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Cardiac Troponin I Levels in Patients with Severe Preeclampsia and Effect of Magnesium Sulfate Treatment on Cardiac Troponin I Levels

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ABSTRACT:

Cardiac troponin I levels in patients with severe preeclampsia and effect of magnesium sulfate treatment on cardiac troponin I levels

Objective: It was aimed to investigate minor myocardial injury in preeclampsia by comparing troponin I levels in pregnant women with preeclampsia and normal pregnant women, and to examine the effect of magnesium sulfate treatment on cardiac troponin I levels.

Material and Method: The study included two groups as one preeclemptic group consisting of 25 pregnant women with preeclampsia (group 1) and a control group consisting of 25 pregnant women who do not have any medical or obstetric problem. Mean serum cardiac troponin I levels measured before and after magnesium sulfate treatment in pregnant women with preeclampsia were compared to troponin I levels in healthy pregnant women.

Results: There was no statistically significant difference between the two groups regarding their demographical properties (p>0.05). As for the comparison of mean cardiac troponin I levels between groups, there was marked and statistically significant difference between Group I (0.0944±0.044 ng/mL) and Group II (0.006±0.002 ng/mL) (p<0.05). In patients with preeclampsia (Group I), troponin I levels were higher before magnesium sulfate treatment (0.094±0.044 ng/mL) compared to levels measured after treatment (0.0048±0.0017 ng/mL), and the difference was statistically significant (p<0.05).

Conclusion: In our study, levels of troponin I, which is the best known indicator of minor myocardial injury, was higher in pregnant women with severe preeclampsia compared to the control group, suggesting myocardial injury related to hypertensive diseases in pregnancy. In addition, it was determined that magnesium sulfate treatment reduced troponin I levels and did not cause myocardial injury.

Keywords: Magnesium sulfate treatment, preeclampsia, troponin I

ÖZET:

Ağır preeklamptik hastalarda kardiak troponin I düzeyi ve magnezyum sülfat tedavisinin kardiak troponin I düzeyine etkisi

Amaç: Preeklamptik gebeliklerdeki troponin I değerleri normal gebelerdeki değerlerle karşılaştırılarak preeklampsideki minör myokardiyal hasar araştırmak ve magnezyum sülfat tedavisinin kardiak troponin I düzeyine etkisini incelemek amaçlanmıştır.

Gereç ve Yöntem: Çalışmaya; 25 gebeden oluşan preeklamptik grup (grup 1) ve herhangi bir medikal ve obstetrik sorunu olmayan 25 gebeden oluşan kontrol grubu (grup2) olmak üzere iki grup dahil edildi. Preeklamptik gebelere uygulanan magnezyum sülfat tedavisinden öncesinde ve bitiminde troponin I düzeyleri ile saglıklı gebelerdeki troponın I düzeyleri ölçüldü. Peeklampsi hastalarında magnezyum sülfat tedavisi öncesive sonrası bakılan ortalama serum kardiak troponin I değerleri ile saglıklı gebelerdeki troponin I düzeyleri karsılaştırıldı.

Bulgular: İki grup arasında, demografik özellikler açısından istatistiksel olarak anlamlı fark yoktu (p>0.05). Gruplar arasında ortalama kardiak troponin I değerleri karşılaştırıldığında Grup I'de (0.0944±0.044), Grup II'ye (0.006±0.002) kıyasla yüksek düzeyde ve istatistiksel olarak anlamlı fark olduğu saptandı (p<0.05). Peeklampsi hastalarında (Grup I), magnezyum tedavisi öncesi kardiak troponin I değerinin (0.094±0.044), tedavi sonrası değerlerden (0.0048±0.0017) yüksek olduğu ve istatistiksel olarak anlamlı fark olduğu tespit edildi (p<0.05)

Sonuç: Çalışmamızda, minör miyokardial hasarın bilinen en iyi göstergesi olan troponin I'nın preeklamptik gebelerde kontrol grubuna göre yüksek bulunması, gebelikte hipertansif hastalıklarla ilişkili miyokardial hasarı düşündürmektedir. Ayrıca magnezyum sülfat tedavisinin, troponin I düzeyini azalttığı ve miyokardial hasara neden olmadığı sonucuna varılmıştır.

