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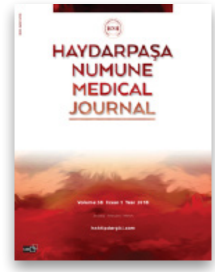

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ORIGINAL ARTICLE

Evaluation of the Gallbladder Dysmotility in the Pregnancy

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Abstract

Introduction: The hormonal changes that occur during the pregnancy increase the risk of developing gallstones. The impact of placental steroid hormones such as elevated estradiol (E2) and progesterone (PGN) continuously affect the biliary lipid storage and gallbladder activity in safe pregnant women. Gallbladder bile quantities of biliary cholesterol begin to increase from the first trimester to the third trimester of pregnancy, along with a steady increase in biliary sludge and gallstone occurrence. Ultrasound is a widely used method of imaging, and has the advantage of being safe for the pregnants. It is generally considered as the first line for gallbladder disease assessment. The study aimed to reveal whether there was a difference in motility marker values such as Fasting Volume (FV), Postprandial Volume (PPV), and Ejection Fraction (EF) between trimesters with the effect of changing steroid hormones. These parameters were also compared between groups of pregnant and non-pregnant people, considering gestation numbers.

Methods: The patient group consists of 50 pregnant women who applied to the gynecology and obstetrics clinic at our hospital. 20 healthy non-pregnant women constituting the control group were also included in the present study. The age and parity of the cases were included in the study. The trimesters of the pregnancies were also recorded for the pregnant group. After the fasting on the day of the examination, gallbladder volumes of the patients were measured. After feeding for 45 minutes, gallbladder postprandial volume measurements were obtained. The gallbladder ejection fractions were calculated using these values (EF: [FV-PPV]×100/[FV]).

Results: When the PPV mean values between the trimesters were observed, significant difference was not found between the 1^{st} and 2^{nd} trimesters (p>0.05) moreover significant difference was found between the 1^{st} and 3^{rd} trimesters and the 2^{nd} and 3^{rd} trimesters (p<0.001).

In the analysis made in terms of EF values, obtained from the pregnant group, the difference between the trimesters was found significant (p<0.05). In terms of EF mean values, any significant difference was not found between 1^{st} and 2^{nd} the trimesters and 2^{nd} and 3^{rd} trimester (p>0.05),but the difference between 1^{st} and 3^{rd} trimesters were found to be significant with the decrease of EF values in 3^{rd} trimester (p<0.05). When comparing control group's mean FV, PPV, and EF valuesto the pregnant women in the 3rd trimester consideringmean FV, TV and EF values, the difference was found to be statistically significant (p<0.001). However, a significant difference between the pregnant and control group was found when examining PPV values (p<0.05).

Discussion and Conclusion: Pregnancy is considered predisposing for gallbladder pathologies, because of the development of the bile stasis depending on insufficient bile excretion and changed bile content especially due to increased PGN and E2 hormone levels in the late period of pregnancy.

When the mean values obtained from the 3^{rd} trimester pregnant women and the mean values of the control group were compared, the increase in FV and PPV and the decrease in EF were at statistically significant levels (p<0.001). These findings

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are expected results due to increases in PGN and E2 serum levels in the last trimester of pregnancy. In this study, there was a significant difference in PPV mean values of only nulliparous ones compared to the other groups (p<0.005), while no significant difference was found between the multiparity groups in terms of EF, FV, and PPV mean values.

When the pregnant group and control groups in the same parity were compared in terms of PPV mean values, the values of the pregnant group were significantly higher in the group with parity 1, compared to the values belonging to the control group. This result is an outcome of the negative effect of the first pregnancy forming bile stasis which is much higher than the following pregnancies.

It was concluded that the gallbladder dysfunction, which is held responsible for the emergence of gallbladder pathologies, the frequency of which increases in pregnancy, becomes more pronounced in the last trimester and in the first pregnancy the women are affected by hormonal changes more than following pregnancies.

Keywords: Ejection fraction; first pregnancy; gallbladder dysfunction; parity.

Epidemiological and clinical researches have shown that females are twice as likely to develop cholesterol gallstones at all ages as males[1]. Cholesterol stones account for >90% of gallstones, and they are comprised of >50% cholesterol[2]. The hormonal changes that occur during the pregnancy increase the risk of developing gallstones. In addition, estrogen therapy also induces lithogenic effects in postmenopausal women and men with prostatic carcinoma. These findings highlight the importance of female sex hormones on gallstone pathogenesis[3,4]. The effects of placental steroid hormones such as increased estradiol (E2) and progesterone (PGN), temporarily impair the biliary lipid metabolism and gallbladder function in healthy pregnant women[5]. Gallbladder bile concentrations of biliary cholesterol starts rising from the first to the third trimester of pregnancy, along with a progressive increase in the occurrence of biliary sludge and gallstones. Due to those changes, the incidence of pathologies of the gallbladder like sludge and gallstones are increasing. In a study, gallstone and biliary sludge development during pregnancy were detected in 6.3% and 10.9% of the cases, respectively[6]. Another study has shown that the incidences of biliary sludge and gallstones were 5.1% by the second trimester, 7.9% by the third trimester, and 10.2% by the 4 to 6 weeks postpartum[7].

