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Original Research Article

A study on correlation of liver function test and serum bile acid with feto-maternal outcome in patients with intrahepatic cholestasis of pregnancy

Sonam Gupta[1]*, Juhi Srivastava[1], Modhusmita Chetia[1], P. C. Uniyal[2]

[1]Department of Obstetrics and Gynecology, Tirath Ram Shah Charitable Hospital, New Delhi, India
[2]Department of Pediatrics, Tirath Ram Shah Charitable Hospital, New Delhi, India

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***Correspondence:**
Dr. Sonam Gupta,
E-mail: drsonamgupta26@gmail.com

ABSTRACT

Background: Intrahepatic cholestasis of pregnancy (ICP) is the foremost liver disorder, presenting substantial risks and complications to maternal and fetal health. Characterized by pruritus and elevated bile acids and serum transaminases.
Methods: The study focuses on profiling 70 patients of ICP understanding the correlations between liver function tests with serum bile acid and evaluating the impact of ursodeoxycholic acid (UDCA) treatment and also focus on various maternal and fetal outcome.
Results: The study identified a predominance of primigravida (68.6%) of 26-30 years of age (47.1%), often needing hormonal support (34.3%), with a high incidence of abnormal CTG findings (28.6%) and fetal distress (17.1%) with maximum patient with moderate serum bile acid levels. IHCP diagnosis was commonly noted between 32-36.6 weeks GA (57.1%). The treatment with UDCA 300-TDS (in 72.9% patient) was providing relief to about 75% of participants within a week. Most deliveries occurred between 37-39 weeks (70%) GA, predominantly via LSCS (54.3%), NVD (35.7%) and assisted vaginal delivery (10%). PPH was seen in 4.3% patients. Fetal outcomes revealed 40% incidence of meconium-stained liquor and about 12% NICU admissions with no fetal mortality. Most participants (78.6%) had serum bile acid levels in the 10-40 µmol/L range.
Conclusions: Significant correlations were noted between SGOT and SGPT and with ALP and bile acid. In contrast, bilirubin showed no significant correlations. Higher UDCA dosages showed a dose-response relationship, implying their effectiveness in managing ICP.

Keywords: Intrahepatic cholestasis of pregnancy, SGOT, SGPT, Serum bile acid, Ursodeoxycholic acid

INTRODUCTION

Pregnancy induces various physiological alterations that influence maternal health. These changes can interact with existing health predispositions, leading to complications specific to pregnancy.[1] Conditions such as intrahepatic cholestasis of pregnancy (ICP), pre-eclampsia, HELLP syndrome, and acute fatty liver of pregnancy (AFLP) are among the notable liver-disorders specific to gestation, posing several consequences for both mother and child.[2]

Intrahepatic cholestasis of pregnancy stands out as a significant and the most common cholestatic liver disorder in pregnant women, occurring primarily in the third trimester of pregnancy.[2,3] First described in 1883 as "recurrent jaundice", ICP now is addressed a unique liver condition associated with pregnancy, often disappearing

after childbirth. It is characterized by generalized pruritus, typically intensified on the palms and soles and during nighttime, along with abnormal liver functions, in the absence of other liver diseases.[4]

The incidence of ICP exhibits notable variation worldwide and among different ethnic groups.[3,5] Studies indicate that its prevalence has fluctuated over time, ranging from 1 in 1000 to 1 in 10,000 pregnancies in the 1950s, increasing significantly by the 1970s, and then decreasing as awareness of the disorder grew.[5] It affects women across all maternal age groups and can manifest during first pregnancies as well as subsequent ones, with a tendency to recur in the latter. The condition is particularly prevalent among women with a family history of ICP.[6] It has been reported to occur more frequently in South Asia.[7] Epidemiological associations have been liked with pathophysiological mechanisms over the years to strengthen the understanding of ICP in different populations.[8,9]

A hallmark of ICP is the marked elevation in the serum bile acid level. Further, it's common to observe serum aminotransferases at levels exceeding twice the normal range, along with increased alkaline phosphatase (ALP) levels. However, these indicators are not exclusive to cholestasis. Additionally, total bilirubin concentrations seldom surpass 5 mg/dl in this condition.[1]

