Al-Azhar University Journal
for Virus Research and Studies

The value of Serum Amyloid A in Preeclampsia

Samira Yossef El Mallah[1], Lamiaa Mohamed Yosry [1], Magda Ibrahim Mohamed[2], Hanan Mohammed Ateeyah*[3]

[1] Professor of Obstetrics and Gynecology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

[2] Professor of Clinical Pathology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

[3] M.B.CH, AL-Mergeb University-Libya, MSc in Obstetrics and Gynecology, Ain Shams University

***E-mail: d.hanan.m.m.a@gmail.com**

Abstract

Preeclampsia is a common complication of pregnancy and remains a common cause of maternal and fetal mortality. The clinical symptoms of preeclampsia are caused by widespread endothelial dysfunction suggested to be a part of an exaggerated maternal inflammatory response to pregnancy. The objective of this study is to estimate serum amyloid A in pregnant women with preeclampsia. Type of study: Case control study. Study period: from Septemper2019 to August 2021. Study population: The study was carried out on 75 women divided into three groups: Group I (25 women): The control group are healthy pregnant women who had an uncomplicated antenatal course. Group II (25 women): They are women with mild preeclampsia. Group III (25 women): They are women with severe preeclampsia. Serum amyloid A level (SAA) varied significantly in severe preeclampsia compared to mild and control groups. There was statistically significant positive correlation between serum amyloid A level and most of the indices of severity of preeclampsia, including systolic and diastolic blood pressure, liver transaminases, serum creatinine and albuminuria.

Keywords: Angiotensin receptor, Extravillous trophoblast, Serum amyloid A.

1. Introduction

Preeclampsia is a common complication of pregnancy and remains a common cause of maternal and fetal mortality. The clinical symptoms of preeclampsia are caused by widespread endothelial dysfunction suggested to be a part of an exaggerated maternal inflammatory response to pregnancy [1]. The syndrome of preeclampsia is a condition with many manifestations, and suspected organ impairment is monitored by serum marker for hemolysis, coagulopathy, liver and renal function [2].

Serum amyloid A (SAA) is acute phase protein predominantly produced and secreted by hepatocytes. Other cells including lymphocytes, monocytes and macrophages can also produce this protein. The induction of SAA synthesis is triggered by a number of cytokines, chiefly

IL-6 and TNF- predominantly released from macrophage and monocyte at the inflammatory site [3] .
The synthesis is influenced by steroid hormones and adipose tissue (due to IL-6 production in the adipocytes) [4].
Increased baseline levels of SAA analyzed by high sensitivity assays has been recognized as marker of vascular wall inflammation and as clinical marker for the prediction of cardiovascular events [5].
Since preeclampsia is associated with widespread endothelial dysfunction, proposed to be provoked by an increased maternal systemic inflammatory response, the maternal plasma level of SAA might be expected to be increased when compared to normal pregnancy levels. The maternal plasma level of SAA in normal pregnancy could differ from non-pregnant level due to increased hormone levels, increased adipose tissue and/or secondary to modification of inflammatory response in normal pregnancy [6].
The level of SAA, which is a major acute phase protein, has previously been found to be unaltered by pregnancy. In a recent pilot study, the SAA level was found to be increased in women with preeclampsia correlating with other pro-inflammatory cytokines [7].
The main objective of this investigation was estimate serum amyloid A in pregnant women with preeclampsia.

2. Materials and Methods

Type of study: Case control study.

Study period: From Septemper2019 to August 2021.

Study population:
The study was carried out on 75 women divided into three groups:

Group I (25 women):
- The control group are healthy pregnant women who had an uncomplicated antenatal course.

Group II (25 women):
- They are women with mild preeclampsia.

Group III (25 women):
- They are women with severe preeclampsia.

Inclusion criteria:

1. Pregnant women: age 18-35 years old.
2. Gestational age: greater than or equal to 20 weeks.
3. Primigravida.
4. Singleton pregnancy.

Exclusion Criteria:

1. Multiple pregnancy.
2. Smoking.
3. Past history of preexisting medical conditions (chronic hypertension, chronic renal disease, diabetes mellitus, history of preeclampsia and immunosuppression).
4. Clinical signs and symptoms of infection.
5. Active labour or ruptured fetal membranes.
6. History of illicit drug use.
7. Receiving steroid therapy during pregnancy.

All cases in the groups were subjected to:

a) Full history taking including personal history to exclude smoking, medical history to exclude pre-existing disease such as diabetes, hypertension and drug history.
b) Body weight, height and BMI.
c) General and abdominal examination.
d) Ultrasound was done to exclude multiple pregnancy, poly-hydramnios and fetal abnormality.

