Original Article

Comparing the Inflammatory Markers between Women with Eclampsia- Preeclampsia and Normotensive Pregnant Women in Gynecology

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ARTICLE INFO

ABSTRACT

Hypertension is a medical problem during pregnancy and one of the types of hypertensions during pregnancy is eclampsia-preeclampsia. The aim of this study was to compare inflammatory markers between women with eclampsia - preeclampsia and pregnant women with normal blood pressure admitted to the gynecology ward of Shahada Tarnish and Mehrieh hospitals in 1998-99. This descriptive-analytical study was performed with a cross-sectional design. The study population consisted of all patients diagnosed with eclampsia-preeclampsia and pregnant mothers in Shohada-e-Tajrish and Mahdieh Hospitals in Tehran during 2019 to 2020. The study sample consisted of 400 patients who were selected by convenience or convenience sampling method and 200 patients with a diagnosis of eclampsia-preeclampsia were in the experimental group and 200 pregnant women were in the control group. The subjects completed pre-prepared forms for study variables, i.e. information on maternal age, maternal weight, infant weight, gestational age, neutrophil count and lymphocytes. To analyze the collected data, tests such as Pearson correlation coefficient and independent t-test were used and analyzed by SPSS software version 23. The results showed that a statistically significant difference was found between NLR and PLR MPV. Finally, the results of this study showed that platelet count; MPV, NLR, PLR were significantly different in the two groups of preeclampsia patients and pregnant women with normal blood pressure and that these indicators can be used to predict preeclampsia.

GRAPHICAL ABSTRACT
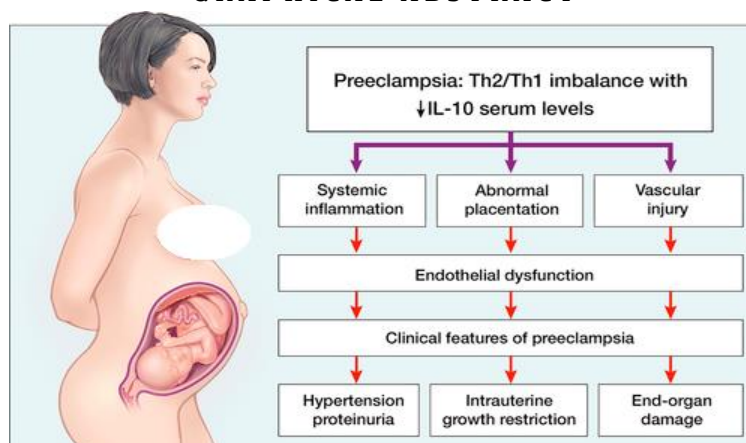
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Introduction

Hypertension becomes a medical problem during pregnancy and one of the types of hypertensions during pregnancy is eclampsia-preeclampsia. Preeclampsia occurs in about 2 to 9% of pregnancies [1-3]. The association of preeclampsia and eclampsia with maternal mortality and morbidity is also well established and is one of the leading causes of maternal death today in development [4-6]. For this reason, factors seem to be cheap and related to prediction and early observation [7]. So far, studies have examined inflammatory markers such as platelet count, lymphocyte, neutrophil, neutrophil to lymphocyte ratio, as well as platelet to lymphocyte ratio and mean platelet volume. These markers have been studied in various diseases such as diabetes mellitus, coronary artery disease, ulcerative colitis, and cancers, resulting in finding a significant relationship with these markers [8-10].

Increased inflammatory cell activity and immunological responses in preeclampsia lead to the release of inflammatory cytokines and autoantibodies and the production of more superoxide, which impairs endothelial function. Preeclampsia is associated with impaired regulation of TH1 and TH_2 inflammatory responses. In different studies, different results have been obtained in terms of lymphocyte, neutrophil count and MPV in patients with preeclampsia [11-13]. Neutrophils circulate in the circulatory system and interstitial villi and are exposed to oxidized lipids, which are the result of impaired blood supply to the placenta. Oxidized lipids during preeclampsia are potent activating factors that increase neutrophil counts; COX_2 update; increased thromboxane and super oxidation [14]. The highest incidence of COX_2 in neutrophils in perpleptics was found in a 2008 study by Cadden et al. and as the number of neutrophils increases, they will be more active. Increased activation of neutrophils, which is seen in normal pregnancies and more severely in preeclamptic patients, can be explained by the increased level of arachidonic acid in these patients [15-17].

