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Measurement of gallbladder volume by ultrasonography in pregnant women

Hamile kadınlarda safra kesesi volümleri

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ÖZET: *Sağlıklı hamile kadınlarda üçüncü trimester ve doğum sonrası ilk 10 gün içinde safra kesesinin ultrasonografik olarak açlık ve postprandial ölçümü açıklandı. Ölçümler 12 saat açlıktan sonra sabah saat 9'da yapıldı. Bazal seviyelerin değerlendirilmesinden sonra 60 dakika içinde 15 dakikalık aralıklarla ölçümler tekrarlandı. Bu işlemin çalışma grubundaki tüm olgulara standart sıvı test yemeği verilerek 1 saat boyunca tekrarlandı. Hamile olmayan kontrol grubunda ortalama bazal safra kesesi hacmi 22.2±4.2 ml olarak tesbit edildi. Hamile kadınlarda üçüncü trimesterde bazal hacim 37.89±10.53 ml olup hamile olmayan kadınlara oranla %70.52 daha yüksek bulundu (p<0.001). Postpartum periyodda ortalama bazal hacim 27.47±6.52 ml idi ve üçüncü trimestere göre azalmıştı (%37.93), (p<0.02). Bazal hacim kontrol grubuna oranla %23.63 oranında artış gösterdi. Test yemeği uygulandıktan sonra postprandial safra kesesi hacmi birkaç dakika içinde bazal değerlere oranla azaldı. Hacim seviyeleri üçüncü trimesterde %10.27'den %39.8'e (p<0.01), postpartum dönemde %14.93'ten %43.28'e (p<0.01), kontrol grubunda ise %19.26'dan %51.62'ye düştü (p<0.02). Postprandial ortalama safra kesesi hacmi üçüncü trimesterde ve postpartum evresinde kontrol grubuna oranla anlamlı farklılık gösterdi (p<0.02). Sonuç olarak hamileliğin üçüncü trimesterde safra kesesinin boşalması sağlıklı hamilelere göre azalmıştı. Bu sonuçlar sık hamileliğin safra taşları oluşturma riski görüşüne destek veren bulgulardır.*

Anahtar kelimeler: **Safra kesesi volümü, ultrasonografi, gebelik**

SUMMARY: *In this study, we investigated fasting and postprandial gallbladder volumes by ultrasonography in three similar healthy groups: a) a control group of non-pregnant women, b) pregnant women in their third trimester and c) women 10 or less days postpartum. Scans were performed at 9 am after a 12 hour fast. After basal measurements were taken, gallbladder volumes were rescanned at 15 minute intervals for 60 minutes. At the of this period, all the volunteers received a standard liquid test-meal and scans were performed again in one hour. The mean basal gallbladder and scans were performed again in one hour. The mean basal gallbladder volume was 22.2±4.2 ml in the non-pregnant (control) group. In the third trimester group, basal volume was 37.89±10.53 ml and 70.52% higher than the non-pregnant group (p<0.001). In the post-partum group, mean basal volume decreased to 27.47±6.52 ml (37.93%) compared to the third trimester group (p<0.02). This basal volume was 23.63% greated than control group (p<0.05). After administration of the test meal, reduced post-prandial gallbladder volumes during the first few minutes were compared to baseline. The percent age of decrease in volumes was reduced by 10.27%-39.8% (p<0.01) in the third trimester group, 14.93%-43.28% in the postportum group (p<0.01, 0.001) and 19.26%-51.62% in the control group (p<0.02, 0.05, 0.01, 0.001). Postprandial mean gallbladder volumes were significantly different in the control group as compared to the third trimester (p<0.002) and postpartum groups (p<0.02, 0.01). In conclusion, incomplete emptying of the gallbladder after eating in the third trimester of pregnancy could contribute to cholesterol-gallstone formation. Therefore, pregnancy may increase the risk of gallstones.*

Key words: **Gallbladder volume, ultrasonography, pregnancy**

IN women, the risk of developing gallstone is directly related to the number of pregnancies (1-5). Two pregnancies increase the risk of having gallstones twofold, and more than four pregnancies nearly quadruples the risk. Although the mechanisms are incompletely defined, significant alterations in biliary lipid metabolism and gallbladder function occur during pregnancy and may contribute to the increased risk (6-8).

During pregnancy the gallbladder is enlarged and empties incompletely. Thus, stasis of lithogenic bile within an enlarged, sluggish gallbladder occurs during late pregnancy and may contribute to the increased risk of gallstones. The results of a recent study suggest that the hypomotility of late pregnancy promotes gallbladder sludge formation (9,10).

If gallbladder emptying were prompt and complete, lithogenic bile and any cholesterol crystals that may have formed would pass uneventfully into the duodenum, interrupting the sequence leading to gallstones (11,12).

In this study we investigated fasting and postprandial gallbladder volumes in three similar groups of healthy, non-obese women a) controls in

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non-pregnant women, b) pregnant women in the third trimester, and c) postpartum women.

