

Comparing Troponin I Level between Preeclampsia and Normotensive Pregnant women

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(Ann Coll Med Mosul 2023; 45 (2):159-165).

Received: 22th July 2023; Accepted: 30th Augu 2023.

ABSTRACT

Background: Pre-eclampsia (PE) is a multi-factorial and multi-systemic disorder precise to gestation; it is classically diagnosed by the hypertension associated with proteinuria and /or target organ damage during pregnancy subsequent to 20th week of conception, in woman who is formerly had normotensive blood pressure.

Aim of the study: To compare the levels of troponin I between pre-eclamptic and normotensive pregnant women.

Patients and Methods: A prospective case-control study was done to achieve the study's aim and carried out in the Obstetrics and Gynecology department at Alkhansaa maternity and childhood teaching hospital, Mosul, Iraq. The data collection period extends from 20th of December 2020 to the 1st of June 2021. One hundred pregnant women were invited to participate in the study. The diagnosis of PE was made by NICE guideline criteria.

Results: The mean GA, gravida, para, and abortion are lower in severe PE. BMI is lower in mild than severe PE and controls. Troponin I levels shows no difference between PE groups concerning the symptoms. No correlation found in Troponin I level between PE groups with proteinuria.

Conclusions: Mean Troponin I levels was higher among PE group than normal.

Keywords: Troponin I, Mild preeclampsia, severe preeclampsia, Normotensive Pregnant women.

مقارنة مستوى التروبونين أي بين تسمم الحمل وضغط الدم الطبيعي لدى النساء الحوامل

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الخلاصة

الخلفية: مقدمات الارتعاج (PE) هي اضطراب متعدد العوامل ومتعدد الأجهزة محدد للحمل؛ يتم تشخيصه بشكل اساسي من خلال ارتفاع ضغط الدم المرتبط بالبييلة البروتينية و/أو تلف الأعضاء المستهدفة أثناء الحمل بعد الأسبوع العشرين من الحمل، لدى المرأة التي كانت تعاني سابقاً من ضغط دم طبيعي.

هدف الدراسة: مقارنة مستويات التروبونين I بين النساء الحوامل المصابات بحالة ما قبل الارتعاج والضغط الطبيعي. **المرضى والطرق:** تم إجراء دراسة الحالات والشواهد لتحقيق هدف الدراسة وتم إجراؤها في قسم أمراض النساء والتوليد في مستشفى الخنساء للأمومة والطفولة التعليمي، الموصل، العراق. تمت فترة جمع البيانات من ٢٠ أيلول ٢٠٢٠ إلى ١ حزيران ٢٠٢١. تمت دعوة مائة امرأة حامل للمشاركة في الدراسة. تم تشخيص الارتعاج وفقاً لمعايير إرشادات NICE

النتائج: متوسط العمر الحملي، الأحمال، الولادات، والإجهاض أقل في حالات الارتعاج الشديدة. مؤشر كتلة الجسم أقل في الحالات الخفيفة من حالات الارتعاج الشديدة ومجموعة الشاهد. لا تظهر مستويات التروبونين I أي فرق بين مجموعات الارتعاج فيما يتعلق بالأعراض. لم يتم العثور على ارتباط في مستوى التروبونين I بين مجموعات الارتعاج المصابة بالبول البروتيني. **الاستنتاجات:** متوسط مستويات التروبونين I كان أعلى بين مجموعة الارتعاج عن المعدل الطبيعي.

الكلمات المفتاحية: تروبونين I، تسمم الحمل الخفيف، تسمم الحمل الشديد، النساء الحوامل ذوات الضغط الطبيعي.

INTRODUCTION

Pre-eclampsia disease (PE) is a multi-factorial and multi-systemic disease precise to gestation; it is classically diagnosed by the hypertension associated with proteinuria and /or target organ damage during pregnancy subsequent to 20th week of conception, in woman who is formerly had normotensive blood pressure¹. Currently, the target organ damage is considered also in the pre-eclampsia even when the proteinuria absent. According to the World Health Organization (WHO), gestational hypertensive disorders are main basis of long-term disability, severe morbidity, in addition to the maternal and the perinatal mortality². The prevalence in Iraq³ was 4.79% which was higher than neighboring countries such as Iran (4.0 %) ⁴ and Jordan (1.3%)⁵.

In PE, the synthesis inhibition of nitric oxide produced by mothers averts embryo implantation⁶. In parallel, oxidative stress provokes release of substances like oxidized lipids, free radicals, cytokines, and serum soluble vascular endothelial growth factor into the circulation of the pregnant women. These abnormalities are responsible for functional disturbance of the endothelium with vascular hyper-permeability, thrombophilia, and hypertension, to balance for the diminished flow in the uterine arteries because of peripheral vasoconstriction⁷.