The underlying causes of intrahepatic cholestasis of pregnancy (ICP) remain elusive, involving a complex interplay of genetic, hormonal, and environmental elements.[10] It's hypothesized that genetic factors make some women more vulnerable to the condition, especially in cases where familial patterns or recurrence in subsequent pregnancies are observed.[11] Hormonal influences, particularly the impact of elevated estrogen levels, have been consistently noted in various situations such as multiple pregnancies, ovarian hyper-stimulation, and ICP's typical emergence in the late second trimester, coinciding with peak estrogen levels. This connection is further highlighted by the similar effects seen in women using high-estrogen contraceptive pills.[12] Environmental factors, including lower levels of selenium and vitamin D, have also been linked to ICP, particularly in geographical and seasonal contexts where these deficiencies are more prevalent. Overall, the etiology of ICP is multifaceted, involving a mix of genetic predisposition and sensitivity to external factors like hormone.[2,13]

ICP is associated with several maternal complications including increased risks of post-partum haemorrhage, operative delivery, severe pruritus with dyslipidemia and deranged coagulation profile, preterm rupture of membrane. Further, increased bile acids and other factors can lead to severe fetal complications, including sudden intrauterine death, preterm birth, meconium-stained amniotic fluid, and neonatal unit admission.[14,2] The immediate treatment upon diagnosing ICP focuses on reducing perinatal morbidity and alleviating maternal discomfort. Ursodeoxycholic acid (UDCA) is the preferred treatment, known to correlate with improved maternal symptoms and fetal outcomes.[15]

Overall, ICP is characterized by a multifactorial etiology and poses significant challenges in both diagnosis and management. ICP's clinical presentation, notably the absence of pruritus in numerous cases, accentuates the imperative need for a diagnostic approach rooted in precision.[16]

METHODS

This hospital-based prospective observational study was conducted in the Department of Obstetrics and Gynecology, Tirath Ram Shah Charitable Hospital, New Delhi from March 2023 to December 2023 after obtaining approval from Institutional Scientific and ethical board. A total 70 patients diagnosed with IHCP were enrolled after taking consent and fulfilling inclusion and exclusion criteria.

Inclusion criteria

All pregnant women (singleton/multiple gestation) diagnosed with Intrahepatic cholestasis of pregnancy were included.

Exclusion criteria

Pregnancy <24 weeks, dermatological lesion with pruritus, acute or chronic liver disease, infective hepatitis, any liver/gall bladder disorder before pregnancy were excluded.

The diagnosis was based on clinical symptoms of persistent pruritus without a skin rash, coupled with biochemical evidence of cholestasis of pregnancy, such as elevated serum transaminases (ALT >40, AST >40 U/L), and Serum Bile acid levels exceeding 10 micromole/L. All the data were entered into a preformed proforma, which included detailed history, General physical and systemic examination and obstetric examination. A comprehensive set of ANC investigations, including complete blood count, blood typing and Rh grouping, blood sugar levels, viral markers (HIV, HBsAg, Anti HCV), Hepatitis A antigen, hepatitis E antigen, VDRL, thyroid profile, liver function tests, kidney function tests, and ultrasound scans with or without color Doppler were performed. Fetal monitoring was done with non-stress tests (NST) and biophysical profile scores.

Patients were monitored with repeated LFT and Serum Bile acid tests. Ursodeoxycholic acid was administered in divided doses to patients based on the levels of LFT and Serum bile acid and follow-up done until delivery. Perinatal and maternal outcomes were analyzed based on LFT and Bile acid levels. Liver function test results were correlated with Bile acid levels.

We initiated our analysis with a thorough descriptive examination of the data. This involved summarizing the central tendencies and variability of LFT parameters and serum bile acid levels using appropriate measures such as means, medians, standard deviations, and interquartile ranges. Further, we analysed data by using software STATA developed by Statacorp wherein we employed Spearman's rank correlation coefficient for non-normally distributed data.

Maternal outcomes included

Onset and severity of symptoms as pruritus, medication and response to medication, gestational age of termination & mode of delivery, abnormal CTG, complications which include sleep disturbances, deranged coagulation profile, preterm labor, operative delivery and PPH, symptomatic relief of pruritus and liver function test determined in all women 2 weeks postpartum.

