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"The Retrospective Analysis Of The Maternal And Fetal Outcomes In Ihcp Patients:-A Comparative Observational Study".

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Abstract:-
Background: *Intrahepatic cholestasis of pregnancy (IHCP) is the most common pregnancy related liver disorder. It typically presents with troublesome itching and can lead to complications for both mother and fetus. The maternal and fetal outcomes in parturients with intrahepatic cholestasis of pregnancy have been retrospectively documented. Thus, we aimed to assess risk factors associated with IHCP as well as maternal and fetal outcome in pregnancy associated with IHCP who underwent delivery at our Zonal Military Hospital. The study was conducted during a last one year period from JAN 2021 to DEC 2021.*
Methods: *This hospital based retrospective analytical observational study enrolled 65 subjects with IHCP and immediately next 65 normal asymptomatic healthy pregnant as controls. The subjects were assessed for demographic parameters, obstetric history, liver function tests. Outcome was measured as various parameters related to delivery and maternal and fetal complications.*
Results: *Out of 130 patients, 65 cases and 65 controls were included in this study. Higher incidence of maternal obstetric complication such as gestational hypertension (p value- <0.02) in IHCP patients. Mean value of ALT, AST and ALP was found significantly raised (p value- <0.001) in IHCP patients.There was no significant increase in meconium stained liquor (MSL) or low APGAR at birth. However, there was a statistically high Pre-term delivery (p value- <0.02) and Low birth weight (p value- <0.02) were noted in the IHCP group in comparison to non-IHCP group.*
Conclusions: *IHCP is associated with higher risk of complications in infants and to lesser extent in mothers. : There is a significant incidence of IHCP in the obstetrical population. The biochemical changes, gestational hypertension, pre-term delivery and low birth weight baby were significantly high in IHCP in pregnancy.*
Keywords: *Fetal complications, Fetal outcome, Intra-hepatic cholestasis of pregnancy (IHCP), Maternal outcome, Pregnancy.*

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I. Introduction:-

Cholestasis can be defined as an interruption in the flow of bile due to obstruction of bile ducts or excretory failure of hepatocytes with accumulation of bile constituents in the blood[1]. In this condition, bile cannot flow from liver to the duodenum.

Obstetric cholestasis is a liver disorder unique to pregnancy, which typically presents with pruritus. However, pruritus is common in pregnancy and the diagnosis of obstetric cholestasis is confirmed by finding abnormal liver function[2].

Intrahepatic cholestasis of pregnancy or obstetric cholestasis is the most common pregnancy related liver disorder and is characterized by pruritus, elevated serum-aminotransferases and bile-acid level with onset in second or third trimester of pregnancy and spontaneous relief of symptoms within second or third week after delivery. It typically presents with troublesome itching and can lead to complications for both mother and fetus[3].

The etiology of IHCP is unclear. Result of insufficient liver capacity to metabolize high amounts of placenta-derived sex steroids during pregnancy is thought to be a cause[4-5].

Some drugs like synthetic estrogens, azathioprine etc. can trigger IHCP. It is also common in multiple pregnancies[6-7].

Variable incidence of IHCP has been noted in Indian population with paucity of data on comparison of various fetal risks with normal pregnant subjects. There is lack of data indicating association of various risk factors for IHCP with maternal and fetal outcome in Indian population.

The present study has been conducted to study the incidence, biochemical changes, maternal and neonatal outcome in IHCP with pregnancy and also to compare with non-IHCP normal pregnancy.

- **Aims and objectives:-**

A retrospective observational study to compare the maternal and fetal outcomes in IHCP gravida patient and non IHCP gravida patient at our zonal hospital with following objectives:-

1. Evaluate the risk factors associated with intra-hepatic cholestasis of pregnancy.
2. Analyse the relationship between IHCP and pregnancy outcomes.
3. The study was done to assess the various maternal and neonatal outcome in pregnancy complicated by IHCP and compare with the non-IHCP controls.

