Pregnancy, Parity and Maternal Age - Predictive Factors for Occurrence of Billiary Pathology (Gallstones and Sludge)?

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Abstract

Background and aims. *Because biliary disorders during pregnancy are a matter of controversy, we studied a variety of factors considered important in the occurrence of gallstones and biliary sludge during this specific period of a woman's life.* ***Methods.*** *In a prospective cohort (Regional University Hospital - Constanța), 176 patients were included in 3 groups: pregnant (divided per trimester), puerperal and matching non-pregnant women (control). Each patient was assessed by anamnesis as well as by fasting and postprandial ultrasound examination of the gallbladder. Results were statistically interpreted.* ***Results.*** *The prevalence for biliary sludge and gallstones was 16.67% and 8.33%, respectively, in the control group; 33.85% and 9.23%, respectively, in the pregnant group and 9.09% and 9.09%, respectively, in the puerperal group.* ***Conclusions.*** *Pregnancy is not associated with a significantly statistic higher prevalence of the cholelithiasis than the non-pregnant status. The prevalence of the biliary sludge, instead, is significantly increased during pregnancy if compared to the non-pregnant status ($p<0.05$). Parity degree is not associated with the prevalence of either cholelithiasis or biliary sludge.*

Keywords: *gallbladder, pregnancy, gallstones, billiary sludge*

Introduction

The occurrence of biliary pathology during pregnancy can be explained not only by the modified hormonal status but also by a number of morphological and functional disorders that take place at the gallbladder's level, disorders that can induce sludge and stones formation[(1)].

There is, still, a lot of controversy in the medical literature related to pregnancy involvement in sludge and gallstones' occurrence[(2)].

Study Design

Our working hypothesis was that gallbladder disturbances (stones or sludge) occur more frequently during pregnancy than in the non-pregnant status.

The study, prospective cohort type, included 176 patients admitted in the I[st] and III[rd] Departments of Obstetrics and Gynecology and II[nd] Medical Department of the Regional University Hospital - Constanța.

The patients were divided into three groups: pregnant - 130 patients, puerperal (1 to 30 days after a delivery, at least 28 weeks of gestation) - 22 patients and control (24 patients): non-pregnant women, with the same age as the pregnant and puerperal patients, hospitalized for renal colic (after colic's remission), connective tissue disorders (SLE, rheumatoid arthritis, and scleroderma), hematological disorders (thrombocytopenic purpura, anemia), respiratory disorders (acute and chronic bronchitis, pneumonias) and chronic hepatitis.

The rejection criteria were: hiperemesis gravidarum, gallbladder or pancreatic disorders (acute pancreatitis, biliary colic, acute cholecystitis).

A follow-up chart was obtained for each patient, including age, gestational age or number of postpartum days, number of pregnancies and number of births as well as presence of biliary sludge or gallstones.

Ultrasound examination was performed in recumbent position, left lateral and orthostatic position, through right oblique recurrent subcostal views, sagital views under the right costal edge and through intercostals views. The ultrasound measurements were performed by the same physician to all the patients, on the same machine.

Patients were included after having given their written consent. The study's objectives and methodology were approved by the Ethical Comity for Research of the University of Constanța.

Statistic evaluation

Before starting the study, the size of the groups was statistically determined in order to obtain results with a >95% confidence and 5% maximal admitted error. The preemptive analysis resulted in 22 individuals necessary for unitary treated (not subdivided) groups (control and puerperal) and 118 individuals for the study group (pregnant), were a subdivision per trimesters was performed.

The comparison between groups was performed using the "MS Excel 2003©" and "Matematica 3©" programmes. We used the "t" - Student test, the "$\chi 2$" test and „ANOVA" Analysis of Variance. A level of 95% was considered significant.

Results and discussions

The pregnancy's influence on gallbladder pathology represents the theme of a number of controversial studies in the medical literature.

Some authors are in favor of the pregnancy-induced risk of gallstones' occurrence[3-17]. They report a 3-45% prevalence of biliary disorders (biliary lithiasis and biliary sludge) during pregnancy[16,18,19]. In some of these studies the prevalence of biliary disorders is higher in multipara[18], in the third trimester and in older pregnant women[19].

Contradictory (fewer) results express no pregnancy-induced risk for gallstones[20] or even no biliary stones developed during pregnancy[21] as well as no influence of parity, maternal age at the first pregnancy or the menarche age[22].

The prevalence for biliary sludge and lithiasis according to each group in our study is revealed in Table 1.

