

THE RELATIONSHIP OF INFLAMMATORY FACTORS AND KETON UREA IN EVALUATIONS OF PATIENT WITH HYPER EMESIS GRAVIDARUM SEVERITY.

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Abstract

Objective: This study aims to investigate the role of inflammation in the severity of hyperemesis gravidarum (HEG).

Methods: This prospective study was conducted in the Department of Obstetrics and Gynecology at Thi-Qar University in Bint-alhuha Hospital between September 2023 and January 2024 . The patients that were defined as HEG should have the following

symptoms: Persistent nausea and vomiting, presence of at least one positive ketonuria test in a random urine analysis, fetal heartbeat positivity at 4-14 weeks of gestation, and singleton pregnancy. Total blood count including white blood cell (WBC), neutrophil (NEU), lymphocyte (LYM),hemoglobin, hematocrit, and platelet were analyzed. NEU-to-LYM (NLR) and platelet-to-LYM ratios (PLR) were calculated.

Results: Forty-two patients were evaluated in the first trimester of pregnancy. Patients with HEG had similar age, gravida, parity, gestational weeks. NLR and PLR levels were statistically higher in the sever group. There is no differences in term of ketone body.

Conclusion: Measurement of inflammatory markers, such as WBC, NLR, PLR, and CRP levels, might provide valuable knowledge in HEG diagnosis.ketone body has invaluable role in severity but NLR level is a better indicator for predicting the diagnosis and severity of the disease according to our study findings.

Keywords: Hyperemesis gravidarum, inflammation, C-reactive protein, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio

INTRODUCTION

Nausea and vomiting are common symptoms seen in pregnancy (1)

If the symptoms are minor, nausea during the first trimester can be explained as a result of typical physiological changes. Hyperemesis gravidarum (HEG), a severe form of nausea and vomiting in pregnancy, can induce electrolyte imbalance, dehydration, fluid and acid-base imbalance, nutrition insufficiency, ketonuria, and weight loss

of more than 5%. (1,2) The incidence of nausea and vomiting is 85% in pregnancy, but only 0.3%-2% of pregnant women will have HEG (3,4) HEG's etiopathogenesis has been studied extensively, however the specific reason is unknown. The disorder is thought to be caused by a combination of variables, including maternal endocrinology, immunology, and psychology .

Furthermore, placental development and pregestational gastrointestinal condition may be linked to the pathogenesis (5). HEG risk factors include primigravida, multiple gestation, molar pregnancy, previous failed pregnancy, and a history of HEG.

Researchers discovered that inflammation has a role in the pathogenesis of the disease and is closely associated to the intensity of symptoms. The current data are insufficient to explain the function of inflammation in HEG pathogenesis, yet inflammation may be linked to the development of HEG.

Proinflammatory cytokines, including IL-6, TNF- α , and CRP, have been linked to HEG etiology and disease progression. (6,7).In recent years, many hematological indicators have been utilized to assess the inflammatory status of different diseases. neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are simple markers that have been shown to reflect inflammation and disease activity in several disorders, including ulcerative colitis, spontaneous bacterial peritonitis, cancer, and cardiovascular diseases. (8,9).

Oxidative stress is defined as an imbalance of oxidant molecules and antioxidant defenses in humans, which can lead to pathological conditions such as pregnancy and pregnancy problems. It is considered that oxidative stress, which accompanies subclinical inflammation, may cause the start of HEG. (9)

This study aims to investigate the diagnostic value of NLR, PLR, and CRP in patient with HEG in comparison with ketone body according to their severity.

METHOD

From September 2023 to January 2024, this observational analytical study was carried out at Bint-alhuda Hospital's Department of Obstetrics and Gynecology and the supervisor private clinic at Thi-qar University's College of Medicine. A total of 42 patients with HEG. Patients who were defined as HEG should exhibit the following symptoms: Persistent nausea and vomiting, at least one positive ketonuria test in a random urine study, fetal heartbeat positivity at 4-14 weeks of gestation, and singleton pregnancy, patients at least rehydrate in 5-7 days.

Patients with HEG were divided into two subgroups (severe and non-severe) based on the severity of their symptoms; the majority of patients who dehydrated were categorized as severe. Patients with multiple pregnancies, cigarette smoking, chronic illnesses, thyroid issues, gastrointestinal disorders, or urine infections were excluded. Each patient had their age, gestational age, gravidity, and parity documented. The gestational age was established using the date of the previous menstrual period and confirmed by ultrasound.

The whole blood count was tested, which included white blood cells (WBC), neutrophils (NEU), lymphocytes (LYM), hemoglobin, hematocrit, and platelets. NLR and PLR were calculated.

Incidence of sever and non-sever group (positive value of test only) by divide positive sever on total positive and positive non-sever on total positive, and measure relative risk (RR) by divide incidence of positive sever on incidence positive non-sever, $RR > 1$ there is high risk while $RR < 1$ there is low risk.

Using differential count, NLR was computed by dividing the absolute NEU count by the absolute LYM count. PLR was determined by dividing the platelet count by the LYM count. Urine ketones, CRP, were also measured. The ketonuria was rated as 1+, 2+, or 3+.

STATISTIC ANALYSIS

The data was analyzed using the Statistical Program for Social Sciences (SPSS) version 16. The values of HEG and control patients were compared using the Chi squared test. The data were presented as mean \pm standard deviation. The Mann-Whitney U test was used to examine gestational age, gravida, and parity; the findings are shown as mean (minimum-maximum). PLR, CRP, WBC, and NEU counts were all subjected to multivariate analysis. $P < 0.05$ was considered statistically significant.