Numerous vulnerability genes may be present for PE⁸. These genes most likely interact in the hemostatic and cardiovascular systems, in addition to the inflammatory response. One of the markers for the inflammatory reaction was the Troponins which are protein molecule that was a part of cardiac and skeletal muscle. Normal findings of Cardiac troponin T: < 0.1 ng/mL, while Cardiac troponin I: < 0.03 ng/mL. High-sensitivity troponin T was < 14 ng/L for women and < 22 ng/L for men⁹. The routinely original technique used for assessing Troponin, occasionally defined as first generation, may perhaps only identify the unusually high concentrations of Troponin I as those observed in widespread necrosis of myocardium (exceeding 10,000 ng/L), by means of radio-immunoassays on post-mortem investigation of heart tissue¹⁰. Up to date improvement of 5th generation Troponin investigations are 100–1000 times more sensitive than their earlier predecessor¹¹ and has permitted precise measurement of greatly lesser titer than formerly probable, behind to 0.1–5 ng/L^{12,13}.

Aim of the Study

To compare the levels of troponin I in pre-eclamptic women with normal pregnancy.

PATIENTS AND METHODS

A prospective case-control study recruited 100 pregnant women; 50 women with Preeclampsia as cases and 50 women without preeclampsia as controls who attended at time of labor to the Obstetrics and Gynecology department at Alkhansaa maternity and childhood teaching hospital/Nineveh Health Directorate, Mosul, Iraq. The data collection period extends from 20th of December 2020 to the 1st of June 2021.

Ethical Consideration

The study was approved by:

- 1-The Council of the Iraqi Board of medical specialization.
- 2-Approval of Nineveh Health Directorate to the Department of Obstetrics and Gynecology of Alkhansaa maternity and childhood teaching hospital, Mosul, Iraq in order to convey the study.

Sampling Process and Sample Size: A sample of 100 pregnant women ≤ 35 years old was included in the study after meeting the inclusion criteria. The sample divided into three groups: 25 pregnant women with mild PE, 25 with severe PE, and 50 normotensive pregnant women.

The inclusion criteria of the study were: Fifty women with pre-eclampsia and fifty women with normal blood pressure with a viable singleton pregnancy. There were two categories of pre-eclampsia cases (25 of them were with severe mild pre-eclampsia and 25 with severe pre-eclampsia). The diagnosis of PE was done by NICE guideline criteria¹³; Include clinical features, blood pressure measurements, and laboratory investigations such as a complete blood count, renal function test, liver function test, and detection of protein in urine done through GUE and by using urine dipstick testing 1+ = 0.3 g/L, 2+ = 1 g/L, and 3+ = 3 g/L¹⁴.

Mild PE: asymptomatic women with systolic blood pressure ≥140 mmHg or diastolic BP ≥90 mmHg but lower than 160/110 mmHg with proteinuria ≥300 mg/24 hour but less than 5g/24hour.

Severe PE: symptomatic women with systolic BP ≥160 mmHg or diastolic ≥110 mmHg on two instances with 6 hour apart at least while the patient is on bed rest. Proteinuria of 5g or higher/24hour or 3+ or greater on 2 random urine samples were collected at least 24hour apart.

Controls: asymptomatic women with systolic BP ≤ 140 mmHg or diastolic BP ≤ 90 with proteinuria less than 300mg /24 hour.

The exclusion criteria for pre-eclamptic and normotensive pregnant women include chronic hypertension, diabetes mellitus type 1 and 2, cardiovascular disease, multiple gestations, chronic renal disease, smoking, fetal anomalies, autoimmune disease, oligohydrominose, and polyhydrominose.

History and Examination

The last menstrual cycle was used to determine gestational age in some women, while the first trimester ultrasonography was used in others.

Before being included in the study, all pregnant women gave their verbal consent. A questionnaire form was used to facilitate history taking followed by thorough examination done at same time. Blood was taken from all participants, and a full hematological and biochemical examination was performed including Serum Troponin I (ng/ml), blood urea (mmol/l), S. creatinin (mg/dl), S. uric acid (mg/dl), ALT(U/l), AST (U/l), TSB, HB (g/l) and platelet count (PC) were measured.

Color, heart rate, reflexes, muscular tone, and breathing are all factors in the Apgar score. Apgar scoring is used to determine if cyanosis, hypoperfusion, bradycardia, hypotonia, respiratory depression, or apnea symptoms of hemodynamic compromise.