All the women eligible for the study were subjected for sampling. Serum sampling was collected from all women before any intervention such as administration of steroids or Mgso4. Venous blood sample (5cc) was taken from each participant for examination of serum amyloid A. The

collected blood was centrifuged, and the serum was stored to measure the level of serum amyloid A by Enzyme Linked Immune Sorbant Assay (ELISA) technique (method kit: catalog NO: E1225HU in Clinical Pathology Department- Ain Shams University.

3. Results

The results of the present study are demonstrated in the following tables and Figureures.

Table (1): Comparison between control group, mild preeclampsia group and severe preeclampsia group according to demographic data.

Baseline characteristics	Control group (n=25)	Mild preeclampsia group (n=25)	Severe preeclampsia group (n=25)	ANOVA		Post HOC test		
				F	p-value	P1	P2	P3
Age (years)								
Mean ± SD	**28.28±4.92**	**29.80±3.20**	**29.92±3.99**	**1.244**	**0.294**	**0.194**	**0.161**	**0.918**
Range	**18 – 37**	**25 – 34**	**22 – 36**					
BMI [wt/(ht)^2]								
Mean ± SD	**26.38±2.12**	**26.96±1.30**	**27.20±2.23**	**1.191**	**0.310**	**0.292**	**0.138**	**0.661**
Range	**21 – 29**	**24.9 – 28.8**	**21.6 – 29.8**					
Gestational age (wks)								
Mean ± SD	**34.60±3.04**	**33.20±2.52**	**34.08±1.78**	**2.004**	**0.142**	**0.051**	**0.464**	**0.217**
Range	**28 – 39**	**28 – 38**	**30 – 37**					

*F-One Way Analysis of Variance; p-value>0.05 NS; *p-value <0.05 S; **p-value <0.001 HS*

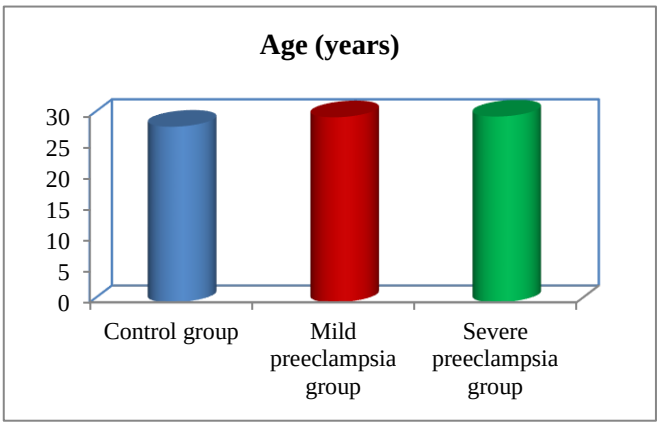

Figure 1: Bar chart between control group, mild preeclampsia group and severe preeclampsia group according to age (years).

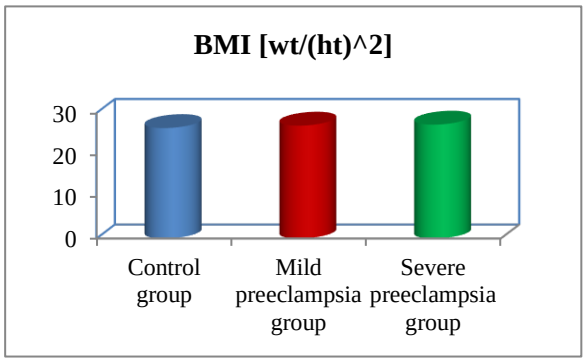

Figure 2: Bar chart between control group, mild preeclampsia group and severe preeclampsia group according to BMI.

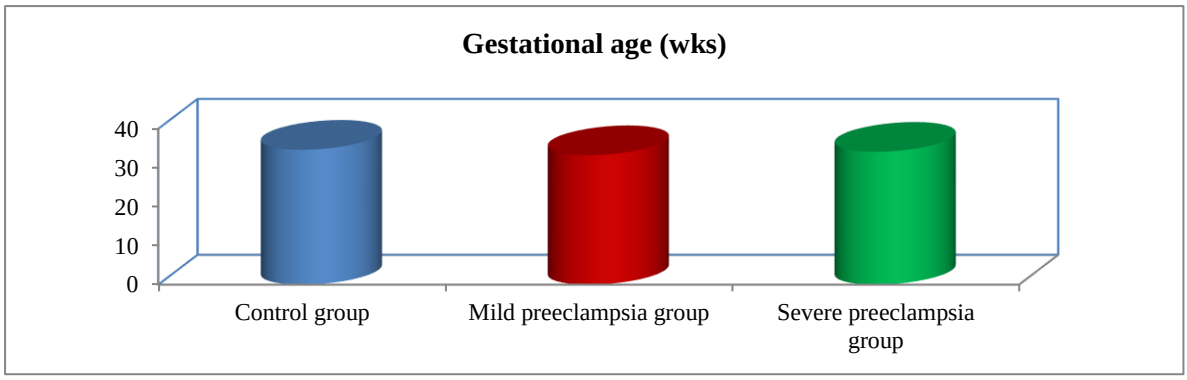

Figure 3: Bar chart between control group, mild preeclampsia group and severe preeclampsia group according to gestational age.

