolic blood pressure (SBP) more than or equal 140 mmHg and less than 160 mmHg. Their diastolic blood pressure (DBP) more than or equal 90 mmHg and less than 110 mmHg together with proteinuria which is 1+ or 2+ developed after 20 weeks of gestation. Group 3: (20 cases) Twenty cases with severe pre-eclampsia, recorded their blood pressure as SBP more than or equal 160 mmHg and DBP greater than or equal 110 mmHg recorded at least two occasions at least six hours apart plus proteinuria which is 3+ or 4+ on urine dipstick. Group 4: (20 cases) Twenty cases with antepartum eclampsia, these are pre-eclamptic patients with eclamptic fits characterized by generalized tonic-clonic convulsions. The cases should fulfill the following criteria: Primigravida, Singleton intrauterine pregnancy and Festational age 28, 32 and 36 weeks. Exclusion criteria: Hypertension, Increased C-reactive protein (infections, inflammatory conditions, malignancy) and Medical disorders (diabetes mellitus, hepatic disorders, renal disorders).Fits should be excluded when patients for group 4 were selected.

Results and conclusions: The serum levels of C-reactive protein were positively correlated with pregnancy duration in pre-eclamptic pregnancy but not in normal pregnancy during the follow up period. As in normal pregnancy, there was a normal drop in the values of C-reactive protein at 32 weeks. The values of C-reactive protein at 28 weeks were 3.19±1.06 mg/L and the levels at 32 weeks were 2.70±1.01 mg/L then the levels raised up again at 36 weeks to be 4.01±1.28 mg/L. This normal drop was lost in pre-eclamptic pregnancy, as there was progressive increase in the values of C-reactive protein longitudinally during 28 weeks, 32 weeks and 36 weeks. The results were positively correlated with the severity of pre-eclampsia as shown in table 7. As C-reactive protein values in mild

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pre-eclampsia were much higher than values in normal pregnancy.

Keywords: CRP, pregnancy, preeclampsia

Introduction

Hypertensive disorders complicating pregnancy are common& form one of the deadly triadalong with hemorrhage and infection that contribute greatly to maternal morbidity & mortality. (1) This disorder complicates about 5-7% of pregnancy worldwide. (2) Detection of pregnancy-associated proteins in maternal serum can indicate severity of the condition and predict the prognosis. In this respect, C reactive protein (CRP), a sensitive indicator marker can be used in this setting.(3) Several attempts have been made to predict the occurrence and severity of the disease. (4) As pre-eclampsia represent the clinical manifestation of endothelial dysfunction which is a part of an excessive maternal inflammatory response to pregnancy, many markers had been used to assess the development and severity of pre-eclampsia as fibronectin, tyrosine kinase-1, uric acid and inhibin-A. (5) C-reactive protein is an inflammatory biomarker, a sensitive index of tissue inflammation and damage. C-reactive protein is a serum glycoprotein produced by the liver during acute inflammation. (6) The circulating value of CRP reflect ongoing inflammation and tissue damage much more accurately than do the laboratory parameters of other acute phase response.. (7) Data suggest that the specific biologic function of CRP may link it to the patho-physiology of pre-eclampsia. (8) The aim of this study was to measure the levels of maternal serum C-reactive protein in pre-eclamptic and eclamptic patients at 28, 32 and 36 weeks of gestation and to find out any possible correlation between these levels and the severity of pre-eclampsia and eclampsia compared with normal values of control group.

Methods

The study will be conducted on eighty primigravida at 28, 32, and 36 weeks of gestation attending El-Shatby maternity university hospital. They will be classified equally into the following groups: Group 1: (20 cases) Twenty normal pregnant women their blood pressure recorded as SBP 130 mmHg or less and DBP is 80 mmHg or less. These patients had no proteinuria, taken as a control group .Group 2: (20 cases)Twenty cases with mild pre-eclampsia, their blood pressure recorded as systolic blood pressure (SBP) more than or equal 140 mmHg and less than 160 mmHg. Their diastolic blood pressure (DBP) more than or equal 90 mmHg and less than 110 mmHg together with proteinuria which is 1+ or 2+ developed after 20 weeks of gestation. Group 3: (20 cases) Twenty cases with severe pre-eclampsia, recorded their blood pressure as SBP more than or equal 160 mmHg and DBP greater than or equal 110 mmHg recorded at least two occasions at least six hours apart plus proteinuria which is 3+ or 4+ on urine dipstick. Group 4: (20 cases) Twenty cases with antepartum eclampsia, these are pre-eclamptic patients with eclamptic fits characterized by generalized tonic-clonic convulsions. The cases should fulfill the following criteria: Primigravida, Singleton intrauterine pregnancy and Festational age 28, 32 and 36 weeks. Exclusion criteria: Hypertension, Increased C-reactive protein (infections, inflammatory conditions, malignancy) and Medical disorders (diabetes mellitus, hepatic disorders, renal disorders).Fits should be excluded when patients for group 4 were selected.