The statistical analysis: The statistical analysis performed by using IBM-SPSS 26. The data

Table (1): Comparison of study parameters among study sampled women.

Characteristics	Mild PE [n = 25]	Severe PE [n = 25]	Control [n = 50]	P-value*
Mean maternal age	27.8 \pm 5.73 ^A	25.3 \pm 6.64 ^A	26.5 \pm 6.00 ^A	0.347
Gravida	2.9 \pm 2.07 ^{AB}	2.08 \pm 1.75 ^B	3.6 \pm 2.25 ^A	0.014
Para	1.2 \pm 1.91 ^B	1.1 \pm 1.79 ^B	2.3 \pm 1.88 ^A	0.012
Abortion	0.76 \pm 1.09 ^A	0.08 \pm 0.40 ^B	0.40 \pm 0.83 ^{AB}	0.017
Mean GA, weeks	38.5 \pm 0.96 ^{AB}	38.0 \pm 0.01 ^B	39.0 \pm 0.92 ^A	0.001
ANC	No. (%)	No. (%)	No. (%)	
Booked	14 (56.0)	14 (56.0)	33 (66.0)	0.591
Non-booked	11 (44.0)	11 (44.0)	17 (34.0)	
Place of ANC	No. (%)	No. (%)	No. (%)	
PHCC	13 (52.0)	9 (36.0)	7 (63.3)	0.262
Private clinics	12 (48.0)	16 (64.0)	4 (36.7)	
Frequency of ANC	No. (%)	No. (%)	No. (%)	
2	3 (12.0)	4 (16.0)	7 (14.0)	0.287
3	2 (8.0)	5 (20.0)	15 (30.0)	
4	3 (12.0)	2 (8.0)	6 (12.0)	
> 4	6 (24.0)	3 (12.0)	4 (8.0)	

*One-way ANOVA-test with Tukey's Pair wise comparisons was used for quantitative data. Means that do not share a letter are significantly different. Chi-square test for categorical variables.

presented by mean and standard deviation and the students-t-test for difference between two independent means and one-way analysis of variance (ANOVA) test for difference among more than two independent means were used with Tukey's Pair wise comparisons. Means that do not share a letter are significantly different. The significance of difference of different percentages was tested using Pearson Chi-square test (χ^2 -test). Pearson correlation was calculated for the correlation between two quantitative variables with its t-test for testing the significance of correlation. P-value ≤ 0.05 considered as significant.

RESULTS

Table (1) displays the comparison in study parameters among mild, severe PE cases and normotensive pregnant women, and portrays that, the mean maternal age, BMI, residence, and maternal education show statistically non-significant difference. The mean GA varies among the study groups; (38.5 \pm 0.96) in mild PE, (38.0 \pm 0.01) in severe PE, and (39.0 \pm 0.92) in controls, and difference is very highly statistically significant at (p-value 0.001) with a real honest difference between severe PE and controls. The Gravida of (3.6 \pm 2.25) in controls is statistically differs from that of severe PE but not mild PE. While Para of controls (2.3 \pm 1.88) is statistically differs from that of mild (1.2 \pm 1.91) and severe PE (1.1 \pm 1.79). In abortion, the statistically significant difference appears only between mild and severe PE.

Table (2) demonstrates the comparison in the S. troponin I among mild, severe PE cases and normotensive pregnant women and shows that the difference is non-significant.

Table (2): Comparison in the S. troponin I among study sampled women.

Parameters	Mild PE [n = 25]	Severe PE [n = 25]	Control [n = 50]	P-value
S.Troponin I (ng/ml)	0.010 ± 0.006 ^A	0.008 ± 0.008 ^A	0.009 ± 0.016 ^A	0.932

*One-way ANOVA-test with Tukey's Pair wise comparisons was used for comparing mean age. Means that do not share a letter are significantly different. Chi-square test for categorical variables.

Table (3) illustrates the correlation matrix between S. troponin I and maternal biochemical parameters in the two study sampled women and shows, the correlation of PE and normotensive women with blood urea, serum creatinine, serum uric acid, TSB, Aspartate trans-aminase, Alanine transferase, Hb, and platelets appear to be non-significantly weak.

Table (3): Correlation matrix between S. troponin I and maternal biochemical parameters in the two study sampled women.

