

Evaluation of platelet count and platelet function in intrahepatic cholestasis of pregnancy

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Abstract

Objective: Platelet count (PC) and function have been reported to be increased in inflammatory incident. The aim of the study is to evaluate PC and mean platelet volume (MPV) in patients with intrahepatic cholestasis of pregnancy (ICP) and to compare them to normal pregnancies.

Methods: The patients with ICP and newborns files were retrospectively reviewed at Obstetrics and Gynecology Department, Dicle University between January 2009-December 2011. During the study period 6,743 birth was found in our clinic. Twenty-two patients with ICP identified and 32 subject enrolled as a control group which have no systemic disease or risk factors that may complicate pregnancy. Groups were compared in terms of demographic, biochemical parameters, PC, MPV, and Apgar scores.

Results: The incidence of patients with ICP was found to be 3.2/1000 in this study. The average time to diagnose is 34.2±2.2 gestational weeks. Pruritus (72.7%) were found to be the most common presenting symptom in patients and the 13.6% of patients present jaundice. There was no difference in the average birth weight of newborns and 1-5 Apgar scores between the two groups. Four (18.2%) patients of the ICP developed fetal distress and three of these patients had meconium stained amniotic fluid. There was no fetal distress or meconium stained amniotic fluid in the control group. The average PC in patient and control group were 268.9 x 10⁹ K/uL and 226.5 x 10⁹ K/uL respectively (p=0.037) and MPV were 10.6 fL and 8.9 fL (p=0.004) respectively. Platelet count and MPV were significantly higher in patients with ICP when compared to control group.

Conclusion: Increased platelet count and function in patients with intrahepatic cholestasis of pregnancy may be indicative of inflammation.

Key words: Pregnancy, intrahepatic cholestasis, platelet count, platelet function test.

Gebeliğe bağlı intrahepatik kolestaz olgularında trombosit sayı ve fonksiyonunun değerlendirilmesi

Amaç: Trombosit sayı ve fonksiyonu inflamatuvar hadiselerde artmış olarak rapor edilmektedir. Bu çalışmanın amacı gebeliğe bağlı intrahepatik kolestaz (GBİHK) olgularındaki trombosit sayısı (TS) ve ortalama trombosit hacmini (OTH) normal gebeler ile karşılaştırmaktır.

Yöntem: Dicle Üniversitesi Kadın Hastalıkları ve Doğum Kliniğine Ocak 2009-Aralık 2011 tarihleri arasında GBİHK tanılı hastalar ve yenidoğan dosyaları retrospektif olarak incelendi. Çalışma süresinde kliniğimizde 6743 doğum olduğu izlendi. Çalışmaya, GBİHK tanısı konulan 22 olgu ile gebeliği komplike edebilecek herhangi bir sistemik hastalığı veya risk faktörü olmayan 32 gebe kontrol grubu olarak alındı. Gruplar demografik yönden, biyokimyasal parametreler, TS, OTH ve yenidoğan Apgar skorları açısından karşılaştırıldı.

Bulgular: Kliniğimizde GBİHK insidansı 3.2/1000 olarak bulundu. Tanı anındaki ortalama gebelik haftası 34.2±2.2 olarak saptandı. Kaşıntı (%72.7) en sık başvuru semptomu iken hastaların %13.6'sında sarılık olduğu tespit edildi. Gruplar arasında yenidoğan ortalama doğum ağırlığı ve 1.-5. dakika Apgar skorları arasında farklılık izlenmedi. Hasta grubunda dört (%18.2) olguda fetal distres geliştiği izlendi ve bu hastaların üçünde amniyotik mayi mekonyumlu idi; kontrol grubunda ise fetal distres veya mekonyumlu amniyon mayi saptanmadı. Hasta ve kontrol grubunda ortalama TS sırasıyla; 268.9 x 10⁹ K/uL ve 226.5 x 10⁹ K/uL (p=0.037) olarak izlendi. Yine OTH değerleri sırasıyla 10.6 fL ve 8.9 fL (p=0.004) idi. Trombosit sayısı ve OTH kontrol grubuna göre GBİHK'lı hastalarda istatistiksel anlamlı yüksek saptandı.

Sonuç: Gebeliğe bağlı intrahepatik kolestazlı hastalarda kontrol grubuna göre TS ve fonksiyonlarında artma olması inflamasyonun göstergesi olabilir.

Anahtar sözcükler: Gebelik, intrahepatik kolestaz, trombosit sayısı, trombosit fonksiyon testi.