Table (1): Comparison between control group, mild preeclampsia group and severe preeclampsia group according to blood pressure (mmHg).

Blood pressure (mmHg)	Control group (n=25)	Mild preeclampsia group (n=25)	Severe preeclampsia group (n=25)	ANOVA		Post HOC test		
				F	p-value	P1	P2	P3
SBP (mmHg)								
Mean ±SD	111.00±11.73	144.20±9.32	156.00±10.80	119.739	<0.001**	<0.001**	<0.001**	<0.001**
Range	90 – 150	130 – 180	140 – 180					
DBP (mmHg)								
Mean ±SD	72.60±6.79	91.20±4.40	97.40±6.63	114.178	<0.001**	<0.001**	<0.001**	<0.001**
Range	60 – 90	80 – 100	90 – 110					

F-One Way Analysis of Variance: Post HOC test: P1: Control and Mild Preeclampsia; P2: Control and Severe Preeclampsia; P3: Mild and Severe Preeclampsia; p-value>0.05 NS; *p-value <0.05 S; **p-value <0.001 HS.

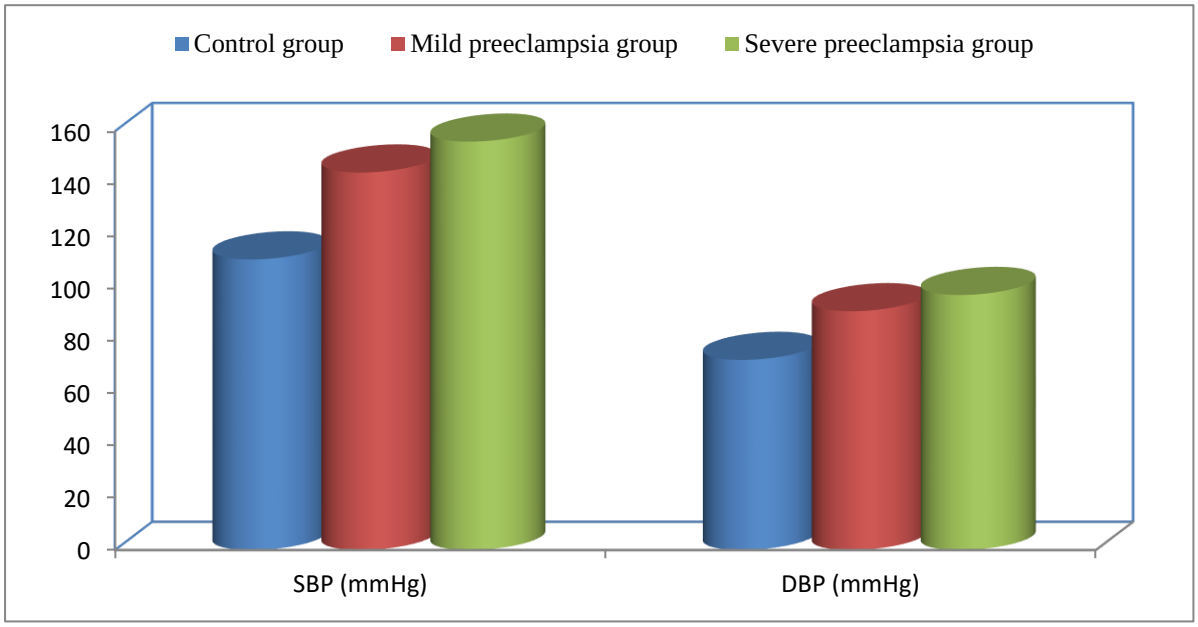

Figure 4: Bar chart between control group, mild preeclampsia group and severe preeclampsia group according to blood pressure.

Table (2): Comparison between control group, mild preeclampsia group and severe preeclampsia group according to laboratory data.