Fetal outcome included meconium-stained liquor, low birth weight, IUGR, prematurity, APGAR score at birth and after 5 min, NICU admission and perinatal death.

RESULTS

A comprehensive overview of the demographic and clinical characteristics of patients suggested a higher prevalence of IHCP among women in their late twenties to early thirties (47.1%) and specially Primigravida (68.6%). Pruritus was present in a substantial 92.9% of the participants, emphasizing its prevalence in ICP cases. However, a history of ICP in previous pregnancies (18.2%) and a family history of IHCP (4.3%) are less commonly reported in the study sample (Table 1).

Table 1: Frequency distribution of study participants by background characteristics.

Background characteristics		N	Percentage
Age groups (in years)	18-25	15	21.4
	26-30	33	47.1
	31-35	20	28.6
	>35	2	2.9
Parity	1	48	68.6
	2	19	27.1
	3	3	4.3
H/O OCP use	No	68	97.1
	Yes	2	2.9
Hormonal support	No	46	65.7
	Yes	24	34.3
Gestational age at diagnosis (weeks)	28-31.6	30	42.9
	32-36.6	40	57.1
	37-39.6	0	0
	>=40	0	0
Pruritus	No	5	7.1
	Yes	65	92.9
H/O IHCP in previous pregnancy	No	18	81.8
	Yes	4	18.2
Family h/o IHCP	No	67	95.7
	Yes	3	4.3
Total		70	

Maternal health conditions such as gestational diabetes mellitus (GDM) and hypertensive disorders of pregnancy may be associated with IHCP but not predominantly. GDM is present in 8.6% of the study participants, whereas hypertensive disorders are slightly more prevalent, affecting 11.4% of the participants. Looking at complications of pregnancy and labor, premature rupture of the membrane (PROM) was reported in 8.6% of cases. Abnormal cardiotocography (CTG) was observed in 28.6% of the participants. This higher percentage might reflect an increased risk of fetal distress or could be linked to other underlying conditions. Fetal distress itself is noted in 17.1% of the cases.

In terms of treatment, the use of ursodeoxycholic acid (UDCA) was predominant, with the 300-TDS dosage being the most common, administered to 72.9% of the participants with 74.29% experienced relief of symptoms within 1 week, 21.43% reported symptom relief between 1 and 2 weeks, and 4.29% experienced relief after more than 2 weeks (Figure 1).

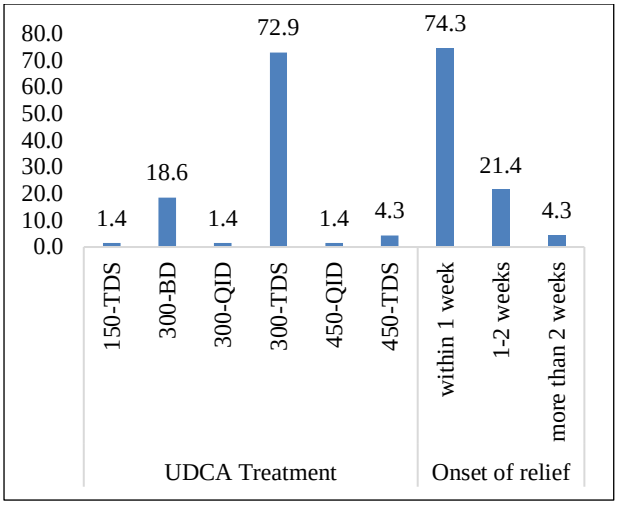

Figure 1: Percentage distribution of study participants by background characteristics-UDCA treatment.

Regarding delivery outcomes data showed that none of the study participants delivered extremely preterm (28-31.6 weeks, n=0) or post-term (>=40 weeks, n=0). When it comes to the mode of delivery, a significant majority of the study participants underwent lower segment caesarean section (LSCS), with 54.3% of deliveries and may be reflective of the complications noted in the study such as fetal distress or abnormal CTG. For postpartum haemorrhage, the vast majority of participants, 95.7%, did not experience this condition, while a small percentage, 4.3%, did (n=3) (Figure 2).