After approval of local ethics committee an informed consent was obtained from every woman included in the study. All the cases were subjected to the following: Proper history taking, Thorough clinical examination, Obstetrics ultrasound for: Fetal biometric measurements, Amniotic fluid index and Placental assessment. Biophysical profile and Doppler umbilical artery blood flow were indicated in intrauterine growth restriction, oligohydraminous and abnormal biophysical score. Laboratory investigations: Ten millimeters of venous blood sample was taken and the following testes were done .Complete blood count, Renal function tests, Complete urine analysis, Blood urea, creatinine and Serum uric acid. Liver function testes: Liver enzymes Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) ,Direct and indirect serum bilirubin, Prothrombin time and activity, Serum proteins :Total proteins and Serum albumin.

C-reactive protein analysis: Laboratory investigations of C-reactive protein were measured three times; one at 28 weeks, second at 32 weeks and finally at 36 weeks gestation except cases of severe pre-eclampsia and eclampsia were measured once at the time of admission. Serum quantitative nephelometric kits for human C-reactive protein were used in our research. Each kit contains a calibrator (affinity purified C-reactive protein). The standard management protocol was adopted in El Shatby Maternity University hospital for cases of pre-eclampsia: Cases of mild pre-eclampsia were prescribed methyl dopa (aldomet 250mg); the doses were adjusted according to the response and the progression together with monitoring and necessary advice. Cases of sever pre-eclampsia and eclampsia were admitted to ICU of El Shatby maternity university hospital and the following protocol is adopted:

Antihypertensive and sedatives: using magnesium sulphate as bolus dose and maintenance in addition to methyl dopa and hydralazine. Termination of pregnancy either by induction of labour or immediate caesarean section when fetal distress, maternal hypertension more than or equal 160/110 not responding to treatment, impending fits or actual fits. Follow up of the cases to detect progression, complication and outcome of maternal and fetal conditions was carried out.

Results

The results of this work will be categorized as follows: Clinical data of the studied cases. Laboratory finding of the four groups: Group 1 normal cases, Group 2 mild cases, Group 3 severe cases and Group 4 eclamptic cases. Comparison of CRP levels between the four studied groups. Follow up of CRP levels in normal pregnant females and cases with mild pre-eclampsia at 28, 32 and 36 weeks of gestation

The mean age of the four studied groups was 27.25±3.83 years old, 29.8±4.71 years old, 26.90±3.78 years old and 28.25±3.193 years old in normal, mild, severe and eclampsia groups respectively. There was no significant difference between the four studied groups regarding afe, p=0.104 (table 1).

The mean systolic blood pressure of the four studied groups was 115.6±5.753 mmHg, 148.0±5.606 mmHg, 188.75±22.668 mmHg and 197.25±25.817 mmHg respectively in normal, mild, severe and eclampsia groups, it was found that there was a highly significant difference between the four studied groups regarding systolic blood pressure (systolic BP), each of the studied groups had a significant difference from other groups (p=0.0001) (table 1).

The mean diastolic blood pressure of the four studied groups was 73.85±4.753 mmHg, 99.40±5.606 mmHg, 118.75±29.668 mmHg and 123.75±8.37 mmHg respectively in normal, mild, severe and eclampsia groups, it was found that there was a highly significant difference between the four studied groups regarding diastolic blood pressure, each of the studied groups had a significant difference from other groups (p=0.0001) (table 1).