MATERIALS AND METHODS

Thirty healthy female volunteers with a mean age of 29.7±10.01 years all within±12% ideal body weight agreed to participate in the study. After the protocol and the test procedures had been explained, all of the subjects completed the protocol. We intended to evaluate each control subject, non-pregnant, pregnant and postpartum woman. Non-pregnant subjects (n:10) were fertile, pergnant women (n:10) were in their third trimester. Postpartum gallbladder volume was measured by the 10th postpartum day.

No subjects had any known illnesses and none were taking any medication. All volunteers had normal fasting serum levels of aspartate aminotransferase, alkaline phosphatase and bilirubin.

Gallbladder volumes and emptying were measured using ultrasonography (13). Using a 3.5 or 5-MHz tranduce, real time ultrasound scans were obtained with Siemens Sonoline SL 2 3.5 MHz. Subjects were scanned supine in the right anterior oblique position by a radiologist trained in ultrasonography. The gallbladder was visualized in the longitudinal and transverse planes, and measurements of maximum length, width, and height were taken in duplicate. The volume of the gallbladder was subsequently calculated using the ellipsoid method (volume=0.52 x length x width x heighth) (14).

Scans were performed at nine am after 12 hours of fasting. After basal measurement, the gallbladder volumes were rescanned at 15 minute intervals for 60 minutes. The end of this period, all the volunteers received a standard liquid test meal that contained 250 cal/250 ml, (protein 16.7%, fat 30%, carbonhydrate 53.3%) Ensure (Abbott) and scans were performed again in one hour. The results are expressed as mean ± SEM unless otherwise stated. For statistical analysis, the Wilcoxon mached paire signed-rank test or the Wilcoxon U test (15) was used where appropriate. The level of significance was set at $p<0.05$.

RESULTS

The mean basal gallbladder volume was 22.2±4.26 ml in the non-pregnant (control) group. In the third trimester group, basal volume was 37.89±10.53 ml and 70.52% higher than in the non-pregnant group ($p<0.001$). In Figure-1, the post-partum groups mean basal volume decreased to 27.47±6.52 ml (37.93%) compared to the third trimester groups ($p<0.02$). This basal volume was 23.63% greater than the control group ($p<0.05$). After administration of the test mean reduced post-prandial gallbladder volume during the first few minutes was compared to baseline. The percentage of volumes reduced 10.27%-39.8% ($p<0.01$) in the third trimester group, 14.93%-43.28% in the post-partum group ($p<0.01$, 0.001) and 19.26%-51.62% in the control group ($p<0.02$, 0.05, 0.01, 0.001). Post-prandial mean gallbladder volumes group in the third trimester group ($p<0.001$) and post-partum group ($p<0.02$-0.01) were significantly different from the control group.

DISCUSSION

This study showed that fasting and post-prandial gallbladder volumes were larger than non-pregnant values in third trimester pregnant women. During fasting, post-prandial volume were reduced to non-pregnant values but still greater than the control in the post-partum group. After the test-meal contraction gallbladder was reduced in a few minutes and compared to baseline.

The reducing gallbladder volumes ratio did not change. Fasting and postprandial volumes of non-pregnant, pregnant and post-partum subjects in

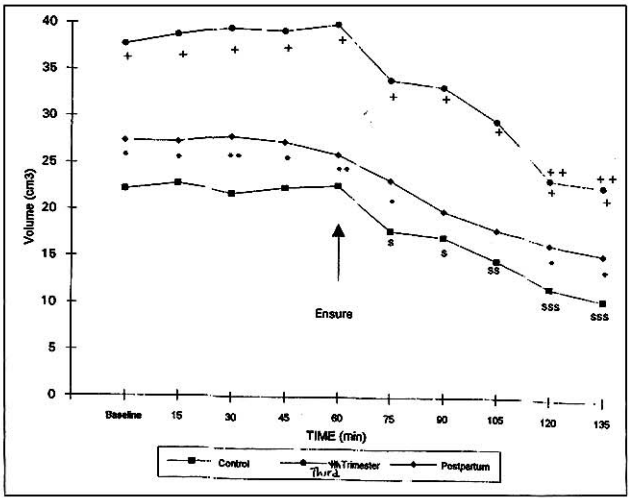

Figure 1. The Mean Values of Gallbladder Volume on Pregnant Women.

+ $p<0.001$ difference from control group in third trimester
++ $p<0.01$ difference from baseline in third trimester group
* $p<0.05$, ** $p<0.01$ difference from control group in post-partum group
s $p<0.05$, ss $p<0.01$, sss $p<0.001$ difference from baseline in control group