Anahtar kelimeler: Magnezyum sülfat tedavisi, preeklampsi, troponin I

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INTRODUCTION

Preeclampsia is a disorder that is specific to humans and its etiology is not completely clear. It generally occurs in nulliparous women after 20th week of gestation; it is a multi-systemic disease observed in 2-3% of all pregnancies (5-7% of nulliparous pregnancies), characterized with hypertension and accompanying proteinuria and/or edema (1). Various theories have been suggested for etiology of preeclampsia. Vasospasm, activation of coagulation system, abnormal hemostasis and altered prostacyclin/thromboxane ratio lead to endothelial cell damage, which is an important component of the disease (2). Preeclampsia that is added on top of the necessary maternal cardiovascular adaptations in pregnancy has been reported to affect structure of intramyocardial vessels, left ventricular mechanics and cause damage in cardiac myocytes (3,4). In patients with hypertension who do not have remarkable myocardial necrosis, cardiac troponin levels were detected above normal, and it was stated that this situation could be explained by subclinical myocardial necrosis (5). Myocardial ischemia is a rare but serious complication of pregnancy. Incidence of myocardial infarction in pregnancy varies between 1/10,000 to 1/30,000, and it is associated with high maternal (30%) and fetal (17%) mortality (6).

As cardiac structural proteins, troponins are specific markers of myocardial ischemia and injury, and they can reveal minor myocardial ischemia that cannot be detected with other biochemical markers. Troponin I is a constituent of the troponin complex that regulates interaction of actin and myosin in striated muscles. Cardiac troponin I has an N-terminal amino acid chain that is immunologically distinct from the skeletal muscle isoforms. Troponin I is released into circulation when there is myocardial damage. Troponin I is defined as one of the sensitive and specific myocardial damage markers in ischemic and non-ischemic situations (7).

In this study, it was aimed to detect possible minor myocardial injury in preeclampsia by comparing serum cardiac troponin I levels in pregnant patient with severe preeclampsia and in healthy pregnant women, and to examine the effect of magnesium sulfate treatment on troponin I levels.

MATERIAL AND METHOD

This study included pregnant women who were diagnosed with preeclampsia between 28th to 41st gestational weeks, who presented to Uludag University Faculty of Medicine Gynecology and Obstetrics Department between 1st June 2008 and 31st December 2008 together with pregnant women who presented to Gynecology and Obstetrics outpatient clinic for routine pregnancy examination and did not have any obstetrics problems, who were between 37th to 41st gestational weeks. The study was designed as a prospective controlled study.

The study was conducted on 50 pregnant women and in two groups; Group I included 25 pregnant women with severe preeclampsia and Group II included 25 pregnant women who did not have any medical and obstetric problems (none of the following: multiple pregnancy, cardiac disease, hypertension, diabetes, renal and hepatobiliary disease, smoking) as control group.

Local ethics committee approval was obtained for the study. All participants were informed about the study and an informed consent was signed by each participant.

Cases who had any of the following were excluded from the study: chronic hypertension, cardiac disease, chronic renal disease, type 1 and 2 diabetes mellitus, gestational diabetes mellitus, connective tissue disease, local or systemic infection, premature rupture of membranes, threat of preterm birth, multiple pregnancies, smoking. Demographical data including age, gravida, parity, number of living children, used medications and systemic diseases were recorded in all of the remaining cases. Working Group criteria were used for the diagnosis of preeclampsia (as patient group with preeclampsia, two or more blood pressure measurements with at least 6 hours intervals were 140/90 mmHg or above, proteinuria >30 mg/dl and dipstick test 1(+) or higher) (8). Classification of severe preeclampsia was made according to ACOG Practice Bulletin criteria (9).

Five cc. venous blood sample was taken before

magnesium sulfate treatment and at the 24th hour of treatment in patients with preeclampsia, and before delivery (before and during labor) in control group. Serum was separated after centrifugation at 3000 rpm, and stored at -20°C until time of analysis for troponin I levels.

In all cases, serum urea, creatinine, uric acid, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH) and serum electrolyte concentrations were analyzed in Uludag University Faculty of Medicine Biochemistry Laboratory using Architect Ci 8200 autoanalyzer. Complete blood count and urinalysis were performed. Troponin I measurement was performed at Uludag University Faculty of Medicine Emergency Biochemistry Laboratory in AxSYM device using Troponin - I ADV (Abbott) assay kit, with microparticle enzyme immunoassay test (MEIT).