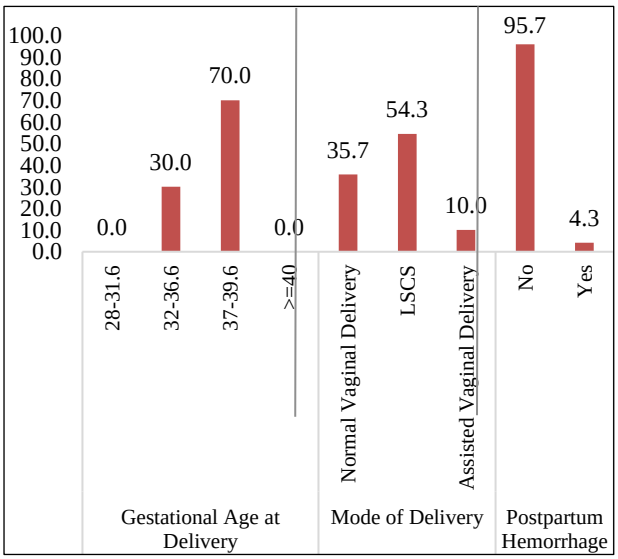

Figure 2: Percentage distribution of study participants by background characteristics-maternal outcomes.

Fetal outcomes showed that 12.9% of the newborns had an APGAR score of less than 7 at birth, however, this decreased to 7.1% by the 5-minute mark, suggesting an improvement in the initial minutes after birth. Birth weight was another factor monitored, with 5.7% of the newborns weighing less than 2.5 kilograms, which is considered low birth weight. The same percentage (5.7%) of the study's newborns experienced fetal growth restriction, a condition where a baby is smaller than expected for the number of weeks of pregnancy. Notably, 40% of the deliveries involved meconium-stained liquor, a sign that the baby might have experienced stress before birth. Neonatal Intensive Care Unit (NICU) admission was necessary for 11.4% of the newborns. No case of fetal death was reported among the study sample (Figure 3).

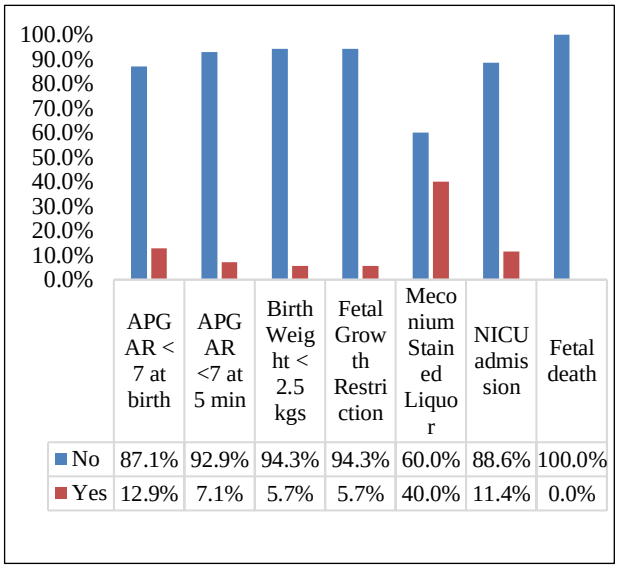

Figure 3: Percentage distribution of study participants by background characteristics-fetal outcomes.

Detailed breakdown of the liver function test results among the study participants, specifically focusing on serum bile acid, SGOT (serum glutamic-oxaloacetic transaminase), and SGPT (serum glutamic-pyruvic transaminase) levels (Table 2).

The mean values of various liver function tests and Total Bile Acid in relation to different maternal characteristics and pathophysiological markers of ICP showed Statistical significance, indicated by p values, with an asterisk denoting a p value less than 0.05, which is typically considered statistically significant (Table 3).

Mean values of various LFTs, presenting the data in relation to specific characteristics and treatment variable with an asterisk denoting a p value less than 0.05, which is typically considered statistically significant (Table 4).

The analysis of liver function tests in relation to maternal and fetal outcomes reveals several correlations and associations with ICP. Statistical significance is indicated by p values, with an asterisk denoting a p value less than 0.05, which is typically considered statistically significant (Table 5).