Table 1. The mean values of gallbladder volume on pregnant women

Groups	*The Mean Volume in Different Time (X±SEM)* (min)										
	Baseline	15	30	45	60	Ens	75	90	105	120	135
Control	22.2±4.2	22.8±3.4	21.8±3.4	22.4±4.2	22.7±3.8		17.9±3.6	17.2±4.4	14.7±4.4	11.9±3.5	10.7±3.2
Third Trimester	37.8±10.5	38.8±11.5	39.5±12	39.2±12.5	39.9±12.9		34.0±10.2	33.2±11.1	29.6±8.6	23.5±7.3	22.8±7.1
Pospartum	27.4±6.5	27.9±5.7	27.3±5.2	27.3±5.2	26.0±5.5		23.3±5.5	20.0±4	18.0±4.1	16.6±4.3	15.5±4.2
p value between third trimester	<0.001	<0.001	<0.001	<0.001	<0.001		<0.001	<0.001	<0.001	<0.001	<0.001
Differ, between third trimester	70.52	69.79	80.97	74.88	75.79		89.52	92.91	101.50	97.15	96.15
p value from baseline in third trimester							NS	NS	NS	<0.01	<0.01
Differ, from baseline in third trimester							10.27	12.38	21.83	37.82	39.80
p value between potpartum and control	<0.05	<0.05	<0.01	<0.02	<0.01		<0.02	NS	NS	<0.02	<0.02
Differen. from baseline in postpartum (%)							14.93	26.87	34.44	39.39	43.28
Differen. between third trimester and potpartum (%)	37.93	41.87	41.64	43.94	53.38		45.49	65.26	64.46	41.50	40.08
p value between baselineand control							<0.05	<0.02	<0.01	<0.001	<0.001
differ from baselinein control (%)							19.26	22.55	33.84	46.21	51.62

this study were nearly identical (6,7,16).

Because the hormonal changes of pregnancy are complex (17), it is not possible to identify with certainty the mediator, or mediators, of the alterations in gallbladder function.

The increase in volume and reduction in emptying are not due to alteration in meal-induced CCK release (18). Nevertheless, progesterone, a known inhibitory of smooth-muscle contraction (19-23), is a likely candidate. One study showed direct correlation of fasting and residual volume with serum progesterone concentrations up to 80 mg/ml (7). This is consistent with, but not proof of, progesterone mediation (7). As there was a highly significant direct correlation between serum progesterone and week of pregnancy, and the correlation of each of these variables with fasting and residual volume was identical, it cannot be concluded that progesterone caused the effects (7). The changes in gallbladder function could be due to other factors in pregnant women.

The volume of bile in the gallbladder after an overnight fast is the result of several variables, including the amount of bile secreted, its distribution between the gallbladder and intestinal tract, and the concentrating ability of the gallbladder (24).

During fasting, the movement of bile between the gallbladder and the small intestine is determined by the degree of resistance provided by intravesicular pressure to the pressure of the sphincter of Oddi, intraduodenal pressure, or both. Since the serum concentration of progesterone, a smooth-muscle relaxant, increases during pregnancy, decreased tone or increased receptive relaxation of the gallbladder may contribute to its enlargement. It is interesting, however, that eventhough the serum progesterone concentration is twice as great in the third trimester as in the second, the gallbladder seemed to behave similarly in both trimesters (6).

Increased gallbladder volume during fasting could be due to decreased water absorption by the gallbladder mucosa. The large amount of water normally absorbed from the gallbladder produces an eight to ten fold increase in the concentration of the organic components of bile (25). Water absorp-

tion is dependent on active absorption of sodium, which is mediated by the sodium pump in the gallbladder epithelium (26). The activity of the sodium pump, believed to be sodium-potassium ATPase (ATP-phosphohydralase, EC 3.6.1.3), may be decreased by estrogens, which are present in large concentrations in the serum in late pregnancy. Sodium-potassium-ATPase activity is reduced in the livers of pregnant hamsters (27), and in the guinea pigs gallbladder (28) in vitro it is inhibited by 17 ß-estrodiol (29). Active water secretion by the gallbladder mucosa has not been observed, except after the administration of vasoactive intestinal peptide in pharmacologic amounts (30).

Gallbladder contraction is mediated via the gastrointestinal hormones cholecystokinin (CCK) and motilin. Cholecystokinin is the major hormone that mediates postprandial gallbladder contraction (31). Recent studies using specific CCK receptor antagonists have provided conflicting information on the role of CCK in maintenance of the "resting tone" of the gallbladder (32,33). It seems likely that the large volume of bile in the gallbladder mucosa and diminished tone of the gallbladder muscle are probably caused by the high serum concentrations of estrogens and progesterone, respectively (6).

Progesteron impairs the gallbladder response to exogenously administered CCK in animals (23). High levels of progesterone or estrogen or both could reduce the release of cholecystokinin from the intestinal mucosa, but no relevant informations is available (6). As part of a larger study where gallbladder contraction was stimulated intraduodenal infusion of an amino acid mixture it was found that the effects of pregnancy on gallbladder emptying were identical to those described; thus, delayed gastric emptying was not a cause of dimished gallbladder contraction (6).

The secretion of CCK in pregnant and non-pregnant woman was measured. Neither contraction of the gallbladder nor CCK secretion after a liquid mixed meal differed significantly between the pregnant women group and the control group (18). These findings agree with earlier studies using dye dilution techniques (34), but contradict those obtained in studies of pregnant animals (23,35). Therefore, these results suggest that the mechanism of increased gallbladder volume in pregnant women could be explained by high levels of progesteron or estrogen, or both or the reduction in the release of CCK from intestinal mucosa (6).

In conclusion, incomplete emptying of the gallbladder after eating in third trimester of pregnancy could contribute to cholestrol-gallstone formation and pregnancy may thus increase the risk of gallstones.

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