The prevalence of biliary lithiasis in our control group is smaller than the one reported nationally, in 1995 (16.9%), while the one of biliary sludge is similar to the national one[3]. This difference in biliary lithiasis' prevalence may be explained by our specific analyzed population: women with ages up to 44 years old, situated in a restricted geographical area: Dobrogea.

The prevalence of biliary lithiasis and biliary sludge for the pregnant group in our study is within the ranges cited by others. However, the peculiarity of our results consists in the reduced prevalence of gallstones compared to that of biliary sludge during pregnancy. In our patients, pregnancy was not statistic significantly associated with biliary lithiasis but it was with biliary sludge.

We found that the patients with gallstones have a higher medium age than the ones without stones (Table 2). This is consistent with the medical literature which considers age as a risk factor for gallstones' occurrence[5,7]. Among women with biliary lithiasis the medium age was the youngest in the pregnant group and the highest in the control group; the difference was statistically significant ($p<0.05$) (Figure 1). Patients' age was also younger in the pregnant group with biliary sludge than in the control group. Our results are in favor of the concept that that the younger the maternal age the higher the risk of biliary lithiasis.

We found no gallstones during the first trimester of pregnancy; the prevalence increasing with the trimester, but without statistical significance. The prevalence of biliary sludge significantly ($p<0.05$) increased with each trimester of pregnancy (Table 3, Figure 2).

In our study there was no statistical difference between the medium parity of the control, puerperal

Table 1 Prevalence of biliary sludge and biliary lithiasis in the studied groups

	Sludge (%)	Biliary lithiasis (%)
Control	17.39	8.69
Puerperal	9.09*/**	9.09
Pregnant	33.85	9.23

** = p<0.05 between the puerperal and the control group*
*** = p<0.05 between the puerperal and the pregnant group*

and pregnant subgroups with biliary stones or sludge and the one of the equivalent subgroups but without stones or sludge (Table 4). The same results were obtained when comparing the subgroups with biliary stones or biliary sludge, respectively, with the corresponding ones without any biliary pathology: neither biliary stones nor sludge (Table 4). This is in contradiction with other authors, in favor of the parity as a risk factor in this pathology[18].

Our study found a 18.18% - prevalence of biliary pathology in the post partum. This is smaller than reported by others - 31.4% in the immediate puerperal period (1-6 days) or at 1 year[7]. In the same way, the prevalence of puerperal biliary lithiasis is smaller in our group (9.09%) than reported by others in the immediate postpartum period (12.2%)[15]. A possible explanation could be related to our detection of the pathology in a larger (1-30 days) post partum period than only the immediate puerperium (1-6 days), so the stones dissolution could have taken place, as reported elsewhere[4-7,9-12,14-19,23,24].

The prevalence of biliary sludge found in our puerperal group is significantly smaller than the one of the pregnant ($p < 0.05$) or of the control group ($p < 0.05$). This observation suggests the role of pregnancy in the occurrence of biliary sludge and the

Table 2 Medium age of the studied subgroups according to the presence of biliary lithiasis, biliary sludge

Group	Control		Puerperal		Pregnant	
	+BL	- BL	+ BL	- BL	+ BL	- BL
Medium Age (Years)	36.50	32.68	29	28	26*	25
	+Sludge	-Sludge	+Sludge	-Sludge	+Sludge	-Sludge
Medium Age (Years)	36	32.32	27*	28.11	25.11	24.94