Table 1: Comparison between the studied groups according to clinical parameters:

	Normal N=20	Mild N=20	Severe N=20	Eclampsia N=20	F (p)
Maternal age Range (years) Mean ± SD (years)	19.00-33.00 27.25±3.84	23.00-38.00 29.75±4.71	20.00-36.00 26.90±3.78	22.00-33.00 28.25±3.19	2.124 (0.104)
P1		0.136	0.38	0.422	
P2			0.22	0.230	
P3				0.279	
Systolic BP Range (mmHg) Mean ± SD (mmHg)	108.00-125.00 115.60±5.75	140.00-155.00 146.85±5.58	140.00-230.00 188.75±22.70	160.00-230.00 197.50±19.50	121.073* (<0.001)
P1		<0.001*	<0.001*	<0.001*	
P2			<0.001*	<0.001*	
P3				0.078	
Diastolic BP Range (mmHg) Mean ± SD (mmHg)	65.00-82.00 73.85±4.92	90.00-107.00 99.40±5.78	110.00-140.00 118.00±7.85	110.00-140.00 119.75±8.35	193.117* (<0.001)
P1		<0.001*	<0.001*	<0.001*	
P2			<0.001*	<0.001*	
P3				0.423	

*Significant difference

- P1= Comparison between normal and mild, severe and eclamptic group
- P2= Comparison between mild and both severe and eclamptic group.
- P3= Comparison between severe and eclamptic group.

Hemoglobin level (Hb level) in normal group was 11.44±0.627g/dl, in mild pre-eclampsia it was 10.627±0.85g/dl and in severe pre-eclampsia it was 10.17±0.987g/dl, in eclampsia the Hb level was 9.635±0.591 g/dl. There was a significant decrease in Hb level in eclampsia group than the other groups, on the other hand it was found that there was a significant increase in Hb level in normal group than the other groups, while mild and severe pre-eclampsia had no difference regarding the Hb level (p=0.0001) (table 2).

Hematocrite level (Hct level) in normal group was 35.26±3.47mg/L, in mild pre-eclampsia it was 41.00±3.46% and in severe pre-eclampsia it was 32.87±2.83%, in eclampsia the Hct level was 30.55±2.92%, there was a significant difference in Hct level in the four groups (p=0.0001) (table 2).

Platelet count in normal group was 298.15±18.48x103/L, in mild pre-eclampsia it was 207.2±6.026x103/L and in severe pre-eclampsia it was 141.25±42.08x103/L, in eclampsia the platelet count was 111.25±29.86x103/L, there was a significant decrease in platelet count in eclampsia group than the other groups, on the other hand it was found that there was a significant increase in platelet count in normal group than the other groups (p=0.0001) (table 2)

Table 2: Comparison between the studied groups according to the complete blood count

	Normal N=20	Mild N=20	Severe N=20	Eclampsia N=20	F (p)
Hb Range (g/dl) Mean ± SD	10.30-12.50 11.44±0.63	9.10-12.00 10.66±0.80	8.70-12.10 10.18±0.99	8.60-10.40 9.64±0.59	19.864* (<0.001)
P1		0.04*	0.037*	0.022*	
P2			0.086	0.011*	
P3				0.029*	
Hct Range (%) Mean ± SD	29.70-39.90 35.21±3.48	31.30-83.30 41.00±10.45	26.00-36.00 30.55±2.93	30.00-39.50 32.87±2.83	11.680* (<0.001)
P1		0.003*	0.014*	0.212	
P2			<0.001*	<0.001*	
P3				0.215	
Platelet count Range (cmm/micro liter) Mean ± SD	65.00-82.00 73.85±4.92	90.00-107.00 99.40±5.78	110.00-140.00 118.00±7.85	110.00-140.00 119.75±8.35	193.117* (<0.001)
P1		<0.001*	<0.001*	<0.001*	
P2			<0.001*	<0.001*	
P3				<0.001*	

*Significant difference

- P1= Comparison between normal and mild, severe and eclamptic group
- P2= Comparison between mild and both severe and eclamptic group.
- P3= Comparison between severe and eclamptic group.

Serum urea shows a significant difference in the studied groups, the mean value in normal group was 16.05±3.3mg/L, while in mild group it was found 16.50±4.33mg/L, in severe group serum urea was 25.85±4.97mg/L, finally in eclampsia group the serum urea was 30.5±5.29mg/L, there was a significant increase in serum urea in mild group than normal and in severe group than normal and mild and highly increased in eclampsia than all other groups (p=0.0001) (Table 3).