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Introduction

Intrahepatic cholestasis of pregnancy (ICP) is a pregnancy-specific liver disease with unclear etiology which may start at any week after 30th gestational week, usually may recover by delivery. The symptoms mostly complained by the patients are the itching especially on extremities and excoriated skin caused by itching.^[1] Many causes have been accused in the etiology of cholestasis of pregnancy; however, the primary reason cannot be explained clearly. Increased bile acid levels in the cases of intrahepatic cholestasis of pregnancy cause itching on skin and jaundice. It has been reported that risks such as preterm labor, amniotic fluid with meconium, fetal distress and intrauterine fetal loss are increased in terms of fetus.^[2,3] Platelet count (PC) and its function have increased in systemic inflammatory disease.^[4] In this study, we aimed to evaluate PC and its functions in ICP cases and to compare them with the control group.

Methods

In this study, 22 patients who applied to Obstetrics and Gynecology Department of Dicle University in between January 2009 and December 2011 and diagnosed as ICP were evaluated. Data during applications were collected from hospital archives and patient files. Patients were evaluated in terms of age, gravida, parity, number of living children, gestational week, newborn Apgar scores, liver function tests, full blood count, urinalysis, and biochemical parameters. Platelet count (PC) and mean platelet volume (MPV) were compared between patient group and control group. Patients were examined by abdominal USG in order to exclude liver and bile duct pathologies and cases without any pathology were included into the study. Patients who were found to have allergic diseases, dermatitides, chronic liver diseases, disease that may cause biliary obstruc-

tions (cholelithiasis – choledocholithiasis), hypothyroidism, hyperthyroidism, hypertensive diseases that may affect liver functions (preeclampsia, eclampsia, HELLP), pregnancy-induced acute hepatic lipidosis by differential diagnosis and patients who did not give birth in our clinic were excluded from the study.

Steroid treatment was applied to 12 (54.5%) patients at 28th-34th gestational week in order to provide fetal lung maturation. Thirty-two pregnant who had no systemic disease or risk factor that may complicate the pregnancy were included into the control group.

Data were evaluated on SPSS (Statistical Package for Social Sciences) for Windows 15.0 (SPSS, Inc., Chicago, IL, USA), Epi info and Excel for statistical analysis. Numerical data were controlled by Kolmogorov-Smirnov test if they were distributed regularly or not, and Mann-Whitney U test was applied since there was no regular distribution. Results were found statistically significant at 95% confidence interval and when $p < 0.05$. Approval of Ethics Committee of Dicle University was obtained.

Results

Twenty-two patients with ICP diagnosis and 32 patients (as control group) who had no pathology complicating pregnancy were included into this study. It was found that there were 6,743 deliveries in our clinic within the specified period. Demographic and obstetric data of cases are presented in **Table 1**.

It was observed that application symptoms of the patients were itching (72.7%) and jaundice (13.6%). Mean PC and MPV values in patients with ICP were found as significantly increased compared to the control group. Liver function tests and mean PC and MPV values are listed in **Table 2**. Mean diagnosis period of patients during application to clinic after symptoms

Table 1. Comparison of demographic and obstetric data of the groups.

	Patient group (Average \pm SD)	Control group (Average \pm SD)	p
Age, (year)	26.9 \pm 5.4	27.5 \pm 5.7	0.74
Number of gestation	2.2 \pm 1.6	2.9 \pm 2	0.18
Number of delivery	1.1 \pm 1.5	1.7 \pm 1.8	0.19
Number of living children	1.0 \pm 1.3	1.4 \pm 1.5	0.24
Gestational week	34.2 \pm 2.2	33.9 \pm 2.4	0.62

SD: Standard deviation.

Table 2. Comparison of hematologic and biochemical parameters of the groups.

	Patient group (Average \pm SD)	Control group (Average \pm SD)	p
Hemoglobin, (g/dL)	12.06 \pm 1.09	12.02 \pm 1.13	0.88
Hematocrit, (%)	36.10 \pm 3.43	35.29 \pm 2.94	0.36
Leucocyte, (K/uL)	9.97 \pm 3.23	10.17 \pm 2.20	0.78
Platelet count, (fL10 ⁹ /L)	268.9 \pm 85.8	226.5 \pm 59.7	0.037
Mean platelet volume, (fL)	10.6 \pm 2.3	8.9 \pm 1.8	0.004
ALT, (U/L)	227.9 \pm 221.8	18.7 \pm 8.5	<0.001
AST, (U/L)	136.8 \pm 123.4	27.4 \pm 12.3	<0.001
Bilirubin total, mg/dL	1.38 \pm 1.29	0.43 \pm 0.22	0.003
LDH, (IU/L)	391.6 \pm 185.7	263.1 \pm 54.7	0.004

SD: Standard deviation, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, LDH: Lactate dehydrogenase, fL: Femtoliter, K/uL: Cubic milliliter.

appeared was 34.2 \pm 2.2 gestational week and all patients were at or below 37th gestational week.