Laboratory data	Control group (n=25)	Mild preeclampsia group (n=25)	Severe preeclampsia group (n=25)	ANOVA		Post HOC test		
				F	p-value	P1	P2	P3
Serum creatinine								
Mean ±SD	**0.58±0.23**	**0.61±0.23**	**1.12±0.41**	**25.265**	**<0.001****	**0.670**	**<0.001****	**<0.001****
Range	**0.3 – 1.1**	**0.3 – 1.1**	**0.3 – 1.8**					
AST								
Mean ±SD	**15.92±3.38**	**21.00±8.10**	**25.34±7.17**	**12.974**	**<0.001****	**0.058**	**<0.001****	**0.022***
Range	**10 – 23**	**11 – 40**	**16 – 39**					
ALT								
Mean ±SD	**9.62±3.55**	**13.00±2.93**	**18.95±7.82**	**20.341**	**<0.001****	**0.065**	**<0.001****	**<0.001****
Range	**3 – 18**	**9 – 19**	**10 – 36**					
Platelet (x103/mm3)								
Mean ±SD	**226.00±62.76**	**221.68±74.85**	**213.32±51.40**	**0.256**	**0.775**	**0.811**	**0.484**	**0.644**
Range	**98 – 351**	**150 – 417**	**163 – 340**					
HGB (mg/dl)								
Mean ±SD	**10.21±1.33**	**10.28±1.17**	**10.56±0.86**	**0.689**	**0.505**	**0.837**	**0.272**	**0.377**
Range	**7.7 – 13.7**	**7.7 – 12**	**8.5 – 11.8**					
Albuminuria								
Median (IQR)	**0 (0)**	**2 (2)**	**2 (1)**	**84.570**	**<0.001****	**<0.001****	**<0.001****	**0.280**
Range	**0 – 0**	**1 – 3**	**1 – 3**					

F-One Way Analysis of Variance; Post HOC test: P1: Control and Mild Preeclampsia; p2: Control and Severe Preeclampsia; p3: Mild and Severe Preeclampsia, p-value>0.05 NS; *p-value <0.05 S; **p-value <0.001 HS.

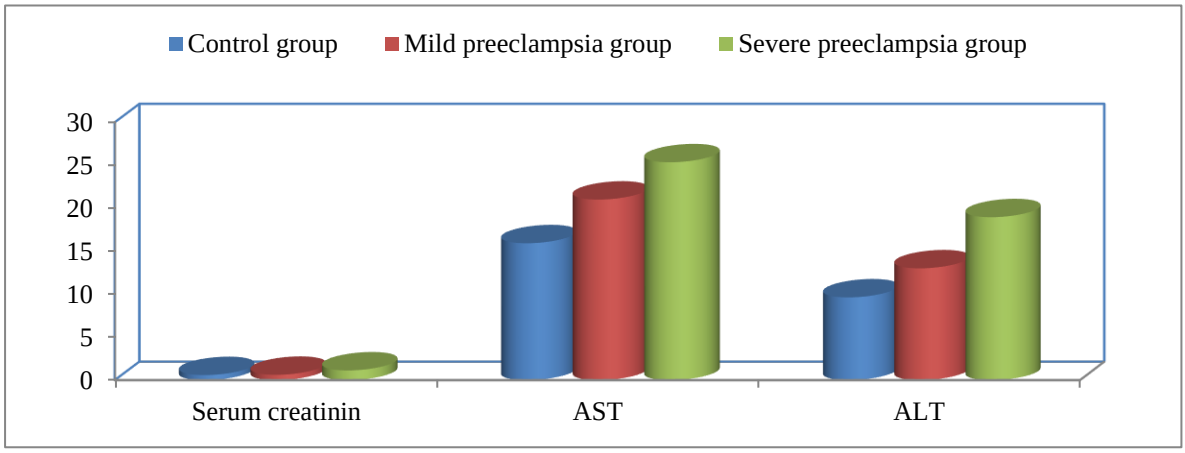

Figure 5: Bar chart between control group, mild preeclampsia group and severe preeclampsia group according to serum creatinine, AST and ALT.

Table.1 shows no statistically significant difference between the three groups according to baseline characteristics. Table.2 shows highly statistically significant increase mean of severe preeclampsia compared to mild and control groups according to their systolic and diastolic blood pressure. Table.3 shows highly statistically significant increase mean of severe preeclampsia compared to mild and control group according to their serum creatinine, AST and ALT, while there was statistically significant decrease mean in control group compared to mild and severe preeclampsia according to albuminuria.

Table (3): Comparison between control group, mild preeclampsia group and severe preeclampsia group according to serum Amyloid A level (ng/dL).