Statistical Analyses

Statistical analyses were carried out on SPSS statistical software version 10.0. Independent Samples t test, Mann Whitney U test, Wilcoxon ranked sum test used in statistical analyses. $p<0.05$ was accepted as statistically being significant.

RESULTS

Distribution of demographical data belonging to preeclamptic and control groups are shown in Table-1. There were no statistically significant differences between the two groups with regards to maternal age, gravida, parity, abortion and BMI ($p>0.05$). In preeclamptic group, mean systolic arterial blood pressure was 164.00±2.51 mmHg and mean diastolic blood pressure was 106.00±1.73 mmHg, whereas in control group mean systolic arterial blood pressure was 111.20±1.85 mmHg and mean diastolic blood pressure was 74.00±1.41 mmHg ($p<0.001$). Mean gestational age at delivery and neonatal birth weight was significantly lower in preeclamptic group compared to the control group ($p<0.001$). When the two groups were compared for delivery type, delivery rate with C/S in the preeclamptic group was 80%, which was significantly higher than the control group ($p<0.05$) (Table-1).

Table-2 shows laboratory measurements in the groups. There were no significant differences in hemoglobin, hematocrit measurements between the groups ($p>0.05$). Mean thrombocyte count was lower in Group I compared to Group II ($p<0.05$). Mean serum AST, ALT,uric acid and LDH levels were significantly higher in Group I compared to Group II ($p<0.05$). As for serum total protein and albumin levels, Group I had significantly lower values compared to Group II ($p<0.05$). Mean Esbach value in Group I (preeclampsia) was 3.59±0.28 gr/day. As for the comparison of mean cardiac troponin I levels between the groups, preeclamptic group (0.0944±0.044 ng/mL) had significantly higher troponin I levels than normotensive group

Table-1: Distribution of demographical properties in groups

Properties	Preeclampsia (n:25) mean±SD (Group-1)	Control (n:25) mean±SD (Group-2)	p value
Age	27.56±0.90	28.28±1.10	0.62[a]
Gravida	1.60±0.19	1.88±0.22	0.34[b]
Parity	0.56±0.19	0.56±0.14	0.58[a]
Abortion	0.04±0.04	0.32±0.14	0.079[b]
BMI	29.44±0.95	27.28±0.58	0.062[a]
Mean systolic arterial pressure (mmHg)	164.00±2.51	111.20±1.85	<0.001[a]
Mean diastolic arterial pressure (mmHg)	106.00±1.73	74.00±1.41	<0.001[a]
Cesarean delivery	20 (%80)	7 (%28)	<0.05[c]
Gestational week	32.79±0.61	38.90±0.19	<0.001[a]
Birth weight (gr)	1612.10±135.00	3278.00±76.00	<0.001[a]

BMI: body mass index, Values are shown as mean±standard deviation, [a]using Student t test, [b]using the Mann-Whitney U test, [c]using Pearson Chi-square test

Table-2: Hematologic Data of Study Participants

Hematologic Date	Preeclamptic Women (n:25) (Grup-1)	Normotensive Pregnant Women (n:25) (Grup-2)	p value
Hemoglobin level (g/dL)	12.610±0.300	12.13±0.30	0.68
Hematocrit count (10^9/L)	37.370±0.890	35.85±0.83	0.42
Platelet count (10^9/L)	198.716±15.157	244.60±14.35	p<0.05
AST (IU/ml)	62.880±15.220	20.28±0.9	p<0.05
ALT(IU/ml)	39.680±8.760	16.52±1.73	p<0.05
Uric acid (mg/dL)	6.800±0.160	2.97±0.16	p<0.05
LDH (IU/dl)	773.120±104.500	228.32±11.10	p<0.05
Total Protein (g/dL)	5.060±0.120	6.73±0.15	p<0.05
Albumin (gr/dl)	2.760±0.090	3,66±0,10	p<0.05
Mean Troponin I (ng/ml)	0.0944±0.044	0.006±0.002	p<0.05

Table-3: Serum cardiac troponin I levels measured before and after magnesium sulfate treatment (ng/mL)

Parameter	Before magnesium sulfate treatment	After magnesium sulfate treatment	p value
TROPONIN I (ng/ml)	0.0944±0.044	0.0048±0.001	p<0.05[a]

[a]Wilcoxon signed rank test

(0.006±0.002 ng/mL), which was statistically significant (p<0.05) (Table-2).