According to the general acceptance, parity and duration of the fertility period increase the incidence of gallstones, and the frequency and number of pregnancies are significant risk factors for gallstone formation[6-8].

Ultrasound is a widely used method of imaging, and has the advantage of being safe during pregnancy. It is generally considered as the first line of gallbladder disease assessment. Ultrasound can reliably assess gallstones in >95% of cases. It can also be used to evaluate the fasting and postprandial volumes in its function. The study aimed to reveal whether there was any difference in motility marker values such as Fasting Volume (FV), Postprandial Volume (PPV), and Ejection Fraction (EF) between trimesters with the effect of changing steroid hormones. Thus, we aimed to determine the relationship between trimesters and parity with gallbladder dysmotility which is one of the factors held responsible for the pathogenesis of gallbladder pathologies.

Materials and Methods

The patient group consists of 50 pregnant women who applied to the gynaecology and obstetrics clinic at our hospital. Approval was obtained from the hospital's Institutional Board for the study. Informed consents are obtained from patients who participated in the investigation. Those patients' ages were between 20 and 45 years. Patients who have comorbid diseases such as gallstones, chronic cholecystitis, dyspeptic complaint, diabetes mellitus, hypertension, cardiovascular disease, malignancy, or chronic kidney disease were excluded. 20 healthy non-pregnant women constituting the control group were included in the study. Consent was obtained by explaining the purpose and application of the study to all patients. The age and parity of the cases were included in the study. The trimesters of the pregnancies were also recorded for the pregnant group.

After 8 hours of fasting on the day of the examination, gallbladder volumes of the patients were measured in the lateral decubitus position using a 3.5 MHz convex probe with the Hitachi EUB 6000 model ultrasonography. The volume measurement was made with ultrasound images which were obtained in axial and sagittal planes and calculated with the elliptical formula [Volume(mm^3): Craniocaudal axis(mm)xAnteroposterior axis(mm)xTransverse axis(mm) x0.532] (Fig. 1a). The patients were then fed with 80 grams of chocolate. After waiting for 45 minutes, gallbladder postprandial volume measurements were obtained (Fig. 1b). The gallbladder ejection fractions were calculated using the obtained fasting and postprandial volume values (EF: [FV-PPV]×100/[FV])[6].

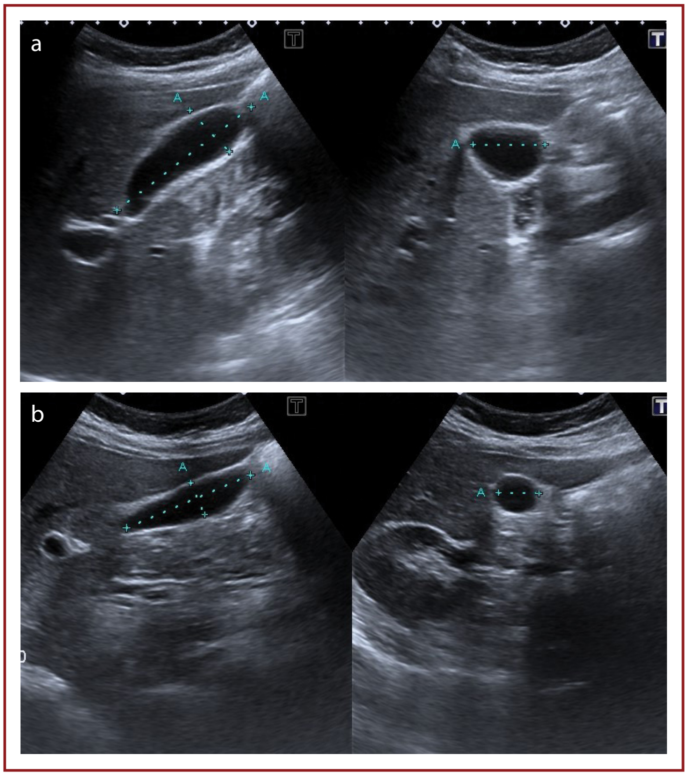

Figure 1a, b. Fasting volume **(a)** and postprandial volume **(b)** measurements were shown in the gallbladder ultrasound images of a 28-year-old pregnant in the axial and sagittal planes.