BL = biliary lithiasis
** = p<0.05 between the pregnant and the control group*

Figure 1. Medium age of the patients with biliary lithiasis according to group

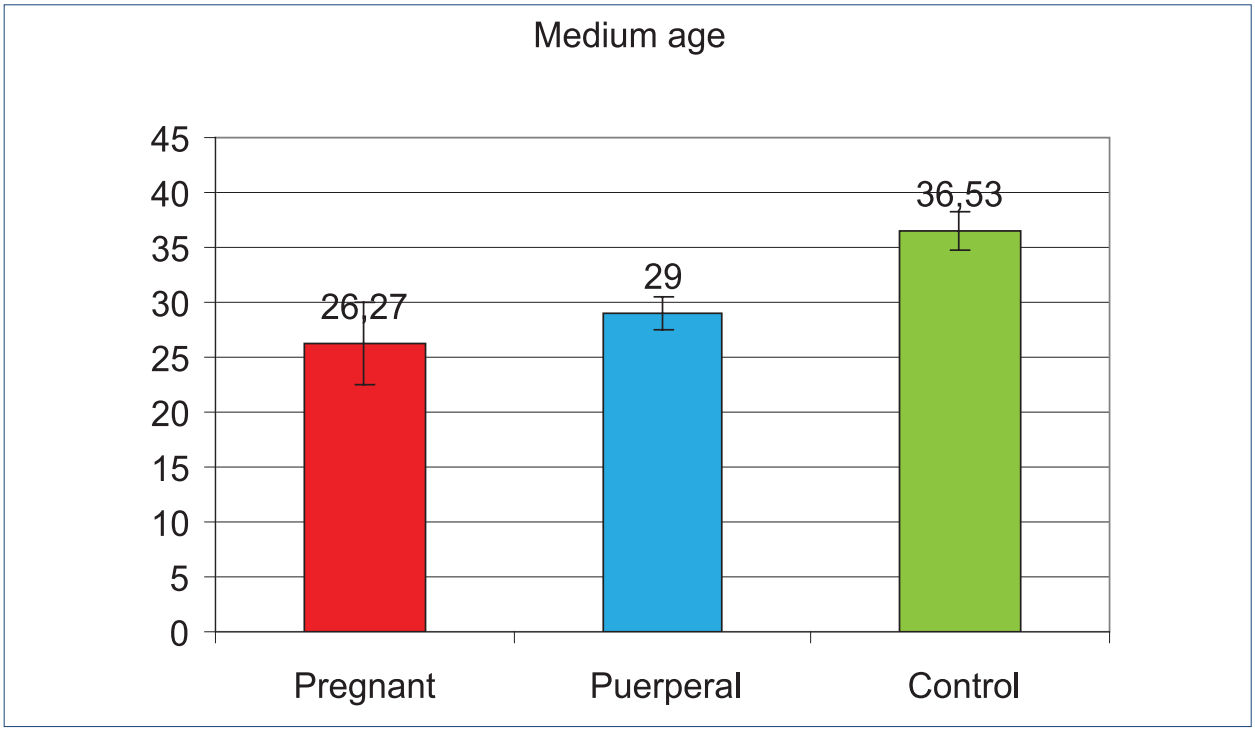

Table 3 Prevalence of biliary sludge and biliary lithiasis according to the trimester of pregnancy

	Trimester I	Trimester II	Trimester III
Sludge (%)	16	25.53*	42.28**
BL (%)	0	8.5	13.79

BL+ biliary lithiasis
** = p<0.05 between the I and II trimester*
*** = p<0.05 between the III and each of the I and II trimester*

