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PERINATAL OUTCOME IN PREGNANCY COMPLICATED BY OBSTETRIC CHOLESTASIS

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Abstract

Objective: *To determine the association of adverse perinatal outcome with obstetric cholestasis in females attending a tertiary care hospital*

Study Design: *Cohort study*

Study place and duration: *Study was conducted at Obstetrics & Gynecology Department, Combined Military Hospital, Bahawalpur during January to July 2025.*

Methodology: *Females were examined for obstetric cholestasis and divided in two groups, exposed and unexposed. All the females were then followed-up in OPD until delivery and were assessed for preeclampsia, small for gestational age, preterm delivery, cesarean section, respiratory distress syndrome and postpartum hemorrhage. All information was gathered by Proforma and SPSS version 25" was used for data analysis. Relative risk was calculated to measure the association of obstetric cholestasis with adverse perinatal outcome, with RR>1 as significant risk factor.*

Results: *The mean age of exposed group was 26.74 ± 3.45 years and unexposed group was 27.04 ± 3.47 years. The mean gestational age at the time of presentation was 33.20 ± 1.65 weeks in exposed females and 32.30 ± 1.97 weeks in unexposed females. Preeclampsia was observed in 6 (12%) vs. 0%, relative risk: 2.136 (95% CI: 1.722, 2.650). Small for gestational age in 24 (48%) vs. 12 (24%), relative risk: 1.641 (95% CI: 1.127, 2.389). Preterm delivery in 37 (74%) vs. 3 (6%), relative risk: 4.269 (95% CI: 2.618, 6.963). Cesarean section in 44 (88%) vs. 26 (52%), relative risk: 3.143 (95% CI: 1.503, 6.574). Respiratory distress syndrome in 41 (82%) vs. 8 (16%), relative risk: 4.741 (95% CI: 2.588, 8.688). Postpartum hemorrhage in 31 (62%) vs. 8 (16%), relative risk: 2.552 (95% CI: 1.701, 3.829).*

Conclusion: *Through this study findings, we may conclude that there is significant association of adverse perinatal outcomes with obstetric cholestasis.*

INTRODUCTION

The most prevalent liver condition during pregnancy, obstetric cholestasis, is linked to a higher risk of unfavourable obstetrical outcomes, such as unexpected foetal death. [1]Geographical distribution and ethnicity have an impact on the incidence and prevalence of obstetric cholestasis. The incidence of obstetric cholestasis ranges from 0.2% to 2% of pregnancies.[2, 3]It is more prevalent in northern Europe and South America.

According to research, between 0.2 and 0.3% of pregnancies in the United States result in obstetric cholestasis. A previous history of obstetric cholestasis, chronic liver illness, chronic hepatitis C, multifetal pregnancy, and advanced mother age are associated with an increased risk of obstetric cholestasis. Between 60-70% cases of obstetric cholestasis return in subsequent pregnancies.[4-6]

Although the exact origin of obstetric cholestasis is unknown, environmental, hormonal, and genetic variables are probably involved. Early detection is crucial since it increases the risk of stillbirth and premature delivery, which are linked to the newborn's mortality and morbidity. Consequently, prompt delivery, treatment, and early detection are essential. [7, 8]Obstetric cholestasis can cause serious problems for both the foetus and the pregnant woman. It can affect the pregnant woman's quality of life and overall health, cause psychiatric issues in the pregnant woman, and cause potentially fatal difficulties for the foetus.[9, 10]

Therefore, the rationale of this study was to determine the association of adverse perinatal outcome with obstetric cholestasis in pregnant females during second trimester. Obstetric cholestasis is a common complication observed among pregnant females and its incidence is rising day by day. It is also associated with perinatal complications. But due to lack of evidence in local population, females are not generally given much attention. Therefore, this study was planned to help the obstetricians to get the evidence and counsel and screen the pregnant females accordingly to prevent perinatal complications.

METHODOLOGY:

After approval from ethical review committee (ERC letter number:1516/TRG/2023, dated: 18thMay 2023), thisCohort studywas conducted at Obstetrics & Gynecology Department, Combined Military Hospital, Bahawalpur during period of 6 months (from January to July 2025).Sample size was estimated as 100 patients (500 in each of groups A and B) by using 5% significance level, 80% power of study and preterm delivery i.e. 33.8% in females exposed to obstetric cholestasis and 11.5% in females unexposed to obstetric cholestasis.[11]Females were enrolled who fulfilled following selection criteria by applying Non-probability, consecutive sampling technique.