Serum creatinine show a significant difference in the studied groups, the mean value in normal group was 0.65±0.167mg/L, while in mild groups was 0.63±0.33mg/L, in severe group serum creatinine was 1.14±0.198mg/L, finally in eclampsia group the serum creatinine was 1.32±0.234mg/L, there was a significant increase in serum creatinine in mild group than normal and in severe group than normal and mild and highly increased in eclampsia than all other groups (p=0.0001) (table 3).

Serum uric acid show a significant difference in the studied groups, the mean value in normal group was 4.295±0.7944mg/L, while in mild group was 5.67±0.572mg/L, in severe group serum uric acid was 7.49±1.878mg/L, finally in eclampsia group the serum uric acid was 8.29±2.175mg/L, there was a significant increase in serum uric acid in mild group than normal and in severe group than normal and mild and highly increased in eclampsia than all other groups (p=0.0001) (table 3).

Table 3: Comparison between the studied groups according to laboratory parameters

	Normal N=20	Mild N=20	Severe N=20	Eclampsia N=20	F (p)
Serum urea (20-40mg/L) Range Mean±SD	10-20 16.05±3.30	10-23 16.50±4.33	18-33 25.85±4.97	20-39 30.50±5.30	49.363* (<0.001)
P1		0.755	<0.001*	<0.001*	
P2			<0.001*	<0.001*	
P3				0.002*	
Serum creatinine (0.6-1.2mg/L) Range Mean±SD	0.40-0.9 065±017	0.10-1.20 0.63±0.33	0.90-1.50 1.14±0.20	0.80-1.80 1.33±0.25	41.711* (<0.001)
P1		0.796	<0.001*	<0.001*	
P2			<0.001*	<0.001*	
P3				0.016	
Serum uric acid (2-6mg/L) Range Mean±SD	2.70-5.60 4.30±0.79	4.60-6.60 5.65±0.58	4.80-11.60 7.48±1.87	5.50-12.40 8.29±2.18	28.236* (<0.001)
P1		0.006*	<0.001*	<0.001*	
P2			<0.001*	<0.001*	
P3					

*Significant difference

- P1= Comparison between normal and mild, severe and eclamptic group
- P2= Comparison between mild and both severe and eclamptic group.
- P3= Comparison between severe and eclamptic group.

The mean value of aspartate transferase (AST) was 33.25±7.369 U/L in normal group, 32.55±4.01 U/L in mild group, 177.75±100.95 U/L in severe group and 180.55±103.821 U/L in eclampsia, there was a significant increase in AST in severe and eclampsia group than normal and mild group, on the other hand there was no significant difference between normal and mild group but there were significant difference between severe and eclampsia group. (Table 4)

The mean value of alanine transferase (ALT) was 30.30±5.10 U/L in normal group, 38.25±3.39 U/L in mild group, 232.5±121..20 U/L in severe group and 236.85±127.63 U/L in eclampsia, there was a significant increase in ALT in severe and eclampsia group than normal and mild group, on the other hand there was no significant difference between normal and mild group but there were significant difference between severe and eclampsia group. (Table 4)

The mean value of serum bilirubin was 0.589±.219 mg/L in normal group, 0.71±0.271 mg/L in mild group, 2.04±1.067 mg/L in severe group and 2.29±1.03 mg/L in eclampsia, there was a significant increase in serum bilirubin in severe and eclampsia group than normal and mild group, on the other hand there was no significant difference between normal and mild group and also there was no significant difference between severe and eclampsia group. (Table 4)

It was found that there was a slightly higher significant in total protein in normal group than the other groups.

total protein was 6.08±0.522 g/dl in normal group, in mild group it was 5.35±0.406 g/dl and in severe group it was 5.29±0.84 g/dl, finally in eclampsia was 5.44±0.85 g/dl. (Table 4)

The mean value of albumin was 2.66±0.273g/dl in normal group, in mild group it was 2.26±0.32 g/dl, in severe group it was found that the albumin was 1.98±0.44 g/dl, and in eclampsia albumin was 1.085±0.425 g/dl, there was a significant decrease of albumin in severe and eclampsia group than normal and mild cases. (Table 4)