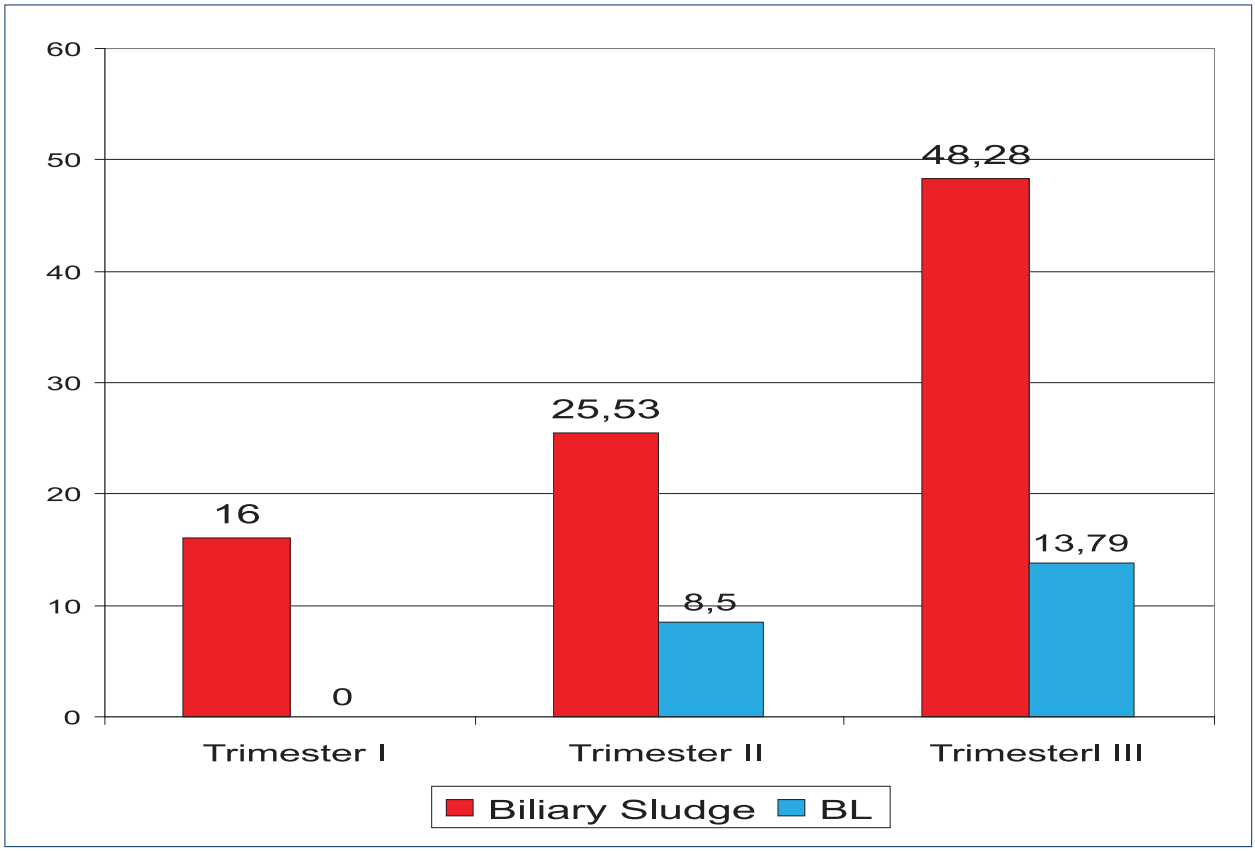

Figure 2. Pregnant patients with biliary lithiasis/ biliary sludge according to trimester

Table 4 Medium parity of the studied subgroups related to the presence/absence of biliary sludge and biliary lithiasis

	Control		Puerperal		Pregnant	
	+ Sludge	- Sludge	+ Sludge	- Sludge	+ Sludge	- Sludge
Medium Parity	0.75	1.26	1.00	1.65	1.40	1.55
	+ BL	- BL	+ BL	- BL	+ BL	- BL
Medium Parity	0.50	1.23	1	1.65	1.33	1.57

BL = biliary lithiasis

Table 5 Medium parity of the studied subgroups related to the presence of biliary sludge, biliary lithiasis or no biliary pathology

	Parity (medium number of pregnancies)			
	+ Sl	- p	+ BL	- p
Control	0.75	1.18	0.50	1.18
Puerperal	1.00	1.72	1	1.72
Puerperal	1.40	1.55	1.33	1.55

Sl = biliary sludge; BL = biliary lithiasis; p = biliary pathology

rapid reaction of the puerperal women to the physiological cholecystokinetic stimuli, with consecutive disappearance of the biliary sludge.

Conclusions

Our study suggests that:

1. Pregnancy is not associated with a higher prevalence of the cholelithiasis than the non-pregnant status. The prevalence of the biliary sludge instead, is significantly increased during pregnancy.

2. The age of biliary pathology occurrence (especially of lithiasis) is smaller in pregnant patients than in non-pregnant ones.

3. Parity degree is not related to the prevalence of cholelithiasis or biliary sludge.

4. The risk of biliary sludge increases throughout the pregnancy.

Age may play a role in the process.