RESULT

The outcomes of 42 patients were analyzed. Everyone has HEG in the first trimester of pregnancy. Eighteen were severe, while twenty-four were not.

Table 1 compares demographic features between sever and non-severe. Healthy pregnant women and HEG patients shared similar ages, gravida, parity, and gestational week.

Table 2 presents the univariate analysis of laboratory data in severe and non-severe patients with RR. The univariate analysis revealed that the severe group had significantly higher levels of WBC, NEU, CRP, NLR, and PLR.

Table 3 shows the values of ketone body and relation to severity of HGE shows small number of patients with +2, +3 and +4 has sever symptoms, Urine ketone was not statistically significant and differed between the two groups ($p=0.503$).

NLR levels were evaluated by the chi-square test, and it was statistically significantly high in the sever group compared with the nonsever group ($p=0.008$).

Table 1

Subject	Subgroup	HEG		P value
		Sever	Non sever	
Age	15-29 y.o	10	18	0.175
	30-39 y.o	8	6	
Gravida and parity (G P)	G1 P0	6	10	0.894
	G2 P1	6	6	
	G3 P0	0	1	
	G3 P2	4	5	
	G4 P3	1	3	
Gestational age	4-9 weeks	4	5	0.547
	10-15 weeks	14	19	

DISCUSSION

outcomes of 42 patients were analyzed. Everyone has inflammation and oxidative stress are important in the pathogenesis of HEG (7, 8). NLR, PLR, and CRP are indicators that indicate both acute and chronic inflammation. The study's goal was to compare and evaluate inflammatory markers in pregnant women with severe and non-severe HEG

Our data demonstrated that WBC, NEU, CRP, NLR, and PLR levels were considerably higher in patients with severe HEG than in non-severe patients. (10) Their findings revealed an increase in NLR and PLR in patients with severe HEG. (10) noted that NLR and PLR were raised as a normal immunological response of circulating leukocytes to HEG-associated physical stress, resulting in NEU amplification and LYM count reduction

Our study's findings of higher NEU and serum CRP levels support the role of inflammation in the pathogenesis and severity of HEG. However, our findings demonstrate elevated levels of NLR and PLR. This could be attributed to the recent start of HEG symptoms and the severity of nausea and vomiting

Platelets are dynamic blood particles whose major purpose, along with coagulation factors, is to maintain hemostasis or prevent bleeding. Platelets interact with one another, as well as with leukocytes and endothelial cells, looking for areas of injury where they might become activated (12). Platelets can be influenced by a variety of reasons other than inflammatory processes during pregnancy, including hemodilution and aggregation, which are typically reflected in laboratory data as a reduction. Furthermore, hormones such as estrogen, which rise during pregnancy, might impair platelet function and lead to hypercoagulability. Platelets are shown to contribute to the inflammatory process, microbial host defense, wound healing, angiogenesis, and remodeling (13). Platelet activation can be linked to platelet size

STUDY LIMITATION

The limitations of this study are listed below. To better understand the pathophysiology of severe HEG, it would be beneficial to study serum levels of proinflammatory markers like ILs and TNF- α . Alternatively, one of our study's key strengths is the availability of complete data for each patient, as well as the exclusion of individuals with HEG risk factors such as chronic and systemic endocrine, immunologic, or GI disorders.

Table 2

Invx	HEG		Relative risk IR sever IR non-sever	P value
	Sever	Non-sever		
Hb	11.41(9-14)	11.69(9.6-14.2)	71.4/28.57=2.5	0.161
HTC %	38.26(31-45)	38.8(33-44.4)	47/52.9=0.88	0.739
WBC	9.26(3.98-14.8)	8.72(3.79-15.9)	50/50=1	0.326
NEU	7.34(1.98-13)	6.13(1.34-12.9)	50/50=1	0.058
LYM	1.4(0.228-2.8)	1.93(0.4-3)	0/1=0	0.359
PLT	217(120-355)	243.33(116-351)	50/50=1	0.076
NLR	8.84(1.58-32.3)	4.94(0.64-23.5)	58.8/41.1=1.42	0.008
PLR	244(69.5-1083)	174(56.8-600)	57.89/42.1=1.37	0.077
CRP	9.6(0.2-66)	1.5(0.08-14)	26.6/73.3=0.36	0.591

Table 3

Ketone body	Sever	Non sever	P value
+	3	5	0.503
++	6	13	
+++	4	6	
++++	2	3	

CONCLUSION

Measurement of inflammatory markers such as WBC and CRP levels, as well as NLR and PLR, may provide useful information in HEG diagnosis since inflammation contributes to the pathogenesis of severe HEG. CRP levels are OK, but our study found that NLR levels are a stronger predictor of disease diagnosis and severity.

ETHICS

Ethics Committee Approval: This prospective study was conducted in the Department of Obstetrics and Gynecology at Thi-Qar University Hospital, Faculty of Medicine

Informed Consent: Was obtained from all patients.

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Table 1 :- Comparison of demographic findings

	HEG		P value
	Sever	Non - sever	
Age	27(15-36)	26(16-34)	0.175
Gravida	1(1-4)	1(1-4)	0.894
Parity	0(0-3)	0(0-3)	0.942
Gastational weeks	11(4-14)	10(4-14)	0.547