The mean value of prothrombin time was 12.55±1.19 in normal group, 12.85±1.39 in mild group, 15.03±1.38 in severe group and 17.00±1.28 in eclamptic group. There was a significant increase in prothrombin time in severe and eclampsia group than normal and mild group, on the other hand there was no significant difference between normal and mild group but there were significant difference between severe and eclampsia group. (Table 4)

The mean value of prothrombin activity was 92.70±6.86 in normal group, in mild group it was 91.55±8.34, in severe group it was found that prothrombin activity was 89.20±6.46, and in eclampsia group was 77.49±6.00, there was a significant decrease of prothrombin activity in severe and eclampsia group than normal and mild cases. (Table 4)

finally in eclampsia group the serum creatinine was 1.32±0.234mg/L, there was a significant increase in serum creatinine in mild group than normal and in severe group than normal and mild and highly increased in eclampsia than all other groups (p=0.0001) (table 3).

Table 4: comparison between the studied groups according to liver profile.

	Normal	Mild	Severe	Eclampsia	F (p)
AST (U/L) Range Mean±SD	24.00-45.00 33.25±7.37	24.00-40.00 32.55±4.11	70.00-360.00 77.75±100.96	80.00-426.00 180.55±103.82	27.112* (<0.001)
P1		0.976	<0.001*	<0.001*	
P2			<0.001*	<0.001*	
P3				0.903	
ALT (U/L) Range Mean±SD	24.00-46.00 30.30±5.10	29.00-45.00 38.25±4.51	95.00-420.00 232.25±111.95	100.00-505.00 236.85±127.63	37.090 (<0.001)
P1		0.768	<0.001*	<0.001*	
P2			<0.001*	<0.001*	
P3				0.864	
Bilirubin (mg/L) Range Mean±SD	0.30-1.00 0.59±0.22	0.30-1.00 0.71±0.29	0.80-4.20 2.03±1.05	1.00-4.50 2.30±1.03	27.110* (<0.001)
P1		0.622	<0.001*	<0.001*	
P2			<0.001*	<0.001*	
P3				0.262	
Serum proteins (g/dl) Range Mean±SD	5.00-6.81 6.09±0.52	4.70-6.00 5.31±0.38	4.20-6.00 5.29±0.84	4.10-6.90 5.44±0.85	6.164* (0.001)
P1		0.001*	<0.001*	0.003*	
P2			0.926	0.546	
P3				0.486	

Albumin (g/dl) Range Mean±SD	2.00-3.10 2.67±0.27	1.80-2.80 2.26±0.32	1.40-3.00 1.98±0.45	1.60-2.80 2.09±0.43	13.026* (<0.001)
P1		0.001*	<0.001*	<0.001*	
P2			0.022*	0.154	
P3				0.377	
Prothrombin time Range (seconds) Mean±SD	11-14 12.55±1.19	11-16 12.85±1.39	12-17 15.03±1.38	15-19 17.00±1.28	50.257* (<0.001)
P1		0.001*	<0.001*	<0.001*	
P2					
P3					
Prothrombin activity Range Mean±SD	79-100 92.70±6.86	78-100 91.55±8.34	79-100 89.20±6.49	70-89 77.49±6.00	20.053* (<0.001)
P1		0.472	<0.001*	<0.001*	
P2			<0.001*	<0.001*	
P3				<0.001*	

*Significant difference

- P1= Comparison between normal and mild, severe and eclamptic group
- P2= Comparison between mild and both severe and eclamptic group.
- P3= Comparison between severe and eclamptic group.

The mean value of high sensitive C-reactive protein (hs CRP) at 28 weeks was 3.19±1.06 mg/L in normal patients, while in mild eclampsia was 7.64±3.38 mg/L, in severe eclampsia hs CRP was 11.99±6.40 mg/L, in eclampsia the mean value of hs CRP was 27.40±14.51 mg/L, there was a significant increase in s CRP in mild group than the normal group, (p=0.021). Mild group show a significant decrease in hs CRP than severe and eclampsia group. Finally, eclamptic group showed a significant increase tan the severe group, i.e. the eclampsia group had the highest value of hs CRP (table 5), Fig. (1), shows the box plot graph of hs CRP level in different groups, the graph shows the range of 95.0% of the data, the mean of the value and the standard deviation of the data, from Fig. (1), it was found that the normal group had a wide range of data, and eclampsia showed the highest value and the largest range.