Results

The mean age of the pregnant group was 26.74±4.86 and the mean age of the individuals in the control group was 29.25±4.62. Parity rates of the pregnant group were examined, there were 23 (46%) with 1 parity, 11 (22%) with 2 parities, and 16 (33%) with 3 parities; in the control group the findings were as follows: 6 women (30%) with 1 parity , those with 2 parities were 9 (45%) and those with 3 parities were 5 (25%). In the results obtained by performing a One-way Analysis of Variance (ANOVA) from the pregnant group, there was found to be a significant difference between the trimesters. When Bonferroni test was performed to examine the difference between the trimesters, there was no significant difference between the 1st and 2nd trimester in terms of PV ($p>0.05$), and the difference between the 1st and 3rd trimesters and the 2nd and 3rd trimesters was significant due to the effect of increasing mean values. It was found to be at the level ($p<0.001$).

In the analysis made in terms of EF values, obtained from the pregnant group, the difference between the trimesters was found significant ($p<0.05$). In terms of EF mean values, significant difference was not found between 1st and 2nd the trimesters and 2nd and 3rd trimesters ($p>0.05$), and a significant difference between 1st and 3rd trimesters was found with the decrease of EF values in 3rd trimester ($p<0.05$) (Table 1). There was no statistically significant difference when the FV, PPV, and EF mean values of the 1st and 2nd trimester pregnancy and the FV, PPV, and EF mean values of the control group were compared. When comparing control group's FV, PPV, and EF mean values to pregnant women in the 3rd trimester FV, TV and EF mean values, the difference found was statistically significant ($p<0.001$). As the Mann-Whitney U test (Wilcoxon Rank Sum Test) tested FV and EF mean values of pregnant group and control groups according to parities, PPV averages of the same groups were not found between the pregnant group and control group values ($p>0.05$). However, a significant difference between the pregnant and control group was found when examining PPV values ($p<0.05$) (Table 2).

Discussion

Neural stimulation of emptying gallbladder is mediated by parasympathetic and sympathetic innervation; the former is responsible for the contractility of the gallbladder, and of the latter mediate smooth muscle relaxation in the gallbladder[9]. Pregnancy is considered predisposing for gallbladder pathologies, because of the development of the bile stasis depending on insufficient bile excretion and changed bile content especially due to increased PGN and E2 hormone levels in the late period[10,11].

Also, Maringhini et al.[12] showed that gallbladder hypomotility increased the formation of sludge in the late stages of pregnancy. In studies conducted on gallbladder motility in pregnant women, it was reported that FV and PPV values doubled, late in pregnancy[4,5,12].

In the study conducted by Kapıcıoğlu et al.[13], FV values were 75% higher in the last trimester pregnant women than the control group ($p<0.001$). In the same study, the PPV mean value was found to be significantly different from

Table 1. Mean values of FV, PPV and EF of the control group and pregnant group according to trimesters

	FV (MV±SD mm^3)	PPV (MV±SD mm^3)	EF (MV)
Pregnant group			
First trimester	22.11±9.6	7.86±3.10	60.73±6.5
Second trimester	23.05±9.33	11.31±5.65	49.30±22.7
Third trimester	41.44±12.75	23.69±6.67	41.30±15.1
Control group	22.73±7.09	8.52±3.26	60.20±15.36

FV: Fasting volume; PPV: Postprandial volume; EF: Ejection fraction; MV: Median value, SD: Standard deviation.

Table 2. FV, PPV and EF mean values of pregnant and control groups' according to same parities

	Parity 1			Parity 2			Parity 3		
	FV(MV± SD-mm^3)	PPV(MV± SD-mm^3)	EF	FV(MV± SD-mm^3)	PPV(MV± SD-mm^3)	EF	FV(MV± SD-mm^3)	PPV(MV± SD-mm^3)	EF
Pregnant group	25.68±8.11	13.20±7.02	48.00±20.54	22.72±11.64	10.11±6.13	55.63±18.74	33.56±17.82	16.24±10.20	51.12±21.49
Control group	21.55±4.86	7.41±2.37	64.83±10.38	23.64±7.84	7.30 ±3.08	66.77±13.53	22.50±9.05	12.04±1.95	42.80±10.61

FV: Fasting volume; PPV: Postprandial volume; EF: Ejection fraction; MV: Median value, SD: Standard deviation.

the control group in the last trimester pregnant women (p<0.02). This, results in insufficient excretion of the gallbladder, especially in the last trimester. In this study, average FV values reach approximately two times the 1st trimester values in the 3rd trimester and PPV average values reach three times the 1st trimester values. On the other hand, the average EF values decrease up to approximately 50% of the 1st trimester average values in the 3rd trimester. These results are similar to the ones obtained in other studies[4,13].