In the patient group, it was confirmed that four (18.2%) cases had fetal distress and it was found that amniotic fluid was stained by meconium in three of these patients. In the control group, no fetal distress and amniotic fluid with meconium was observed. Newborn birth weights and Apgar scores of patients are shown in **Table 3**. There was no neonatal mortality in any newborn.

Discussion

ICP incidence was found as 0.32% in this study. Kurt et al.^[5] found that incidence of Central Anatolia is 1.4%. Incidence of the disease varies regionally; while it was reported as 0.32% in the USA and as 0.2-1.5% in Europe, it was reported high as 6.5-27.6%.^[1,6-9]

The etiology of the disease is complex and it is considered that factors such as hormones, diets etc. High level of liver function test (ALT, AST) is the most significant indication accompanying the diagnosis. ICP is

diagnosed by the presence of liver function test abnormality and excluding other etiological reasons causing jaundice and itching. Itching was a symptom in 72.7% of patients during application. Jaundice generally becomes evident 1-4 weeks after itching.^[1] HELLP syndrome should be considered particularly during differential diagnosis, because preterm labor is required in the treatment of HELLP syndrome while the management of ICP cases can be followed up to term by appropriate treatment and follow up. In both cases where hepatic enzyme is found high, HELLP syndrome diagnosis is ruled out due to non-existence of hypertension, proteinuria and thrombocytopenia.^[1]

The disease should be followed-up closely after diagnosis and medical treatment should be applied. Although chenodeoxycholic acid may be given, ursodeoxycholic acid should be preferred since it is safer for both mother and baby and its advantage of decreasing preterm labor risk by perinatal morbidity.^[10] Placental ischemia has been reported in the cases of intrahepatic cholestasis of pregnancy; placental ischemia and oxygenation disorder may cause fetal complications

Table 3. Comparison of newborn results of the groups.

	Patient group (Average \pm SD)	Control group (Average \pm SD)	p
Newborn birth weight (gram)	2,467	2,486	0.92
Apgar 1st minute	5.2 \pm 1.0	5.2 \pm 1.3	0.84
Apgar 5th minute	7.5 \pm 1.0	7.8 \pm 1.3	0.30

SD: Standard deviation.

such as fetal distress, preterm labor, fetal cardiac dysrhythmia and baby with meconium. Nevertheless, pathophysiology of fetal adverse effects have not been understood clearly yet. It has been considered that abnormal contractions occurring in chorionic vessels have major roles on placental pathologies.^[11,12]

Platelets are the smallest shaped elements of the blood and they have a role in thrombosis. However, they also include mediators in the granules secreted which have vasoconstrictor effect. Activated platelets include granules which include pro-inflammatory mediators (thromboxane A₂, serotonin, leukotriene) and free oxygen radicals; they cause thrombotic activity to increase and micro-vascular circulation to get disorder. Effects of platelets which are in the circulation of pro-thrombotic activity are bigger. MPV is a cheap, easy and effective method for the evaluation of platelet functions; its high level is a parameter showing the increase of platelet synthesis and function.^[4,13,14] MPV was found significantly high in diseases such as rheumatoid arthritis associated with inflammation, ankylosing spondylitis, acute ischemic stroke, familial Mediterranean fever and acute pancreatitis.^[4,15-17]

In the literature, the only study comparing PC and MPV in ICP cases was conducted by Kebapçılar et al.^[18] In their study, 40 cases with ICP were compared with 40 control pregnant. Consequently, they reported that patient group had lower 1st and 5th minute Apgar scores and higher MPV values compared to the control group. In our study, there was statistically significant difference between the MPV values of patients with ICP and the control group; however, Apgar scores were found similar.

Conclusion

Consequently, PC and increase in the functions of patients with ICP compared to the control group may be an indication of inflammation.

Conflicts of Interest: No conflicts declared.

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