Lymphocytes are also responsible for the adaptation of the immune system, which plays this role by producing antibodies. On the other hand, neutrophils are the first line of defense against wound infection or other tissue damage, which seems to decrease lymphocyte production with increasing neutrophil count [18] (Figure 1).
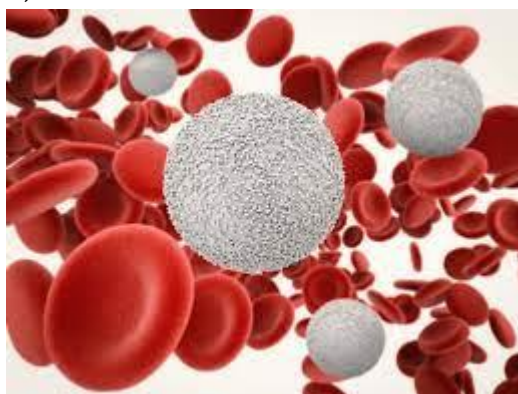
**Figure 1:** Lymphocytes: Levels, ranges, and functions

As an inflammatory marker in preeclamptic patients, in preeclampsia, from fetal maternal vascular involvement to increased immune response to maternal antigens, systemic inflammatory response and placental dysfunction are all involved in preeclampsia [19-21]. Increased vascular resistance in preeclampsia facilitates platelet aggregation and increases coagulation system activity as well as dysfunction of the endothelial system. In preeclampsia, a decrease in platelet count is common [22-24]. This phenomenon is due to an increase in circulating plasma volume and on the other hand due to platelet consumption due to increased intravascular coagulation [25]. It is a common finding in preeclampsia and the rate of platelet

decline is often associated with the severity of the disease [26-28].

Platelet volume is a marker that can be used to differentiate physiological thrombocytopenia of pregnancy and increase bone marrow activity due to increased platelet intake [30-32]. Following a decrease in platelet count, the bone marrow begins to produce new platelets, which are larger and more active in size. Mean platelet volume (MPV) indicates platelet size and TURN OVER above platelets [33-35]. This factor is accepted as a marker of platelet function and is routinely checked during CBC [36-38]. Also, an increase in the mean platelet volume indicates a greater number of granules in the platelets and a greater release of cytokines and thromboxane. Based on the available evidence, we decided to examine inflammatory markers such as neutrophil and lymphocyte count, platelet count and MPV, neutrophil to lymphocyte ratio and platelet-to-lymphocyte ratio in preeclampsia and normal pregnancy patients so that we could identify these factors in the next step[39] (Figure 2).
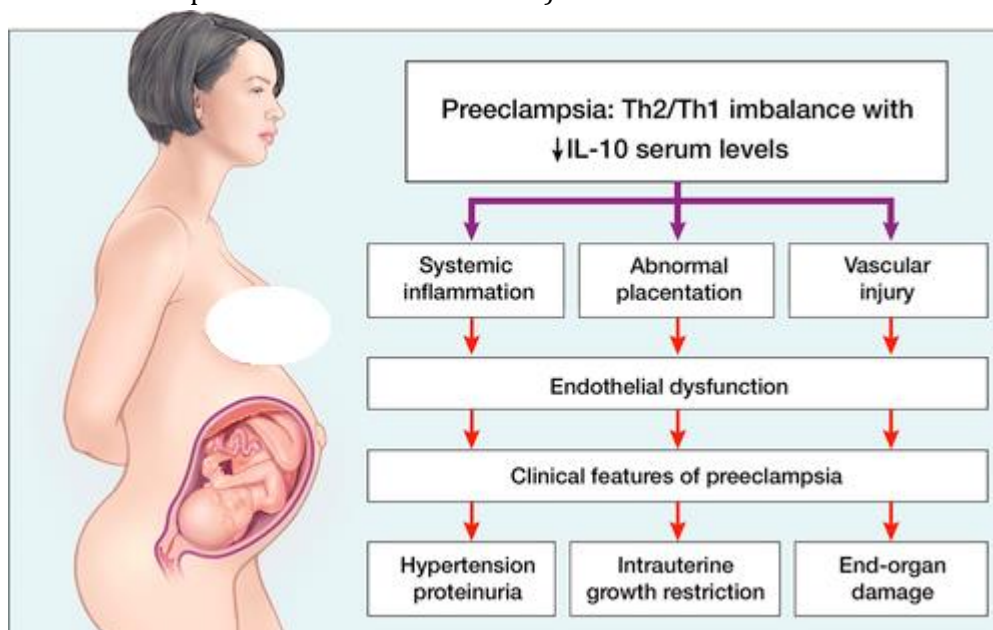
Figure 2: Preeclamptic Women Have Decreased Circulating IL-10 (Interleukin-10) Values