In preeclampsia patients (Group I), there was statistically significant difference in mean serum cardiac troponin I levels that were measured before and after magnesium sulfate treatment. Cardiac troponin I levels before magnesium sulfate treatment (0.094±0.044 ng/mL) were higher than the levels measured after the treatment (0.0048±0.0017 ng/mL) (p<0.05) (Table-3).

DISCUSSION

Preeclampsia is a multisystemic disease involving renal, placental and cerebral damage mediated by capillary injury and vasospasm. Prevalence of preeclampsia in pregnancies is 3-4%, and it is one of the leading causes of maternal and fetal morbidity and mortality in underdeveloped and developing countries (10). It is characterized with hypertension and accompanying proteinuria that occurs after 20th week of gestation especially in nulliparous women. Despite extensive research, etiopathology of preeclampsia has not been completely understood (11). Endothelial dysfunction, inflammatory events, oxidative stress, disturbances in renin-angiotensin system, prostaglandins, nitric oxide, endothelins, genetic predisposition and immunological factors have been put forward in studies related to etiopathogenesis of preeclampsia (12). As a result, vasoconstriction takes place and blood pressure rises (12). Myocardial ischemia is a rare but serious complication of pregnancy (13).

Detection of abnormal enzyme levels is helpful for diagnosis of myocardial ischemia in pregnancy (14). It is stated that minor myocardial injury can be better detected with cardiac troponins which are protein markers, rather than the enzyme activity assays. Detection of minor cardiac injury has significance with regard to estimation of risks in the patient. Determination of risk state and treatment protocol is important for assessment of disease prognosis (15). The reason why cardiac troponin I is the most cardioselective marker has been explained by some findings. According to these findings, cardiac troponin I is present only in heart muscle both in adults and also in embryonic life. It is not expressed by the skeletal muscle. Antibodies that are used to

detect cardiac troponin I do not cross-react with troponin I derived from the skeletal muscle. It does not become elevated in acute and chronic muscular diseases, following exercise or in renal failure, where CK-MB becomes elevated. Its elevation is correlated with echocardiographically proven myocardial infarction. Its concentration in cardiac muscle is 13 times higher compared to CK-MB.

For this reason, troponin I is regarded as the most specific marker for demonstration of myocardial injury in pregnant women (16). Barton et al. (17) described histological changes that occur in myocardium in preeclampsia. Microvascular abnormalities were detected in endomyocardial biopsy samples that are similar to changes in other organ systems of pregnant women with preeclampsia; and changes in the structure of mitochondria of myometrial cells were also detected in heart muscle cells. The myocardial injury shown pathologically by Barton et al. was further supported with the studies that found increased troponin I levels in circulation.

Although there are many studies investigating troponin I levels in various groups, there are few published studies about troponin I levels in pregnancy. Shivvers et al. (18) found normal serum troponin I levels before delivery, during the active phase of labor and at post-partum period in normal pregnant women, and concluded that troponin I levels were not influenced by the physiological events in labor.

Narin et al. (19) found higher troponin T levels in babies of preeclamptic mothers (0.70 ng/ml) compared to the control group (0.10 ng/ml), and stated that this elevation might be related to mild cardiac injury that can be observed in babies of preeclamptic mothers, and that pathophysiological problems that occur in the placenta of pregnant women with preeclampsia could be responsible for this situation.

Since troponin that is detected in serum of pregnant women has a molecular weight of 24,000 Da, it is not possible to pass through placenta; it is present as a double complex in circulation. In addition, there are no studies about placental production of troponin I (3). In their study investigating troponin I levels in pregnant women with preeclampsia and gestational hypertension, Fleming et al. (3) found mean troponin I levels as 0.118 ng/mL in hypertensive pregnant women and as 0.03 ng/mL in the control group ($p<0.0001$). Mean troponin I levels in preeclamptic group (0.155 ng/mL) was found to be higher than the group with gestational hypertension (0.0089 ng/mL) ($p<0.05$). Fleming et al. suggested that elevated troponin I levels can be observed in pregnancy in association with hypertension and that it indicated subclinical myofibrillary injury. In their study investigating troponin I and CK-MB levels in pregnant women with preeclampsia, Agar et al. (20) found mean troponin I levels as 0.88 ng/mL in pregnant women with preeclampsia and as 0.10 ng/mL in control group ($p<0.05$). They did not find a difference in CK-MB levels between the two groups. Similarly, Fleming et al. (3) detected higher troponin I levels in preeclamptic patients compared to healthy pregnant women.