Serum Amyloid A level (ng/dL)	Control group (n=25)	Mild preeclampsia group (n=25)	Severe preeclampsia group (n=25)	ANOVA		Post HOC test		
				F	p-value	P1	P2	P3
Mean ±SD	2.35±0.90	5.62±3.37	15.24±11.21	24.437	<0.001**	0.032*	<0.001**	<0.001**
Median (IQR)	2.2 (0.5)	4.8 (2.2)	11 (25)					
Range	1.2 – 5	2.5 – 16	2.5 – 32					

Kruskall Wallis test Mann-Whitney test: P1: Control and Mild Preeclampsia; p2: Control and Severe Preeclampsia; P3: Mild and Severe Preeclampsia, p-value>0.05 NS; *p-value <0.05 S; **p-value <0.001 HS

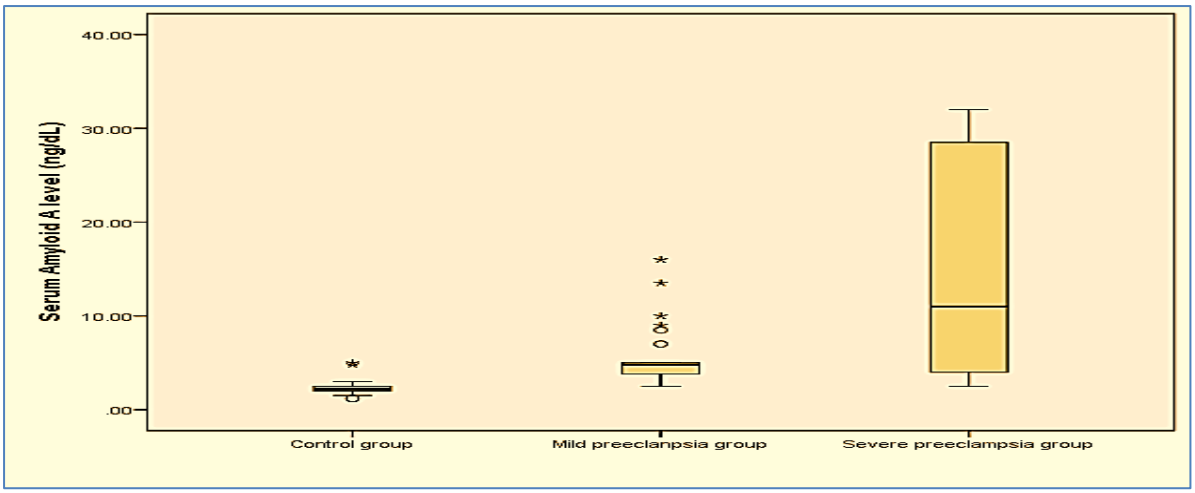

Figure 6: Box plot between control group, mild preeclampsia group and severe preeclampsia group according to serum Amyloid A level (ng/dL).

Table (4): Correlation between serum amyloid A level with all parameters, using Spearman's Correlation coefficient in all the study group.

Parameters	Serum Amyloid A level (ng/dL)	
	R	p-value
Age (years)	-0.037	0.754
BMI [wt/(ht)^2]	0.139	0.235
Gestational age (wks)	-0.042	0.717
SBP (mmHg)	0.411	<0.001**
DBP (mmHg)	0.490	<0.001**
Creatinine	0.518	<0.001**
AST	0.443	<0.001**
ALT	0.564	<0.001**
Platelet (x103/mm3)	-0.148	0.205
HGB (mg/dl)	0.115	0.327
Albuminuria	0.379	0.002*

r- Spearman's Correlation coefficient, p-value >0.05 NS; *p-value <0.05 S; **p-value <0.001 HS

Table.4 shows highly statistically significant increase mean of severe preeclampsia compared to mild preeclampsia and control group according to their serum amyloid A level. Table.5 Positive correlation and significant between serum amyloid A level (ng/dl) with SBP, DBP, Creatinine, AST, ALT and albuminuria.