Material and methods

Instruments
The forms were prepared in advance according to the study variables and the study findings were recorded. Google Scholar, PubMed, Scopus, Web of Science databases were thoroughly searched to review the texts, and similar articles were cited to review and design the study.

B- Methods of study
This descriptive-analytical study was performed on 400 pregnant women, 200 of whom were healthy pregnant women and 200 of whom were diagnosed with eclampsia and preeclampsia in the obstetrics and gynecology ward of Shohada-e-Tajrish and Mahdieh hospitals in Tehran over a period of 2 years. Written consent was obtained from patients to participate in the study and the study is approved by the ethics committee of the medical school of Shahid Beheshti University. Demographic and clinical information is extracted through interviews and questionnaires as well as patient records. Criteria for excluding these patients from the study are the use of anti-inflammatory drugs, inflammatory diseases and blood-related diseases [40-42].

Dialysis patients are also excluded from the study [43-45]. Information such as mother's age, maternal weight, baby weight, maternal blood pressure, BMI, and gestational age extracted from the patients' file [46-48]. Blood MPV level in tubes containing EDTA was evaluated with Sysmex SE 9500 automatic device and Roche Indianapolis [49-50]. The number of neutrophils and lymphocytes as well as platelets was

obtained from CBC and then their ratio was obtained by dividing the number of neutrophils into lymphocytes and dividing the number of platelets by lymphocytes.