In their study investigating the effect of magnesium sulfate treatment on serum cardiac troponin I levels, Atalay et al. (21), found serum cardiac troponin I levels were significantly higher in patient group with severe preeclampsia (0.20 ng/mL) compared to the control group (0.02 ng/mL) ($p<0.05$). They found mean cardiac troponin I level in the group with severe preeclampsia was higher before magnesium sulfate treatment (0.20 ng/mL) compared to levels measured after the treatment (0.09 ng/mL) ($p<0.05$).

There is a few study in literature in which serum cardiac troponin I levels were not found elevated in preeclampsia. In that study by Joyal et al. (22), mean serum cardiac troponin I levels in patient group with preeclampsia (0.008 ng/mL) was found to be lower than the levels in control group (0.01 ng/mL) ($p>0.05$) and In that study by Aydin et al. (23) was not determined between the preoperative and postoperative cTn-I levels (p4 0.05) between normal pregnant women and those with severe pre-eclampsia. In the Aydın et al.'s (23) study, a relation was not determined between pre-eclampsia and increased cTn-I levels.

According to this, troponin I levels were not elevated during labor in preeclampsia, which is not in support of the development of acute myocardial injury. This result is in contrast with other published studies.

In our study, mean serum cardiac troponin I level was significantly higher in patient group with severe preeclampsia (0.0944 ng/mL) compared to control group (0.006 ng/mL) ($p<0.05$). In addition, serum cardiac troponin I levels were significantly higher before magnesium sulfate treatment in patients with severe preeclampsia (0.0944 ng/mL) compared to levels measured after the treatment (0.0048 ng/mL). Our results were consistent with the results of the study by Atalay et al. (21).

Cardiac myofibrillary injury can be suspected to some extent in association with hypertensive diseases in pregnancy. Rather than being a rare complication, this injury can be a frequent feature of the disease. Detection and monitoring of this injury can be possible with measurement of troponin I levels. Considering the specificity of troponin I to cardiac tissue, presence of cardiac injury can be demonstrated in pregnant women with preeclampsia. It is stated that pregnant women with preeclampsia have increased risk for cardiovascular disease in their future life. In their meta-analysis, Bellamy et al. (24), detected increased risk for hypertension, ischemic heart diseases, thromboemboli and stroke in patients with preeclampsia. As for cancer, there was no detected risk escalation in preeclampsia.

Chakraborti et al. (25), reported that hypomagnesaemia caused progressive vasospasm in coronary arteries and suggested that magnesium can be protective for many cardiovascular diseases including ischemic heart disease. This idea is also supported with our study. Our patients were cardiologically asymptomatic. Moreover, long-term, prospective studies with echocardiographic follow-up are necessary in order to examine whether the subclinical myocyte injury that is present in preeclampsia would affect left ventricular functions in the future, and whether post-partum cardiomyopathy would be more prevalent in patients with preeclampsia.

CONCLUSION

In conclusion, levels of troponin I, which is the best indicator of minor myocardial injury, were elevated in pregnant women with preeclampsia, which suggests minor myocardial injury associated with hypertensive diseases in pregnancy. In addition, it was concluded that magnesium sulfate treatment did not cause myocardial damage. Vasodilatation and anti-thrombocytic effects of magnesium sulfate may be playing role in reducing troponin I levels. Anyway, further studies are needed in order to determine significance and value of these results for follow-up and prognosis of preeclampsia.