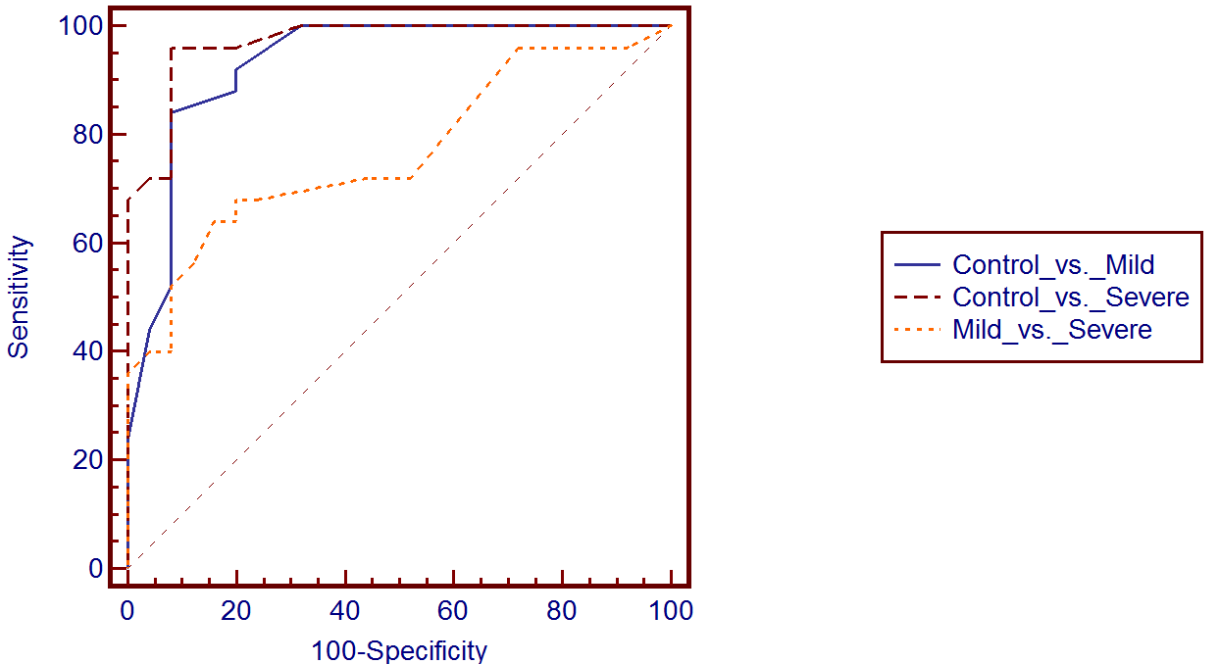

Figure 7: Receiver-operating characteristic (ROC) curve for prediction of preeclampsia using the Serum Amyloid A level (ng/dL).

	Cut-off	Sen.	Spe.	PPV	NPV	AUC
Control vs. Mild	**>3**	**84%**	**92%**	**91.35**	**85.2%**	**0.931**
Control vs. Severe	**>3**	**96%**	**92%**	**92.3%**	**95.8%**	**0.970**
Mild vs. Severe	**>7**	**68%**	**80%**	**77.3%**	**71.4%**	**0.766**

Receiver operating characteristics (ROC) curve was used to define the best cut off value of serum amyloid A level (ng/dL)

4. Discussion

Hypertension is among the most common medical disorders during pregnancy and affect 5% to 10% of all pregnancies [8].

The pathogenesis of preeclampsia has not been elucidated until present. However, it is known that preeclampsia is characterized by an excessive maternal inflammatory response [9].

Serum amyloid A (SAA) is acute phase protein predominantly produced and secreted by hepatocytes. Other cells including lymphocytes, monocytes and macrophage can also produce this protein. The induction of SAA synthesis is triggered by a number of cytokines, chiefly IL-6 and TNF predominately released from macrophage and monocyte at the inflammatory site [3]. Increased baseline levels of SAA analyzed by high sensitivity assays has been recognized as marker of vascular wall inflammation and as clinical marker for the prediction of cardiovascular events [5].

Since preeclampsia is associated with widespread endothelial dysfunction, proposed to be provoked by an increased maternal systemic inflammatory response, the maternal plasma level of SAA might be expected to be increased when compared to normal pregnancy levels. The maternal

plasma level of SAA in normal pregnancy could differ from non-pregnant level due to increased hormone levels, increased adipose tissue and/or secondary to modification of inflammatory response in normal pregnancy [6].

The level of SAA, which is a major acute phase protein, has previously been found to be unaltered by pregnancy. In a recent pilot study, the SAA level was found to be increased in women with preeclampsia correlating with other pro-inflammatory cytokines [7].

The aim of this case control study is to estimate serum amyloid A in pregnant women with preeclampsia.

This case control study was carried out at Al-Zahraa and AL-Sayed Galal University Maternity Hospital during the period from September 2019 to August 2021 .

In currant study, we found as shown in Table -1 the mean value of age among cases of preeclampsia without severe features was (29.80±3.20), and among cases of preeclampsia with severe feature was (29.92± 3.99). On other hands, we found the mean value of age in control group was (28.28± 4.92). With no statistically significant difference between cases and control as regard the age (P-value 0.294).

In agreement with this study [10]., study was conducted to examine serum amyloid A (SAA) levels in 25 normotensive and 25 preeclampsia pregnant women. The mean ages of the preeclampsia and control groups were (27.80± 5.09) and (28.32± 5.38), respectively. There was no statistically significant difference for the age of individuals in the two groups (P>0.05) [10].

In contrast, Ramesh et al., study included 100 cases of preeclampsia and 200 controls. The mean age of cases (21.16y) was less than the controls (23.56y) (Ramesh et al., 2014). This may be explained by different sample size and different exclusion and inclusion criteria .

Also, we found as shown in table (1) the mean value of BMI among cases of mild and severe preeclampsia were (26.96±1.30) and (27.20±2.23) respectively, whereas the mean value of BMI of the control group was (26.38±2.12). With no statistically significant difference between cases and control as regard BMI (P- value=0.661).