All the mentioned information was collected in both control and patient procedures. The variables were collected from all groups and then the data was fed into SPSS software version 23 and the relationship between the variables was appraised with tests such as Pearson coefficient correlation. Also, the comparison between the parameters in terms of variables was made with tests such as independent t-test (Figure 3).
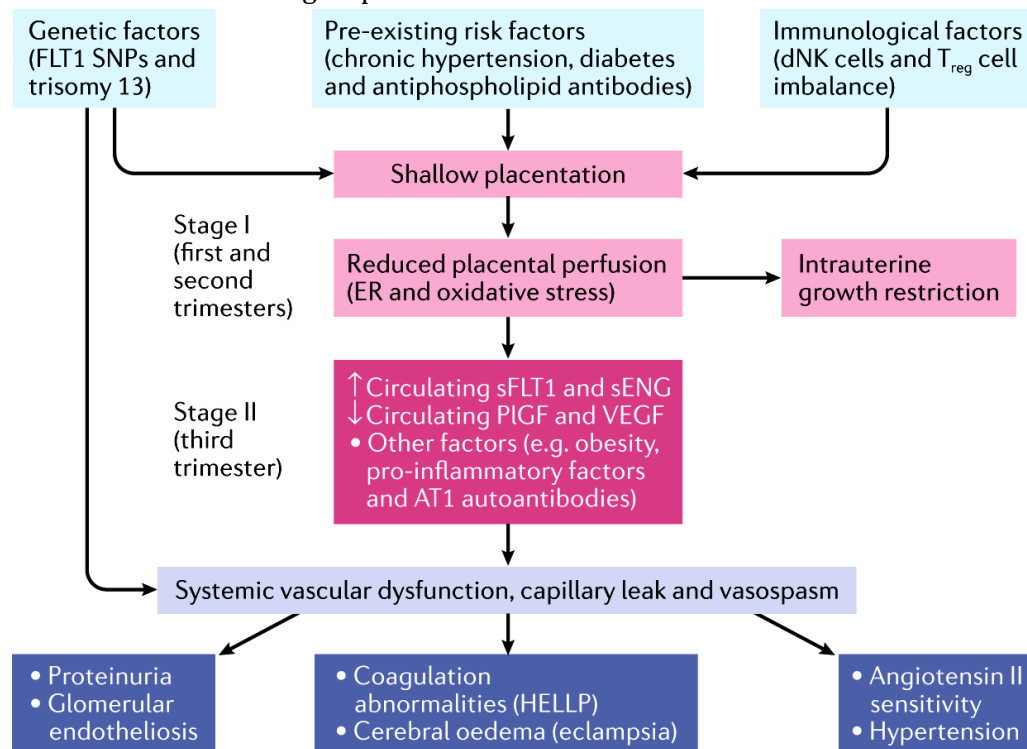
Figure 3: Pre-eclampsia: pathogenesis, novel diagnostics and therapies

C- Data analysis method

The data obtained in the research stage was fed into SPSS v23 software and then the relationship between the variables was examined by calculating the correlation coefficient. Also, the effect of possible confounding factors was investigated using the regression method.

Table 1: Variables under the study

	Total	Normal	Preeclampsia	P-value
Platelet count	253.1+125	274.4+91	149+231.9	<0.05
Number of neutrophils	7.66+2314	5665+1527	2100+8467	<0.05
Lymphocyte count	2335+574	2319+522	623+2352	<0.05
MPV	9.7+1.32	9.55+1.27	1.3+10	<0.05
NLR	3.21+1.6	2.6+1.6	1.3+3.82	<0.05
PLR	116.2+74	126.4+67	78+106	<0.05

Exclusion criteria were as follows:
 ➢ History of inflammatory diseases such as rheumatic diseases;
 ➢ History of blood diseases that affect neutrophils, lymphocytes and platelets;
 ➢ Taking statins and other anti-inflammatory drugs;
 ➢ History of heart failure;
 ➢ History of kidney disease;
 ➢ History of liver disease;

> History of coagulopathy; and
> Cancer history.

This descriptive-analytical study was performed on 400 pregnant women, 200 of whom were normotensive pregnant women and 200 of whom were admitted to the gynecology and obstetrics ward of Shohada-e-Tajrish and Mahdieh hospitals in Tehran with a diagnosis of eclampsia and preeclampsia over a period of 2 years from 2019. The data of healthy pregnant women and women with preeclampsia is presented in Table and 3.

Table 2: variables (Pvalu)

	Total	Normal	Preeclampsia	P-value
Mother's age	26.3+15	14+25.5	16+27	>0.05
Weight	10+74	6.6+73.4	8.6+75.4	>0.05
Height	5+163.7	4.6+164.6	5.1+162.8	>0.05
Gestational age	2.6+35.9	1+38	2+33.7	>0.05
BMI	3.5+27	2.3+26.7	3.2+27.9	>0.05
Baby weight	612+2764	406+3237	372+2291	>0.05
Systolic pressure	22.6+133.8	10+112.7	5+154.9	>0.05
Diastolic pressure	15+86.6	6.6+73.5	8.9+99.8	>0.05

Table 3: Table of variables (Preeclampsia)

	Total	Normal	Preeclampsia	P-value
Platelet count	253.1+125	274.4+91	231.9+149	<0.05
Number of neutrophils	7066+2314	5665+1527	8467+2100	<0.05
Lymphocyte count	2335+574	2319+522	2352+623	<0.05
MPV	9.7+1.32	9.55+1.27	10+1.3	<0.05
NLR	3.21+1.6	2.6+1.6	3.82+1.3	<0.05
PLR	116.2+74	126.4+67	106+78	<0.05