High sensitive C-reactive protein (hs CRP) at 32 weeks in normal group was 2.70±1.01 mg/L, in mild group it was found that the mean value of hs CRP was 8.86±3.55 mg/L, in severe group the mean value of hs CRP was 12.02±5.11 mg/L, finally in eclampsia group the mean value of hs CRP was 28.62±9.89 mg/L, statistically it was found that there was a significant increase in hs CRP in mild, severe and eclampsia than normal group, also it was found that mild group showed a significant decrease in hs CRP than severe and eclampsia group. Finally, eclamptic group showed a significant increase than severe group, i.e. the eclampsia group had the hightest value of hs CRP (table 5), Fig. (2), shows the box plot graph of hs CRP level in different groups, the graph shows the range of 95.0% of the data, the mean of the value and the standard deviation of the data, from Fig. (2), it was found that the normal group had a wide range of data, and eclampsia showed the highest value.

High sensitive C-reactive protein (hs CRP) at 36 weeks in normal group was 4.01±1.28 mg/L, in mild group it was found that the mean value of hs CRP was 10.54±3.53 mg/L, in severe group the mean value of hs CRP was 13.20±1.57 mg/L, finally in eclampsia group the mean value of hs CRP was 28.02±16.40 mg/L, statistically it was found that there was a significant increase in hs CRP in mild, severe and eclampsia than normal group, also it was found that mild group showed a significant decrease in hs CRP than severe and eclampsia group. Finally, eclamptic group showed a significant increase than severe group, i.e. the eclampsia group had the highest value of hs CRP (table 5), Fig. (3), shows the box plot graph of hs CRP level in different groups, the graph shows the range of 95.0% of the data, the mean of the value and the standard deviation of the data, from Fig. (3), it was found that the normal group had a wide range of data, and eclampsia showed the highest value.

Table 5: comparison between studied groups according to the hs CRP level

	Normal	Mild	Severe	Eclampsia	F (p)
hsCRP 28 weeks Range (mg/L) Mean±SD (mg/L)	2.10-7.00 3.19±1.06	2.40-15.90 7.64±3.38	6.70-21.80 11.99±6.40	13.00-56.00 27.40±14.51	30.002* (<0.001)
P1		0.021*	0.001*	<0.001*	
P2			0.041*	<0.001*	
P3				<0.001*	
32 weeks Range (mg/L) Mean±SD (mg/L)	2.00-6.40 2.70±1.01	2.60-18.10 8.86±3.55	6.50-21.70 12.02±5.11	11.40-48.00 28.62±9.89	59.775* (<0.001)
P1		<0.001*	<0.001*	<0.001*	
P2			0.047*	<0.001*	
P3				<0.001*	
36 weeks Range (mg/L) Mean±SD (mg/L)	2.50-8.00 4.01±1.28	5.50-19.00 10.54±3.53	11.80-15.40 13.20±1.57	15.80-56.00 28.02±16.40	26.491* (<0.001)
P1		<0.001*	0.004*	<0.001*	
P2			0.0380	<0.001*	
P3				<0.001*	

*Significant difference

- P1= Comparison between normal and mild, severe and eclamptic group
- P2= Comparison between mild and both severe and eclamptic group.
- P3= Comparison between severe and eclamptic group.

This procedure is a useful way to evaluate the performance of classification schemes in which there is one variable with two categories by which subjects are classified.

Statistics: area under the ROC curve with confidence interval and coordinate points of the ROC curve. Plots: ROC curve.

Methods: the estimate of the area under the ROC curve can be computed either non-parametrically or parametrically using a bi-negative exponential model.