In agreement with us, [10], found there was no statistically significant difference noted between the groups regarding BMI [10].

This study showed non-significant difference between the study groups as regard gestational age as p=0.142, the mean value of gestational age among cases of mild preeclampsia was 33±2 and cases of severe preeclampsia was 34±1. Whereas the mean value of gestational age among the control group was 34 ±3.

In agree with this study [10], found no statistically significant differences were noted between the groups regarding the gestational age [10] .

In disagreement with this study [11], found the mean gestational age of the preeclampsia group was significantly lower than the control group (p=0.0006).

Also, we found as shown in table (2) there was highly statistically significant difference between cases and control as regard SBP and DBP. We found that the mean value of the SBP among the control was (111 ±11.73) and the DBP was (72.60±6.79), the mean value of SBP among cases of mild preeclampsia was (140.20± 9.32) and of the DBP was (91.20± 4.40) and the mean value of SBP among cases of severe preeclampsia was (156± 10.80) and of the DBP was (97.40± 6.63) (p-value < 0.001 for all).

In agree with us, [12] found the systolic and diastolic blood pressure was statistically higher among the preeclampsia groups compared to the control [12].

In current study, we found as shown in table (3) the mean value of serum creatinine among cases of mild preeclampsia was (0.61±0.23) and cases with severe feature was (1.12±0.41) while in the control group was (0.58±0.23) with significant statistical difference (p<0.001).

This result disagrees with [12], as they found no significant between the groups with respect to the levels of creatinine [11].
We also found, as shown in table (3) the mean value of AST among cases of mild preeclampsia was 21±8.10 and among cases of severe preeclampsia (25.34±7.17) while in the control group was (15.92±3.38) with significant difference ($p<0.001$). And we found that the mean value of ALT among cases of mild preeclampsia was (13±2.93) and among cases of severe preeclampsia (18.95±7.82) while in the control group was (9.62±3.55) with significant difference ($p<0.001$).
This result agrees with [12], they found statistically significant difference between the preeclampsia group and control group in terms of mean AST, ALT ($P<0.001$) [12].
In current study, we found as shown in table (3) the mean value of platelet among cases of mild preeclampsia was (221.68± 74.85) and among cases of severe preeclampsia was (213.32±51.40) while platelet mean in the control group was (226±62.76). And mean value of Hb among cases of mild preeclampsia (10.28±1.17) and mean value of Hb among cases of severe preeclampsia was (10.56±0.86) while Hb mean in the control group was .(1.33±10.21)
In accordance with us, [11] found no statistical differences between preeclampsia and healthy pregnant women in terms of the Hb level and platelet [11].
We also found, shown in table (3) the median value (IGR) of albuminuria among cases of mild preeclampsia was 2(2) and among cases of severe preeclampsia was 2(1), while in the control group no albuminuria was found.
Among the cases, we found as shown in table (4) the mean value of serum amyloid A for cases of mild preeclampsia was (5.62 ±3.37) mg/l and for cases of severe preeclampsia was (15.24±11.21) mg/l. While in the control group was (2.35 ±0.09) mg/l.
To the best of our knowledge, there are a limited number of studies on SAA levels in pregnant women with preeclampsia, and different conflicting results have been reported [10]; [13].
In accordance with our finding, a pilot study of [10], in which SAA levels of normal pregnant women and preeclampsia patients were evaluated, the SAA levels of preeclampsia group were found to be significantly higher than that of normal pregnant women (SAA: 28.2(7.2-135) ng/l vs. 7.8(4.65-24.6) ng/l, respectively ($p=0.0001$). They reported that SAA appeared to be a marker of inflammation in preeclampsia [10].
Also, [14], conducted a study including 36 patients with mild preeclampsia, 36 with severe preeclampsia and 33 normotensive pregnant women and observed significantly higher SAA levels in the severe preeclampsia than in mild preeclampsia and normotensive pregnant groups [14].
In disagreement with us, [13], showed that plasma levels of SAA were evaluated in pregnant women with and without preeclampsia, and no significant increase was reported in the SAA levels of pregnant women with preeclampsia as compared to those without preeclampsia. In addition, they suggested that an elevated plasma level of SAA in healthy and preeclampsia pregnant women should be considered pathologic because it may be caused by an inflammatory condition other than preeclampsia. They explained the absence of increased SAA levels by impaired hepatic function in preeclampsia, but they did not investigate hepatic function [13].
In current study, we found as shown in table (5) a statistically significant correlation between Amyloid A and SBP ($R=0.411$ & $P< 0.001$) and DBP ($R=0.490$ & $P<0.001$).
This in line with [14]., as they found a positive correlation was detected between SAA levels and median arterial pressure [14].