Applied Objectives

If there is a link between eclampsia and preeclampsia and the level of inflammatory markers that can be easily measured in the laboratory, these markers can be used to predict the development of eclampsia and preeclampsia in high-risk women [52].
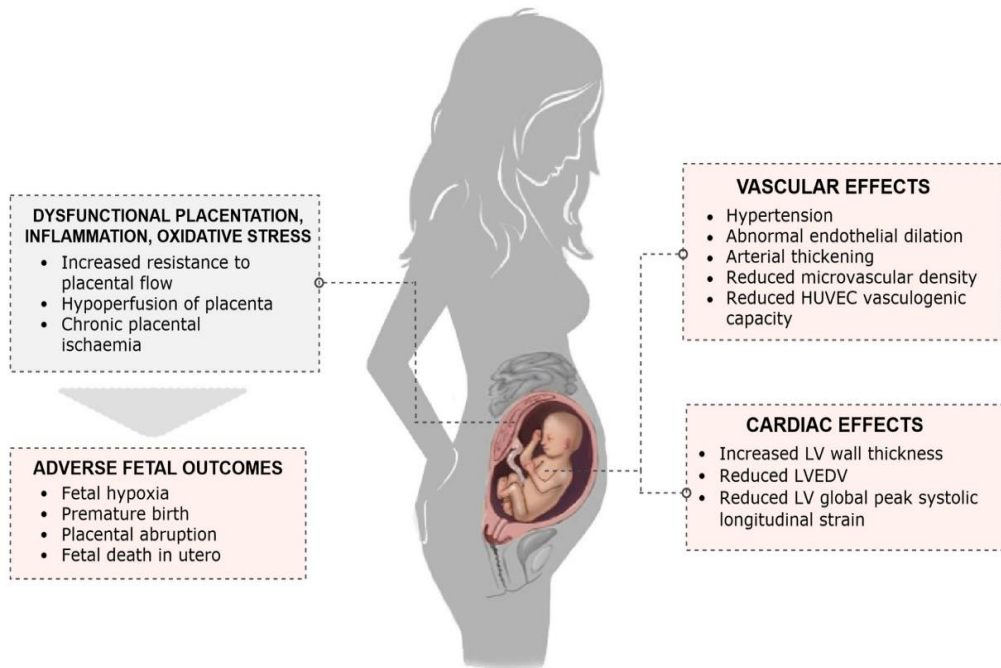
Figure 4: Preeclampsia: Risk Factors, Diagnosis, Management, and the Cardiovascular

Conclusion

In this study, we first investigated whether there was a statistically significant difference between our inflammatory variables in the two groups of preeclampsia and normal. After proving this relationship, we performed studies with a larger sample size. Among the plans that can be done in relation to the study of these inflammatory factors, their study in the first trimester of pregnancy and then follow up patients to determine whether the factors NLR, PLR, MPV can be used as predictors of early preeclampsia and its severity used. Also, due to the fact that the pathophysiology of preeclampsia is related to vascular injury and complications, the cardiovascular complications of these mothers can be followed in the long run. As we know, aspirin is used as a prophylactic drug in preeclampsia in cases of low PAPPA or high PI of uterine artery. Due to the inflammatory process in the process of preeclampsia, these factors such as NLR, PLR, MPV are used as determining factors. Aspirin should be used properly because using these tests is an easy and inexpensive way. On the other hand, considering that thrombocytopenia can occur in pregnant women, MPV can be used to differentiate physiological thrombocytopenia from preeclampsia. Given that we expect the inflammatory response to increase and also the change in hematologic factors after delivery to return to normal, these factors can be examined in the interval of 4 to 6 weeks after delivery to be able to confirm or deny this hypothesis.

Funding

Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

We have no conflicts of interest to disclose.

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