Table 2: Descriptive statistics-liver function test.

		N	Percent	Min.	Max.	Mean	Std. Dev
Serum bile acid	<10 µmoI/l	6	8.6	7.0	9.0	8.5	0.8
	10-40 µmoI/l	55	78.6	10.0	39.0	18.6	6.2
	40-100 µmoI/l	9	12.9	41.0	85.0	53.7	15.7
	>100 µmoI/l	0	0	-	-	-	-
	Total	70	-	7.0	85.0	22.2	14.6
SGOT	40-100 IU/l	57	81.4	55.0	99.0	80.6	9.9
	100-200 IU/l	11	15.7	105.0	173.0	142.8	23.6
	>200 IU/l	2	2.9	289.0	310.0	299.5	14.8
	Total	70	-	55.0	310.0	96.6	43.7
SGPT	40-100 IU/l	47	67.1	59.0	100.0	83.2	9.6
	100-200 IU/l	21	30.0	101.0	190.0	133.7	31.8
	>200 IU/l	2	2.9	280.0	304.0	292.0	17.0
	Total	70	-	59.0	304.0	104.3	44.1

Table 3: Mean values of liver function test by mother's profile and obstetric characteristics.

Background characteristics			**Mean values**				
			Total bilirubin	**Total SGOT**	**Total SGPT**	**Total ALP**	**Total bile acid**
Mother's profile	P value		0.667	0.817	0.828	0.412	0.643
	Age group (years)	18-25	0.640	94.5	103.1	142.4	21.4
		26-30	0.606	97.2	101.6	124.4	22.1
		31-35	0.605	100.1	111.3	139.6	24.3
		>35	0.650	69.0	87.5	117.5	10.5
	P value		0.064	0.768	0.937	0.506	0.718
	Parity	1	0.633	99.0	105.4	136.1	23.1
		2	0.574	92.5	101.2	122.7	20.6
		3	0.567	84.7	106.3	134.3	18.0
	P value		0.616	0.427	0.558	0.836	0.714
	OCP use	No	0.613	95.9	103.8	132.2	22.1
		Yes	0.650	121.0	122.5	138.5	26.0
	P value		0.378	0.211	0.225	0.291	0.087
	Hormonal support	No	0.607	91.9	99.7	128.5	20.1
		Yes	0.629	105.7	113.2	139.8	26.4
Maternal health conditions	P value		0.633	0.011*	0.009*	0.012*	0.011*
	Gestational diabetes mellitus	No	0.613	92.6	100.2	128.6	20.9
		Yes	0.633	139.3	148.5	173.2	36.5
	P value		0.494	0.000*	0.001*	0.028*	0.001*
	Hypertensive disorder of pregnancy	No	0.611	90.2	98.3	128.5	20.2
		Yes	0.638	146.5	151.1	162.8	37.9
Pregnancy/ labor complications	P value		0.437	0.296	0.389	0.145	0.380
	PPROM/PROM	No	0.617	98.3	105.7	134.6	22.7
		Yes	0.583	78.7	89.3	108.5	17.2
	P value		0.282	0.106	0.067	0.300	0.180
	Abnormal CTG	No	0.606	91.3	98.2	129.1	20.7
		Yes	0.635	110.0	119.6	140.7	26.0
	P value		0.478	0.008*	0.011*	0.019*	0.036*
	Fetal distress	No	0.610	90.4	98.2	127.1	20.6
		Yes	0.633	126.8	133.6	158.0	30.3
Total			0.61	96.62	104.30	132.38	22.22

*Indicates statistical significance at p<0.005.

Table 4: Mean values of liver function tests by IHCP characteristics and treatment variables.