Pregnancy may be a risk factor for biliary sludge, but not for cholelithiasis. ■

References

1. Abraham G.E., Odell W.D., Swerdloff R.S. et al. - Simultaneous radioimmunoassay of plasma FSH, LH, progesterone 17-hydroxyprogesterone, and estradiol-17b during the menstrual cycle, J Clin Endocrinol Metab, 34: 312, 1972.
2. Abraham G.E., Samojlik E., Kyle F.W. et al. - Radioimmuinoassay of plasma 16a-hydroxyprogesterone, Analytical Letters, 6: 675, 1974.
3. Acalovschi M., Grigorescu M. - Litiaza biliară, Addendum la Gherasim L, Medicină Internă, vol 3, Ed Medicală, 1999, pag 1-8.
4. Behar J. - Clinical aspects of gallbladder motor function and dysfunction, Curr Gastroenterol Rep, 1999, Apr, 1 (2): 91-4.
5. Basso L., Mc Collum P.T., Darling M.R., Tocchi A., Tanner W.A. - A study of cholelithiasis during pregnancy and its relationship with age, parity, menarche, breast-feeding, dysmenorrhea, oral contraception and a maternal history of cholelithiasis, Surg Gynecol Obstet, 1992, Jul, 175 (1): 41-6.
6. Kapicioglu J., Gurbuz S., Danalioglu A., Senturk O., Uslu M. - Measurement of gallbladder volume with ultrasonography in pregnant women, Can J Gastroenterol, 2000 May, 14 (5): 403-5.
7. Maringhini A., Marceno M.P., Lanzarone F., Caltagirone M., Fusco G., Cuonzo G., Cittadini E., Pagliaro L. - Sludge and stones in gallbladder after pregnancy. Prevalence and risk factors, J Hepatol, 1987, Oct, 5 (2): 218-223.
8. Mutsukura T. - Gallstone disease in pregnancy, Nippon Rinsho, 1993, Jul, 51 (7): 1870-1874.
9. Norgaard P., Kristiansen V.B., Rosenberg J. - Uncomplicated gallstone disease and pregnancy, Ugeskr Laeger, 2001, Apr, 16, 163 (16): 2236-9, review (abstract Medline).
10. Pazzi P., Gambrini S., Buldrini P., Gullini S. - Billiary sludge: the sluggish gallbladder, Dig Liver Dis, 2003, Jul, 35 suppl 3: S, 39-45 review.
11. Ryan J.P. - Effect of pregnancy on gallbladder contractility in the guinea pig, Gastroenterology, 1984, Sept, 87 (3): 674-678.
12. Tierney S., Qian Z., Yun B., Lipsatt A.P., Pitt A.H., Jostre S., Lillemoe K.D - Gender influences sphincter of Oddi response to cholecistokinin in the prairie dog, Am J Physiol, 1995, Oct, 269 (4 Pt 1) G 476-480.
13. Tsimoyiannis E.C., Antonion N.C., Tsaboulas C., Papanikolau N. - Cholelithiasis during pregnancy and lactation. Prospective Study, Eur J Surg, 1994, Nov, 160 (11): 627-631.
14. Valdivieso V., Severin C., Espinoza R., Orellana P., Otero C.G., Huenchullan C., Icarte G., Sepulveda R. - Study of volume and kinetics of gallbladder emptying in non-pregnant, pregnant and puerperal women, Rev Med Chil, 1996, Feb, 124 (2): 198-203 (abstract Medline).
15. Valdivieso V., Covarrubias C., Siegel F., Cruz F. - Preganacy and cholelithiasis: pathogenesis and natural course of gallstones diagnosed in early puerperium, Hepatology, 1993, Jan, 17 (1): 1-4.
16. Van Bodegraven A.A., Bohmer C.J., Manoliu R.A., Paalman E., Van der Klis A.H., Roex A.J., Kruishoop A.M., Deville W.L., Lourens J. - Gallbladder contents and fasting gallbladder volumes during and after pregnancy, Scand J Gastroenterol, 1998 Sep, 33 (9): 993-997.
17. Zhuang X., Li L. - A case control study of gallstone disease in female population in Taicang, Zhonghua Lui Xing Bing Xue Za Zhi, 2000, Feb, 21 (1): 44-7 (abstract Medline).
18. Gilat T., Konikoff F. - Pregnancy and the biliary tract, Can J Gastroenterol, 2000 Nov, 14 suppl D: 55D - 59D, review.
19. Hossain G.A., Islam S.M., Mahmood S., Chakrabarty R.K., Akhter N. - Gallstone in pregnancy, Mymensingh Med J, 2003, Jul, 12 (2): 112-16.
20. Scott L.D. - Gallstone disease and pancreatitis in pregnancy, Gastroenterol Clin North Am, 1992, Dec, 21 (4): 803-15.
21. Basso L., Mc Collum P.T., Darling M.R., Tocchi A., Tanner W.A. - A study of cholelithiasis during pregnancy and its relationship with age, parity, menarche, breast-feeding, dysmenorrhea, oral contraception and a maternal history of cholelithiasis, Surg Gynecol Obstet, 1992, Jul, 175 (1): 41-6.
22. Sali A., Oatsw J.N., Acton C.M., Elzarka A., Vitetta L. - Effect of pergnancy on gallstone formation, Aust N Z J Obstet Gynaecol, 1989, Nov, 29 (4): 386-389.
23. Alba-Quintanilla F., Posadas-Robledo F.J. - Ultrasonic evaluation of the gallbladder during pregnancy, Ginecol Obstet Mex, 1977 Feb, 65: 39-42.
24. Davis A., Katz V.L., Cox R. - Gallbladder disease in pregnancy, J Reprod Med, 1995 Nov, 40 (11): 759-62.