Inclusion Criteria: Pregnant females, who fall in age range 18 -40 years, presenting at gestational age >16 weeks were enrolled in the study. Exposed females were those who presented with obstetric cholestasis. Obstetric cholestasis was diagnosed when female had pruritus and abnormal liver function tests (ALT & AST >40 IU). Exposed females were those who did not had obstetric cholestasis.

Exclusion Criteria: Pregnant females with cholelithiasis, acute or chronic viral hepatitis, primary biliary cirrhosis, multiple pregnancies, allergic skin diseases and acute fatty liver of pregnancy were not included in the study.

After taking informed consent, demographic details of females were noted.Females were examined for obstetric cholestasis and divided in two groups.All the females were then followed-up in OPD until delivery.During follow-up visits, females were examined for blood pressure and if blood pressures was ≥140/90 mmHg, then proteinuria was also assessed on dipstick and positive dipstick results were accounted and females were marked as having preeclampsia. Meanwhile, females underwent transabdominal ultrasound and fetal well-being was assessed. If fetal weight was <10th centile, then small for gestational age was noted. At the time of delivery, gestational age was noted and if delivery occurred before completion of 37 weeks of gestation, then preterm delivery was noted. Mode of delivery was also noted. All deliveries were conducted by researcher and if cesarean section was done, it was also conducted by researcher with single surgical team. At birth, neonates were also examined by consultant pediatrician and presence of respiratory distress syndrome was noted. All the females were shifted to post-delivery wards and were followed-up there for 24 hours and postpartum blood loss was observed. If

blood loss was more than 500 ml after vaginal delivery or more than 1000 ml after cesarean section, postpartum hemorrhage was labeled. All information was gathered by Proforma.

Data Analysis: Statistical software '"SPSS version 25" was used for data analysis. 2x2 table was developed in order to calculate relative risk to measure the association of obstetric cholestasis with adverse perinatal outcome, with RR>1 as significant risk factor. P-value ≤0.05 was considered as significant.

RESULTS:

In thisCohort study, we enrolled total 100 females and divided them in two groups based on their exposure to obstetric cholestasis. The mean age of exposed group was 26.74 ± 3.45 years and unexposed group was 27.04 ± 3.47 years. The mean BMI of exposed females was 24.02 ± 2.97 kg/m^2 and unexposed females had mean BMI of 23.66 ± 3.01 kg/m^2. In exposed group, there were 10 (20%) uneducated females while 22 (44%) had education up to matric or below, 14 (28%) were inter-pass and only 4 (8%) had education up to graduation level. In unexposed group, there were 11 (22%) uneducated females while 15 (30%) had education up to matric or below, 21 (42%) were inter-pass and only 3 (6%) had education up to graduation level. All the females were housewives. In both groups most of the females were coming from rural areas (69%). The mean gestational age at the time of presentation was 33.20 ± 1.65 weeks in exposed females and 32.30 ± 1.97 weeks in unexposed females. Mostly females were multigravida. Anemia was present in half of females in exposed group while in 40% females in unexposed group. History of cholestasis in previous pregnancy was positive in 40 (80%) females in exposed group while in 9 (18%) females in unexposed group. Table-I

The mean liver function test levels were significantly high in exposed females (ALT:116.44 ± 55.42 vs. 35.64 ± 37.22, ALT: 165.72 ± 139.28 vs. 117.32 ± 270.98, Bilirubin: 56.42 ± 69.83 vs. 28.72 ± 57.74, Alkaline phosphatase: 366.86 ± 122.66 vs. 203.36 ± 86.38, and GGT: 48.08 ± 10.82 vs. 31.08 ± 11.88, $p<0.05$, except for ALT) as compared to unexposed females. Table-II