Background characteristics			Mean values				
			Total bilirubin	Total SGOT	Total SGPT	Total ALP	Total bile acid
IHCP Diagnosis	P value		0.946	0.996	0.940	0.971	0.637
	Gestational age at diagnosis (weeks)	24-31.6	0.613	96.6	103.8	132.6	21.3
		32-36.6	0.615	96.7	104.7	132.2	23.0
	P value		0.133	0.613	0.799	0.614	0.429
	Pruritus	No	0.680	87.0	99.4	123.2	17.2
		Yes	0.609	97.4	104.7	133.1	22.6
	P value		0.003*	0.924	0.716	0.789	0.961
	IHCP in previous pregnancy	No	0.544	91.1	100.6	123.4	20.2
		Yes	0.700	92.8	107.5	128.5	20.5
	P value		0.805	0.956	0.780	0.747	0.832
	Family h/o IHCP	No	0.615	96.6	104.0	132.7	22.1
		Yes	0.600	98.0	111.3	124.7	24.0
Treatment	P value		0.999	0.000*	0.000*	0.000*	0.000*
	Treatment with ursodeoxycholic acid	450-QID	0.600	289.0	304.0	310.0	76.0
		450-TDS	0.600	217.7	217.7	168.3	60.3
		300-QID	0.600	158.0	166.0	167.0	41.0
		300-TDS	0.618	90.6	98.5	131.6	20.6
		300-BD	0.608	75.8	82.9	115.0	15.2
		150-TDS	0.600	60.0	78.0	80.0	9.0
	P value		0.089	0.508	0.528	0.404	0.467
	Onset of relief	1 week	0.613	100.1	107.2	135.0	23.2
		2 weeks	0.640	88.3	99.2	129.2	20.8
		3 weeks	0.500	78.7	80.3	102.3	13.0
Total			0.61	96.62	104.30	132.38	22.22

*Indicates statistical significance at p<0.005.

Table 5: Mean values of liver function tests by select fetal and maternal outcomes.

Background characteristics			Mean values Total bilirubin	Total SGOT	Total SGPT	Total ALP	Total bile acid
Maternal outcomes	P value		0.306	0.084	0.149	0.191	0.125
	Gestational age - delivery (weeks)	32-36.6	0.633	110.4	116.0	142.4	26.3
		37-39.6	0.606	90.7	99.3	128.1	20.5
	P value		0.394	0.059	0.042*	0.004*	0.037*
	Mode of delivery	Vaginal	0.592	85.6	91.0	116.2	18.0
		LSCS	0.626	107.7	116.3	147.1	26.3
		Assisted	0.629	76.0	86.6	110.6	15.4
	P value		0.741	0.648	0.541	0.719	0.832
	Postpartum hemorrhage	No	0.613	96.1	103.6	132.0	22.1
		Yes	0.633	108.0	119.7	141.0	24.0
Fetal outcomes	P value		0.342	0.000*	0.000*	0.017*	0.001*
	APGAR <7 at birth	No	0.610	89.0	97.1	127.9	20.0
		Yes	0.644	148.0	153.0	163.1	37.1
	P value		0.897	0.000*	0.000*	0.157	0.001*
	APGAR <7 at 5 minutes	No	0.614	91.3	99.3	130.4	20.7
		Yes	0.620	166.4	169.6	158.0	42.4
	P value		0.471	0.000*	0.000*	0.000*	0.000*
	Birth weight	≤ 2.5 kgs	0.650	212.8	214.3	189.0	56.0
		> 2.5 kgs	0.612	89.6	97.6	129.0	20.2
	P value		0.753	0.001*	0.003*	0.019*	0.005*

Continued.

Background characteristics			Mean values Total bilirubin	Total SGOT	Total SGPT	Total ALP	Total bile acid
	NICU admission	No	0.613	90.4	98.9	128.2	20.5
		Yes	0.625	144.8	146.4	164.9	35.8
	P value		0.471	0.000*	0.000*	0.005*	0.000*
	Fetal growth restriction	No	0.612	89.6	97.6	129.0	20.2
		Yes	0.650	212.8	214.3	189.0	56.0
	P value		0.029*	0.056	0.072	0.204	0.070
	Meconium stained liquor	No	0.593	88.5	96.5	127.2	19.6
		Yes	0.646	108.8	115.9	140.2	26.1
Total			0.61	96.62	104.30	132.38	22.22

*Indicates statistical significance at p<0.005.

Table 6: Correlation of liver functions tests with bile acid.