Parameters	Correlation coefficient*	S. Troponin I	
		PE [n = 50]	Normotensive[n = 50]
Bl. Urea	r	- 0.027	0.036
	p	0.850	0.806
S. creatinin	r	0.023	0.027
	p	0.876	0.854
S. uric acid	r	0.198	0.027
	p	0.168	0.854
TSB	r	0.069	- 0.058
	p	0.636	0.688
Aspartate transaminase	r	0.254	- 0.044
	p	0.075	0.760
Alanine transferase	r	0.207	- 0.182
	p	0.150	0.207
Hb%	r	0.064	0.086
	p	0.658	0.551
Platelets	r	- 0.034	0.231
	p	0.814	0.107

* Correlation coefficient was applied.

Table (4) demonstrates the relationship between mean S. Troponin I and albuminuria in PE groups and reveals that the mean of Troponin I is higher among severe PE than mild PE but statistically non-significant differences.

Table (4): Relationship between mean S. Troponin I and albuminuria study sampled women.

Albuminuria	Mild PE	Severe PE	P-value*
+	0.006 ± 0.006	0.007 ± 0.008	0.728
++	0.005 ± 0.004	0.007 ± 0.007	0.453
+++	---	0.009 ± 0.010	---
++++	---	0.010 ± 0.009	---

* Independent T-test of two means was applied.

DISCUSSION

Preeclampsia is one of the most dangerous conditions of pregnancy. PE affects 8.5 million women globally and has a worldwide incidence of 3% to 8%. PE is responsible with up to 40% of fetal mortality and 18% of maternal fatalities. There is currently no safe and effective treatment for PE except delivery of placenta¹⁵.

Maternal age of the pregnant women had no significant difference, which is similar to Markova¹⁶, where the maternal age statistically not differs between normotensive pregnant and severe form of PE. Gravida, Para, were lower in severe PE in statistically significant way than the controls; meanwhile, the mean of Abortion was significantly higher among the mild PE in comparison to severe PE only, similar results found in another study¹⁷. So the low parity is more in severe PE and primi was risk factor for the PE due to young age and new exposure to sperm¹⁸. This is similar to Cot *et al.*, study¹⁹. Abortion is protective against PE through an immunologic mechanism, whereby exposure to fetal antigens through the aborted pregnancies enhances development of maternal-fetal immunologic tolerance²⁰, also due to more exposure to sperm.

In the current work, the gestational age was statistically lower in severe PE than normotensive women which is similar to the result found in Cot *et al.*, study¹⁹ and Stubert *et al.*, study²⁰ which is differ from Raji *et al* study²¹ and Pasupathi *et al* study²². This might be due to the severe PE necessitate earlier termination of the pregnancy to save the mother and their neonates lives.

Troponin I found to be statistically non-significant difference between mild, severe PE, and normotensive pregnant women. The result was analogue to findings of other studies of Tan *et al.*,²³ study, Atis *et al.*,²⁴ study, and Aydin *et al.*,²⁵ study, which found no difference in levels of troponin I in normotensive pregnancy and PE. Another study conducted by Fleming *et al.*,²⁶ study which compare Troponin I between normotensive pregnant women and severe PE showed no statistically significant. Different results reported in other studies Aydin *et al.*,²⁵ study, Fleming *et al.*,²⁶ study, and Atalay *et al.*,²⁷ study where PE was associated with significant higher level for troponin I than normotensive pregnancy.

The assumption behind was the physiological alteration of conception which comprise an enlarged cardiac output with remodeling of left ventricle, well as, diastolic dysfunction, thus on time speculation that Troponin may be prominent in normotensive pregnant. Additionally, Pergialiotis *et al.*,²⁸ study showed normal troponin I levels in healthy normal pregnancy.

The maternal age was inversely and very weakly correlated with Troponin level in a non-significant way, which is similar to Morton study¹³. The present work found no correlation of Troponin I in both study groups regarding BMI. In Acosta *et al.*,²⁹ study, BMI was significantly and inversely correlated with Troponin I.

The investigations done in the present study which include renal function test (Blood urea, uric acid, and Serum creatinine), liver function test (ALT, AST, and TSB), part of complete blood picture, Hb, and platelet count to have no significant correlations with Troponin I level in both PE and normotensive women. Meanwhile, the blood urea, uric acid, s. creatinine, AST, and ALT were higher in severe form of PE pregnant women compared to mild form of PE and pregnant with normal blood pressure; the platelet count was lower in the severe PE. These findings were similar to Cot *et al.*,¹⁹ study.

CONCLUSIONS

The study concluded that:

- Mean Troponin I levels was higher among PE women than normotensive pregnant women but it wasn't real significant statistical difference.
- Comparing Troponin I levels between mild and severe showed no statistical significant difference, although the mean Troponin I was higher among the mild more than the severe PE.

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