REFERENCES

1. *Garovic VN. Hypertension in pregnancy: Diagnosis and treatment. Maya Clin Proc 2000; 75: 1071-6.* **[CrossRef]**
2. *Dekker GA, Sibai BM. Etiology and pathogenesis of preeclampsia: Current Concepts. Am J Obstet Gynecol 1998; 179: 1359-75.* **[CrossRef]**
3. *Fleming S, O Gorman T, Finn J, Grimes H, Daly K, Morrison J. Cardiac troponin I in preeclampsia and gestational hypertension. BJOG 2000; 107: 1417-20.* **[CrossRef]**
4. *Kuzniar J, Piela A, Skret A. Left ventricular function in preeclamtic patients. Am J Obstet Gynecol 1983; 146: 400-5.* **[CrossRef]**
5. *Nunes JP. Cardiac troponin I in systemic diseases. A possible role for myocardial strain. Rev Port Cardiol 2001; 20: 785-8.*
6. *Pettiti D, Sidney S, Quesenberry CP Jr, Bernstein A. Bernstein A. Incidence of stroke and myocardial infarction in women of reproductive age. Stroke 1997; 28: 280-3.* **[CrossRef]**
7. *Atiye Ç, Yusuf T. Miyokard hasarının biyokimyasal belirteçleri. Türkiye Klinikleri Kardiyoloji 2004: 17; 81-5.*
8. *Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure Pregnacy. Am J Obstet Gynecol 2000; 183: 1-22.* **[CrossRef]**
9. *American College of Obstetricians and Gynecologists (ACOG), Practice Bulletin no. 33. Diagnosis and management of preeclampsia and eclampsia. Obstet Gynecol 2002; 99: 159.*
10. *Papageorghio AT, Yu CK, Bindra R, Pandis G, Nicholaides KH; Fetal Medicine Foundation Second Trimester Screening Group. Multicenter screening for preeclampsia and fetal growth restriction by transvaginal uterine artery Doopler at 23 weeks of gestation. Ultrasound Obstet Gynecol 2001; 18: 441-9.* **[CrossRef]**
11. *Bronses IA. Morphological changes in utero-placental bed in pregnancy hypertension. Clin Obstet Gynaecol 1977; 4: 573-93.*
12. *Sibai MD. Diagnosis, prevention, and management of eclampsia. Obstet Gynecol 2005; 105: 402-10.* **[CrossRef]**
13. *Badui E, Enciso R. Acute myocardial infarction during pregnancy and puerperium review. Angiology 1996; 47: 739-56.* **[CrossRef]**
14. *Sheikh AU, Harper MA. Myocardial infarction during pregnancy: management and outcome of two pregnancies. Am J Obstet Gynecol 1993; 169: 279-83.* **[CrossRef]**
15. *Penttilla I, Penttilla K, Rantanen T. Laboratory diagnosis of patients with acute chest pain. Clin Chem Lab Med 2000; 38: 187-97.* **[CrossRef]**

16. *Fromm RE Jr, Varon J. Myocardial injury in critically ill patients. JAMA 1995; 274: 1672-3.* **[CrossRef]**
17. *Barton JR, Hiett AK, O'Connor WN, Nissen SE, Greene JW Jr. Endomyocardial ultrastructurel findings in preeclampsia. Am J Obstet Gynecol 1991; 165: 389-91.* **[CrossRef]**
18. *Shivvers SA, Wians FH Jr, Keffer JH, Ramin SM. Maternal cardiac troponin I levels during normal labor and delivery. Am J Obstet Gynecol 1999; 180: 122-9.* **[CrossRef]**
19. *Narin N, Cetin N, Kiliç H, Başbuğ M, Narin F, Kafali M. Diagnostic value of troponin T in neonates of mild pre-eclamptic mothers. Biol Neonate 1999; 75: 137-42.* **[CrossRef]**
20. *Ağar E, Davas İ, Akyol A, Varolan A, Yazgan A, Baksu B, et al. Preeklamptik gebelerdeki troponin I ve CK-MB düzeylerinin değerlendirilmesi. Şişli Etfal Hastanesi Tıp Bülteni 2006; 40: 12-6.*
21. *Atalay C, Erden G, Turhan T, Yıldıran G, Saracoglu F, Koca Y. The effect of magnesium sulfate treatment on serum cardiac troponin I levels in preeclamptic women. Acta Obstet Gynecol Scand 2005; 84: 617-21.* **[CrossRef]**
22. *Joyal D, Leya F, Koh M, Besinger R, Romana R, Kahn S, et al. Troponin levels in patients with preeclampsia. Am J Med 2007; 120: 13-4.* **[CrossRef]**
23. *Aydin C, Baloglu A, Cetinkaya B, Yavuzcan A. Cardiac troponin levels in pregnant women with severe pre-eclampsia. J Obstet Gynaecol 2009; 29: 621-3.* **[CrossRef]**
24. *Bellamy L, Casas JP, Hingorani A, Williams JD. Pre-eclampsia and risk of cardiovascular disease and cancer in later life: systematic review and meta-analysis. BMJ 2007; 335: 974.* **[CrossRef]**
25. *Chakraborti S, Chakraborti T, Mandal M, Mandal A, Das S, Ghosh S. Protective roleof magnesium in cardiovascular disease: a review. Mol Cell Biochem 2002; 238: 163-79.* **[CrossRef]**