When the mean values obtained from the 3rd trimester pregnant women and the mean values of the control group were compared, the increase in FV and PPV and the decrease in EF were at statistically significant levels (p<0.001). These findings are expected results due to increases in PGN and E2 serum levels in the last trimester of pregnancy.

Increasing parity number and frequency is an important risk factor in gallbladder pathologies[11]. In this study, there was a significant difference in PPV mean values of only nulliparous ones compared to the other groups (p<0.005), while no significant difference was found between the multiparity groups in terms of EF, FV, and PPV mean values.

When the pregnant group and control groups in the same parity were compared in terms of PPV mean values, the values of the pregnant group were significantly higher in the group with parity 1, compared to the values belonging to the control group. This is a finding that supports the negative effects of bile stasis in the first pregnancy to be much more than following pregnancies.

The first drawback of the study is the low number of patients in both groups. The other is that in the postpartum period patients involved in the research have not been followed up.

Conclusion

This present study reveals that the increase in FV and PPV values and decrease in EF values which are leading to the formation of the lithogenic bile together were much higher in the 3rd trimester than in other trimesters. The study also shows that the first pregnancies were more affected by the increase in placental hormones compared to the multiparities. Bile stasis, which becomes more evident in the last trimester of pregnancy, may persist in the postpartum period. In fact, this effect becomes evident in recurrent pregnancies. It is advised for the future researchers to increase the number of the patients and follow-up the same patients' postpartum period. Thus, the long-term effects of bile stasis due to pregnancy can be better defined.

Ethics Committee Approval: Approval was obtained from the hospital's Institutional Board for the study.

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Conflict of Interest: None declared.

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References

1. Figueiredo JC, Haiman C, Porcel J, Buxbaum J, Stram D, Tambe N, et al. Sex and ethnic/racial-specific risk factors for gallbladder disease. BMC Gastroenterol 2017;17:153. [CrossRef]
2. Greenberger NJ, Paumgartner G. Diseases of the Gallbladder and Bile Ducts. In: Jameson J, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J, (editors). Harrison's Principles of Internal Medicine. New York, NY: McGraw-Hill; 2018. p. 339.
3. Kern F Jr, Everson GT, DeMark B, McKinley C, Showalter R, Erfling W, et al. Biliary lipids, bile acids, and gallbladder function in the human female. Effects of pregnancy and the ovulatory cycle. J Clin Invest 1981;68:1229–42. [CrossRef]
4. Braverman DZ, Johnson ML, Kern F Jr. Effects of pregnancy and contraceptive steroids on gallbladder function. N Engl J

Med 1980;302(7):362–4. [CrossRef]

5. Everson GT. Gastrointestinal motility in pregnancy. Gastroent Clin North America 1992;21:751–60.
6. Bolukbas FF, Bolukbas C, Horoz M, Ince AT, Uzunkoy A, Ozturk A, et al. Risk factors associated with gallstone and biliary sludge formation during pregnancy. J Gastroenterol Hepatol 2006;21:1150–3. [CrossRef]
7. Ko CW, Beresford SA, Schulte SJ, Matsumoto AM, Lee SP. Incidence, natural history, and risk factors for biliary sludge and stones during pregnancy. Hepatology 2005;41:359–65.
8. Lindseth G, Bird-Baker MY. Risk factors for cholelithiasis in pregnancy, Res Nurs Health 2004;27:382–91. [CrossRef]
9. Agarwal AK, Miglani S, Singla S, Garg U, Dudeja RK, Goel A. Ultrasonographic evaluation of gallbladder volume in diabetics. J Assoc Physicians India 2004;52:962–5.
10. Davis RA, Kern F Jr, Showalter R, Sutherland E, Sinensky M, Simon FR. Alterations of hepatic Na+,K+-atpase and bile flow by estrogen: effects on liver surface membrane lipid structure and function. Proc Natl Acad Sci U S A 1978; 75:4130–4.
11. Gangwar R, Dayal M, Dwivedi M, Ghosh UK. Gallbladder disease in pregnancy. J Obstet Gynaecol India 2011;61:57–61.
12. Maringhini A, Marcenò MP, Lanzarone F, Caltagirone M, Fusco G, Di Cuonzo G, et al. Sludge and stones in gallbladder after pregnancy. Prevalence and risk factors. J Hepatol 1987;5:218–23. [CrossRef]
13. Kapicioglu S, Gürbüz S, Danalioglu A, Sentürk O, Uslu M. Measurement of gallbladder volume with ultrasonography in pregnant women. Can J Gastroenterol 2000;14:403–5.