Also, we found as shown in table (5), a statistically significant correlation between serum amyloid A and liver transaminase, serum creatinine and albuminuria. With no statistically significant correlation was found between serum amyloid A level and age, BMI, hemoglobin concentration or platelet count.

Similarly, [15], concluded that, there was no significant correlation between serum AA concentration and patient's age (p=0.38) [15].

Foell [16], concluded that, SAA showed a weak association with serum creatinine level Foell [16]

In contrast to our result, a strong association between body mass index and SAA levels was found in Zhao [17], study and this may be due to different category of the patients Zhao [17].

On other hands, there was no significant relation between SAA level and any demographic or clinical manifestation in study by Lofty [18] .

5. Conclusion

An elevated plasma level of serum amyloid A in preeclampsia patients should be considered pathologic, and in this respect, the response of relationship between preeclampsia and SAA levels could be caused by an inflammatory condition associated with preeclampsia.

Recommendations

We recommend the possibility of using serum amyloid A level for prediction of preeclampsia and the use of its level to indicate severity of such disorder in pregnant women.

References

1. Jeyabalan A (2013). Epidemiology of preeclampsia: impact of obesity. Nutrition reviews; 71(1): S18-25.

2. Townsend R, O'Brien P & Khalil A. (2016). Current best practice in the management of hypertensive disorders in ureonanc; PMCID: PMC4968992.

3. Siegmund SV, Schlosser M, Schildberg FA, et al. (2016). Serum amyloid A induces inflammation, proliferation and cell death in activated hepatic stellate cells. PLoS One, 11(3): e0150893.

4. Coelho M, Oliveira T & Fernandes R. (2013). Biochemistry of adipose tissue: an 'endocrine organ. Arch Med Sci; 9(2): 191-200.

5. Al Shahi H, Shimada K and Miyauchi K. (2015). Elevated circulating levels of Inflammatory Markers in Patients with Acute Coronary Syndrome. Int J Vasc Med; 805375.

6. Gathiram P and Moodley J. (2016). Preeclampsia: its pathogenesis and pathophysiology. Cardiovasc J Afr; 27(2): 71-78.

7. Lopalco G, Lucherini OM, Vitale A, et al. (2015). Putative role of serum amyloid- A and proinflammatory cytokines as biomatkers for Behcet's disease. Medicine, 94.(42)

8. Rich-Edwards JW, Ness RB & Roberts JM. (2015). Epidemiology of pregnancy-related hypertension Cheley's Hypertensive Disorders in Pregnancy (Fourth Edition): Elsevier; p 37-55.

9. Estensen ME, Grindheim G, Remme EW, et al. (2015). Elevated inflammatory markers in preeclamptic pregnancies, but no relation to systemic arterial stiffness. Pregnancy hypertension: An international journal

of woman's cardio-vascular health, 5(4): 325-329 .

10. Engin-Üstün Y, Karabulut AB, Özkaplan E, et al. (2007). Serum amyloid A levels are increased in pre-eclampsia. Gynecologic and obstetric investigation, 64(2): 117-120.

11. Erdoğan Ö, Devran F, Tosun M, et al. (2012). Assessment of serum amyloid A levels in preeclamptic women and healthy pregnant women.

12. Uckan K, & Sahin HG. (2018). Serum amyloid A, procalcitonin, highly sensitive C reactive protein and tumor necrosis factor alpha levels and acute inflammatory response in patients with hemolysis, elevated liver enzymes, low platelet count (HELLP): and eclampsia. Journal of Obstetrics and Gynecology Research; 44(3):440-447.

13. Kristensen K, Wide- Swensson D, Lindström V, et al. (2009). Serum amyloid A protein and C- reactive protein in normal pregnancy and preeclampsia. Gynecologic and Obstetric Investigation, 67(4):275-280.

14. Can M, Sancar E, Harma M, et al. (2011). Inflammatory markers in preeclamptic patients. Clinical Chemistry and Laboratory Medicine, 49(9): 1469-1472.

15. Ni XC, Yi Y, Fu YP, et al. (2014). Serum amyloid A is a novel prognostic biomarker in hepatocellular carcinoma. Asian Pac J Cancer Prev, 15(24): 10713-10718.

16. Foell D and Roth J. (2004). Proinflammatory S 100 proteins in arthritis and autoimmune diseases. Arthritis & Rheumatism; 50:3762-3771.

17. Zhao Y, He X, Shi X, et al. (2010). Association between serum amyloid A and obesity: a meta-analysis and systematic review. Inflammatory Research. 59(5): 323-334.

18. Lofty HM, Marzouk H, Farag Y, et al. (2016). Serum amyloid a level in Egyptian children with familial Mediterranean fever. International Journal of Rheumatology, 2016 .