Correlations					
	Bilirubin	**SGOT**	**SGPT**	**ALP**	**Bile acid**
Bilirubin	1.000	0.038	0.067	0.061	0.070
SGOT	0.038	1.000	0.739**	0.408**	0.802**
SGPT	0.067	0.739**	1.000	0.442**	0.804**
ALP	0.061	0.408**	0.442**	1.000	0.542**
Bile acid	0.070	0.802**	0.804**	0.542**	1.000

**Correlation is significant at the 0.01 level (2-tailed)

Correlation matrix for liver function tests, including bilirubin, SGOT, SGPT, ALP, and bile acid, in the context of ICP is shown in Table 6. Notably, there is a significant positive correlation between SGOT and SGPT, as indicated by a correlation coefficient of 0.739**, suggesting that as SGOT levels increase, SGPT levels also tend to increase. Further, both SGOT and SGPT show significant positive correlations with ALP (0.408** and 0.442**, respectively) and bile acid levels (0.802** and 0.804**, respectively). These strong correlations highlight that as the liver enzymes increase, there is a concomitant increase in bile acid levels, reinforcing the interlinked pathology between liver enzyme elevation and bile acid synthesis or flow abnormalities in ICP. ALP and Bile acid are also positively correlated (0.542**), although this is a moderate relationship compared to the strong correlations seen with SGOT and SGPT. Bilirubin, however, shows no significant correlation with SGOT, SGPT, ALP, or Bile acid, with all correlation coefficients being below 0.1 (Table 6).

DISCUSSION

The objectives of the study were to explore the intricate relationship between liver function test (LFT) and serum bile acid abnormalities and feto-maternal outcomes in cases of intrahepatic cholestasis of pregnancy (ICP). Our findings shed light on significant correlations that not only align with existing literature but also provide novel insights into the clinical management of this condition.

The results resonated with the findings of Glantz et al, who reported that elevated bile acids are strongly associated with preterm labor, which is in line with our observation of increased bile acid levels in the later gestational period (37-39.6 weeks).[17] However, our study extended beyond the scope of previous research by quantifying the specific gradations of LFTs and their direct associations with detailed maternal and fetal outcomes. For instance, we have delineated how specific ranges of SGOT and SGPT correlate with the mode of delivery, a factor not extensively covered in the current body of research. Our analysis indicates that elevated LFTs, particularly in the higher gradations, are frequently observed in cases requiring LSCS delivery.

Our study's findings indicated a clear correlation between elevated liver enzymes and various fetal outcomes in ICP cases. Notably, the concentration of liver enzymes SGOT and SGPT is significantly associated with fetal distress markers such as meconium-stained liquor and poor APGAR scores. This aligns with the research conducted by Williamson et al, who emphasized the impact of liver dysfunction on fetal well-being in ICP.[18] Our data suggest that as liver enzyme levels increase, particularly in the higher ranges (SGOT and SGPT levels between 100-200 IU/L), the incidence of meconium-stained liquor rises. This could imply a direct or indirect influence of maternal liver function on the fetal environment, potentially exacerbating fetal stress.

Moreover, our analysis shows a significant relationship between liver enzyme levels and APGAR scores.

Newborns with APGAR scores less than 7 at birth are more frequently observed in mothers with elevated SGOT and SGPT levels. This is particularly noteworthy in the context of studies like that of Geenes et al.[19] The APGAR score, a critical indicator of neonatal vitality, appears to be inversely related to the severity of liver enzyme elevations, underscoring the need for enhanced monitoring and possibly early intervention in pregnancies complicated by elevated LFTs.

Furthermore, the necessity for NICU admission also shows a concerning association with higher liver enzyme levels. This observation is crucial as it not only highlights the immediate postnatal challenges but also raises questions about the long-term developmental and health consequences for these infants, as discussed in the study by Kawakita et al.[20]

The intricate pathophysiology underlying intrahepatic cholestasis of pregnancy (ICP) and its impact on maternal and fetal health is a complex interplay of genetic, hormonal, and environmental factors. Our study's findings contribute to understanding this complexity, particularly in relation to the role of bile acids and liver enzymes.