Preeclampsia was observed in 6 (12%) females in exposed group while nil in unexploded group. The relative risk was 2.136 (95% CI: 1.722, 2.650), depicting that females exposed to obstetric cholestasis had two times higher chance of developing preeclampsia. Small for gestational age was observed in 24 (48%) females in exposed group while in 12 (24%) females in unexploded group. The relative risk was 1.641 (95% CI: 1.127, 2.389), depicting that females exposed to obstetric cholestasis had more than one times higher chance of having small for gestational age babies. Preterm delivery was observed in 37 (74%) females in exposed group while in 3 (6%) females in unexploded group. The relative risk was 4.269 (95% CI: 2.618, 6.963), depicting that females exposed to obstetric cholestasis had four times higher chance of developing preterm delivery.Cesarean section was observed in 44 (88%) females in exposed group while in 26 (52%) females in unexploded group. The relative risk was 3.143 (95% CI: 1.503, 6.574), depicting that females exposed to obstetric cholestasis had three times higher chance of developing cesarean section.Respiratory distress syndrome was observed in 41 (82%) neonates in exposed group while in 8 (16%) neonates in unexploded group. The relative risk was 4.741 (95% CI: 2.588, 8.688), depicting that females exposed to obstetric cholestasis had four times higher chance of developing respiratory distress syndrome.Postpartum hemorrhage was observed in 31 (62%) females in exposed group while in 8 (16%) females in unexploded group. The relative risk was 2.552 (95% CI: 1.701, 3.829), depicting that females exposed to obstetric cholestasis had more than two times higher chance of developing postpartum hemorrhage. Table-II

Table I: Basic demographics of females enrolled in exposed and unexposed group (n = 100)

	Group	
	Exposed	Unexposed
n	50	50
Age, in years	26.74 ± 3.45	27.04 ± 3.47
BMI, in kg/m^2	24.02 ± 2.97	23.66 ± 3.01
Education level		
Uneducated	10 (20%)	11 (22%)
Under matric	22 (44%)	15 (30%)
Intermediate	14 (28%)	21 (42%)
Graduate	4 (8%)	3 (6%)
Occupation		
Housewife	50 (100%)	50 (100%)
Residence		
Rural	34 (68%)	35 (70%)
Urban	16 (32%)	15 (30%)
Socioeconomic status		
Low	22 (44%)	20 (40%)
Middle	28 (56%)	30 (60%)
High	Nil	Nil
Gestational age at presentation, in weeks	33.20 ± 1.65	32.30 ± 1.97
Parity		
Primigravida	11 (22%)	17 (34%)
Primiparous	16 (32%)	9 (18%)
Multiparous	23 (46%)	24 (48%)
Anemia	25 (50%)	20 (40%)
Cholestasis in previous pregnancy	40 (80%)	9 (18%)
Huqqa cigarette	0 (0%)	3 (6%)

Table II: Laboratory findings of females in exposed and unexposed group (n = 100)

	Group		P-value
	Exposed	Unexposed	
n	50	50	
AST, IU/L	116.44 ± 55.42	35.64 ± 37.22	0.000
ALT, IU/L	165.72 ± 139.28	117.32 ± 270.98	0.264
Bilirubin, mg/dl	56.42 ± 69.83	28.72 ± 57.74	0.033
Alkaline phosphatase, IU/L	366.86 ± 122.66	203.36 ± 86.38	0.000
GGT, IU/L	48.08 ± 10.82	31.08 ± 11.88	0.000

Table III: Perinatal outcomes of females in exposed and unexposed group (n = 100)

	Group		p-value	RR (95% CI)
	Exposed	Unexposed		
n	50	50		
Preeclampsia	6 (12%)	0 (0%)	0.035	2.136 (1.722, 2.650)
Small for gestational age	24 (48%)	12 (24%)	0.012	1.641 (1.127, 2.389)

Preterm delivery	37 (74%)	3 (6%)	0.000	4.269 (2.618, 6.963)
Cesarean section	44 (88%)	26 (52%)	0.000	3.143 (1.503, 6.574)
Respiratory distress syndrome	41 (82%)	8 (16%)	0.000	4.741 (2.588, 8.688)
Postpartum hemorrhage	31 (62%)	8 (16%)	0.000	2.552 (1.701, 3.829)

DISCUSSION:

In has been observed that among pregnant females who were exposed to obstetric cholestasis had high risk of preeclampsia [6 (12%) vs. 0%, relative risk: 2.136 (95% CI: 1.722, 2.650)], small for gestational age [24 (48%) vs. 12 (24%), relative risk: 1.641 (95% CI: 1.127, 2.389)], preterm delivery [37 (74%) vs. 3 (6%), relative risk: 4.269 (95% CI: 2.618, 6.963)], cesarean section [44 (88%) vs. 26 (52%), relative risk: 3.143 (95% CI: 1.503, 6.574)], respiratory distress syndrome [41 (82%) vs. 8 (16%), relative risk: 4.741 (95% CI: 2.588, 8.688)], and postpartum hemorrhage [31 (62%) vs. 8 (16%), relative risk: 2.552 (95% CI: 1.701, 3.829)] as compared to females unexposed to obstetric cholestasis.

A similar prospective observational study was carried out by Parihar and Singh on 100 pregnant women. They found that obstetric cholestasis was highly significantly associated with small for gestational age (33.87% vs. 14.26%, p-value: 0.0003), postpartum haemorrhage (19.35% vs. 9.44%, p-value: 0.0122), and Caesarean section (58.06% vs. 35.45%, p-value: 0.0033). They came to the conclusion that obstetric cholestasis can have a negative impact on both the mother's and the fetus's pregnancy outcomes. The prognosis for maternal outcomes is favourable, but prompt and efficient intervention can enhance foetal results.[12]A comparable research by Medda et al. found that low birth weight infants (32.0%), preterm births (22.0%), and foetal discomfort (23%), among 100 pregnant women with obstetric cholestasis.[13]

Numerous studies have demonstrated that the number of tiny for gestational age babies born to women with obstetric cholestasis does not increase.[14, 15]The rate of caesarean sections (58.06%) is equal to the 62% of pregnancies delivered by caesarean section [Elective (32%) + Emergency (30%)] in a research by Medda et al. According to the same study, maternal outcomes included postpartum haemorrhage (10%) and dyslipidaemia (30%).[13]

According to some research, a history of obstetric cholestasis in the past might indicate a significantly elevated chance of developing obstetric cholestasis in the future.In our study, we observed that among exposed females, history of cholestasis in previous pregnancy was positive in 40 (80%) females while in 9 (18%) females in unexposed group.Interestingly, the incidence of obstetric cholestasis was reported by a Danish research conducted countrywide. Additionally, the study found that women who had first-trimester or recurrent obstetric cholestasis were more likely to have first-degree relatives who likewise had a greater chance of developing the condition. [16]All of these results point to the importance of genetic background and ethnicity in the development of obstetric cholestasis.[9]

In a retrospective analysis of 82 pregnant women with obstetric cholestasis, Mazhar et al. discovered that respiratory distress was present in 14.65% of cases, preterm labour in 3.65%, postpartum haemorrhage in 4.87%, and caesarean birth in 28.09% of cases.[17]These finding were not compatible with findings of our study, as in our study, we found significantly higher rates of complication among females with obstetric cholestasis.

In a different research, Sohail et al. found that around 57.2% of pregnant women with obstetric cholestasis gave birth via caesarean section. According to perinatal statistics, 17.1% of newborns had an aberrant CTG pattern, 17.1% had growth restriction, 25.8% had preterm birth, and 2.8% experienced intrauterine mortality.[18]

There is evidence linking elevated bile acids to the causes of unfavourable outcomes, including placental vascular spasm and foetal cardiac arrhythmia. These two hypothesised theories of foetal death in intrahepatic cholestasis of pregnancy are in line with this data.[19]Researchers recommend treating females having obstetric

cholestasis of pregnancy and singleton pregnancies based on their peak bile acid concentration because the studies are unable to provide additional mechanistic evidence to support these models without data on the timings of peak bile acid concentration and associated stillbirth gestation.[19]Regular monitoring of blood total bile acids (e.g., weekly) is necessary to review risk since bile acids can alter quickly as gestation progresses.[8, 20, 21]

CONCLUSION:

Through this study findings, we may conclude that there is significant association of adverse perinatal outcomes with obstetric cholestasis. Thus in future, for females exposed to obstetrics cholestasis, will be given special care and counseled to complete antenatal visit to prevent adverse perinatal outcomes.

CONFLICT OF INTEREST:

None.

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