Area under the curve

Test result Variable(s)	Area	Std. Error(a)	Asymptomatic Sig.(b)	Asymptomatic 95% confidence interval	
				Lower Bound	Upper Bound
hsCRP 28 wks	.915	.056	.0001	.806	1.024
hsCRP 32 wks	.962	.032	.0001	.900	1.024
hsCRP 36 wks	.983	.017	.0001	.951	1.016

The test result variable(s): hsCRP 28 wks, hsCRP 32 wks has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased

a) Under the non-parametric assumption b) Null hypothesis: true area=0.5

Sensitivity, specificity and accuracy of CRP:

The prognostic value of the tests was determined by:

1. Sensitivity of the test: the percent of the positives by the test and the true positives
2. Specificity of the test: the percent of the negatives by the test and the true negatives
3. Accuracy: the percent of agreement between the two tests

Table (6), shows the sensitivity, specificity and accuracy of Hs CRP at different weeks of follow up, receiver operating curve (ROC) also showed the area under the curve for each line presented by period of follow up and measuring hs CRP.

At 28 weeks:

Hs CRP at 28 weeks show cut off value 5.365 and show a sensitivity 90.0%, specificity 92.0% and accuracy 91.5%, (table 6), ROC curve show the area under the curve for hs CRP at 28 weeks was 0.915 with level of significance <0.001.

At 32 weeks:

From ROC curve it was found that the area under the curve was 0.962, this value showed sensitivity 94.0%, specificity 96.0% and accuracy 96.2, the cut off value of hs CRP at 32 weeks was 4.82.

At 36 weeks:

At 36 weeks it was found that the cut off value of hs CRP was 7.21, the sensitivity was 98.5%, the specificity was 96.0% and the accuracy was 98.3%, the area under the curve was 0.983 which was detected by using ROC curve.

Table 6: Sensitivity, specificity and accuracy of hs CRP at different period of follow up in prediction of severity of the disease

	Hs CRP 28 weeks	Hs CRP 32 weeks	Hs CRP 36 weeks
Cut off value	5.365	4.82	7.21
Sensitivity	90.0	94.0	98.5
Specificity	92.0	96.0	96.0
Accuracy	91.5	96.2	98.3

The serum levels of C-reactive protein were positively correlated with pregnancy duration in pre-eclamptic pregnancy but not in normal pregnancy during the follow up period.

As in normal pregnancy, there was a normal drop in the values of C-reactive protein at 32 weeks. The values of C-reactive protein at 28 weeks were 3.19±1.06 mg/L and the levels at 32 weeks were 2.70±1.01 mg/L then the levels raised up again at 36 weeks to be 4.01±1.28 mg/L. This normal drop was lost in pre-eclamptic pregnancy, as there was progressive increase in the values of C-reactive protein longitudinally during 28 weeks, 32 weeks and 36 weeks.

The results were positively correlated with the severity of pre-eclampsia as shown in table 7. As C-reactive protein values in mild pre-eclampsia were much higher than values in normal pregnancy.

Table (7): Follow up pattern of rising levels of hsCRP in the following two groups during different weeks of gestation (28, 32, 36 weeks):

	hsCRP		
	28 weeks	**32 weeks**	**36 weeks**
Normal (mg/L)	3.19±1.06	2.70±1.01	4.01±1.28
t_1 (p)		8.197* (<0.001)	9.004* (<0.001)
t_2 (p)			10.375* (<0.001)
Mild (mg/L)	7.64±3.38	8.86±3.55	10.54±3.53
t_1 (p)		5.489* (<0.001)	12.841* (<0.001)
t_2 (p)			6.830* (<0.001)

t_1 (p): Paired t-test between 28th week vs. other stages

t_2 (p): Paired t-test between 32nd week and 36th week

Discussion

In this study a total number of one thousand pregnant Pre-eclampsia is a disease of pregnancy associated with endothelial cell activation, endothelial cell dysfunction and finally cell damage. Cell activation is a component of systemic maternal inflammatory response found in normal pregnancy. (9) It has been hypothesized that placental hypoxia resulting from utero-placental insufficiency amplifies release of inflammatory stimuli into maternal circulation. (5) In this study, C-reactive protein and white blood cell count were increased early in pregnancy in women who subsequently developed in pre-eclampsia. CRP was much higher in pre-eclamptic and eclamptic groups. Tjoa et al (8) .demonstrated that elevated CRP levels during 1st trimester of pregnancy are indicative of pre-eclampsia & IUGR. Wolf et al (10) reported that pregnant women with higher CRP concentrations presented an increased risk of pre-eclampsia.

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