Elevated bile acids, a hallmark of ICP, known to play a critical role in fetal development and maternal health. When their levels rise, as evidenced in our study, they can induce oxidative stress and inflammation in the liver, leading to cellular damage. This mechanism aligns with the findings of Williamson et al, which suggested that elevated bile acids can disrupt the normal physiological functions of the liver, thereby contributing to the pathogenesis of ICP.[21]

The genetic predisposition to ICP, as discussed in studies like that of Dixon et al, suggests a complex interplay of genetic factors that can influence the susceptibility to ICP and its severity.[22] Our study included data on the prevalence of ICP among different age groups and the recurrence of ICP in subsequent pregnancies. While the research did not directly analyze genetic factors, the observed recurrence and familial patterns suggest a potential genetic predisposition, which aligns with the current scientific understanding of ICP.

Hormonal fluctuations, particularly the elevated levels of estrogens and progesterone during pregnancy, have been shown to exacerbate cholestasis by impairing bile acid clearance, as elucidated in the research by Hayyeh et al.[23] The study's findings that ICP is predominantly diagnosed in the later stages of pregnancy coincide with peak estrogen levels, supporting the hypothesis that hormonal fluctuations contribute to the development and severity of ICP.

The interplay of these factors- bile acids, liver enzymes, genetic predisposition, hormonal fluctuations, and environmental influences-contributes to the complex clinical picture of ICP. This research further demonstrated that hormonal support in pregnant women with ICP is associated with higher mean values of SGOT, SGPT, and total bile acids, suggesting that hormonal therapy could influence the severity of ICP. These findings are consistent with earlier research that has indicated hormonal influences, especially estrogen, are significant in the pathogenesis of ICP.

The study also noted a substantial rate of adverse fetal outcomes, such as preterm birth and meconium-stained amniotic fluid, associated with ICP, aligning with established data. However, the research presents a subtle view of the feto-maternal relationship in ICP, highlighting the complexity of management strategies that must account for both maternal and fetal well-being.

The incidence and demographics of ICP in our study, primarily diagnosed in the third trimester and notably among primiparous women, resonate with the findings of Garg et al and the incidence rates reported by Jhirwal et al and Maiti et al.[16,24,25] The symptomatology and liver function tests, highlighting pruritus and elevated liver enzymes, mirror the classical understanding of ICP's clinical presentation as discussed by Geenes et al and Riely et al, while also reflecting the observations by Marschall et al.[19,26,27] Our categorization of serum bile acid levels into draws parallels with the gradation observed in studies like those by Glantz et al and Agarwal et al, underscoring the consistency in the thresholds applied across different populations.[17,28]

In terms of treatment, the predominant use of Ursodeoxycholic acid (UDCA) and the resulting symptom relief in our study aligns with the literature, particularly with the findings of Kremer et al and the studies by Walker et al and Ovadia et al, although the latter noted some inconclusiveness regarding UDCA's impact on fetal outcomes.[15,29,30] Speaking of feto-maternal outcomes, our study sheds light on the correlation between elevated liver enzymes, bile acid levels, and adverse outcomes such as increased rates of meconium-stained liquor, preterm delivery, and NICU admission. This not only aligns with the observations made by Kant et al, Garg et al, and Maiti et al but also adds a detailed statistical analysis that enriches the existing literature.[31,16,25] Overall, our study corroborates many established findings while also enhancing the understanding of ICP's impact on feto-maternal outcomes, thereby making a significant contribution to the field of obstetric care.

Our study also established that in most of the subjects symptoms disappears after delivery or within 1 week of delivery.

CONCLUSION

The study found a significant association between elevated LFTs and various adverse maternal and fetal outcomes, including the necessity for surgical intervention in delivery, the presence of meconium-stained liquor

indicating fetal distress, and poor/lower APGAR scores signifying immediate neonatal care requirements. Notably, these associations were not only statistically significant but also clinically relevant, underscoring the importance of vigilant monitoring and management of LFTs in pregnant women diagnosed with or suspected of having ICP. The findings advocate for a proactive and individualized approach to managing ICP, emphasizing the need for regular LFT monitoring and tailored care plans. The study highlights the potential of LFTs to serve as valuable indicators for clinical decision-making, from determining the mode of delivery to preparing for potential neonatal intensive care.

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