II. Material And Method:-

1 Study area	Department of Obstetrics and Gynaecology, Zonal Military Hospital.
2 Study population	All Pregnant women with singleton pregnancy attended emergency in labour and all post-delivery patients from labour room record book data at our Zonal Military Hospital, eligible to consider for this study fulfilling the inclusion criteria. Two age groups studied are, Group1:- Pregnant woman with IHCP. Group2:- Pregnant women without IHCP.
3 Sample size	130 (65 in each groups). Sample size $n = \frac{r+1(p^*)(1-p^*)(Z_B+Z_{a/2})^2}{r \quad (p1-p2)^2}$

Data collection technique and tools:-

This hospital based retrospective observational case control study was carried out in Department of Obstetrics and Gynaecology, Military Hospital, Jammu for a period of one year. Study population was divided into group 1 which comprised of pregnant females clinically diagnosed with IHCP as defined by otherwise unexplained pruritus combined with elevated transaminases during pregnancy and group 2 included normal healthy pregnant females without any obvious complaints as controls.

Inclusion criteria:-

❖ Pregnancy with pruritus due to IHCP developing only after 28 weeks of gestation.
❖ All Singleton pregnancy, irrespective of their parity status.
❖ All IHCP and non-IHCP patient from labour room record book data were included in this study.Patients who delivered at our hospital were enrolled and eligible for participation, irrespective of registration status.

Exclusion criteria:-

❖ Pregnancy less than 28 weeks.
❖ Other causes of pruritus, clinical features or lab investigations suggestive of viral hepatitis.
❖ Patients with twin gestation.
❖ Patients with pre-existing medical, surgical risk factors which can affect outcome are excluded such as, rheumatic heart disease, chronic liver disease, kidney disease, connective tissue disorder, major skeletal deformities…. Etc.

Outcome definition and parameters:-

Maternal outcome:-

- Gestational age of termination and mode of delivery.
- Any antepartum or post-partum complication.
- Biochemical markers.

Fetal outcome:-

- Meconium stained liquor.
- Period of gestation on delivery.
- Live born/ perinatal death/ still born/ IUD.
- Birth weight.
- APGAR score.
- NICU admission.
- Neonatal Jaundice.

III. Discussion:-

IHCP is multifactorial including genetics and environmental influences. Incidence varies in different parts of the world. IHCP usually manifests in the third trimester of pregnancy[8].

In present study as we assessed maternal and fetal outcome in intra-hepatic cholestasis of pregnancy and tried to assess the various risk factors associated with IHCP, maternal and fetal outcome and its association with various risk factors of IHCP. This study recruited 65 subjects with IHCP and 65 normal control subjects. Age distribution in two groups was comparable in present study. Mean age of IHCP subjects in present study was found to be 28.88 years. Brouwers et al also performed similar study on subjects with intrahepatic cholestasis. In a prospective population-based study by Geenes et al to assess outcome in severe IHCP, mean age was 29.6 (±6.3) years. Both the studies were in accordance to present study with mean age also similar to population of present study[9].

In this study, 73.68% of IHCP cases and 26.32% of controls developed gestational hypertension. It was statistically significant (p-value 0.02%).

In a study by Shoballi et al with similar objectives also the age of IHCP subjects was found to be 29.18±3.54 and those of the controls was 29.86±4.37 years[10].

IHCP is characterized by pruritus starting in the second or third trimester of pregnancy and disappearing after delivery[11-12].

In present study various parameters of liver damage including total bilirubin, direct bilirubin, aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase were found to be significantly elevated. In this study, 78.05% of IHCP cases and 21.95% of controls showed higher levels of biochemical markers. It was statistically significant (p-value <0.001%). Further frequency of subjects with higher level of these markers was also found to be significantly higher in IHCP group compared to controls. In a study by Brouwers et al, bilirubin and all liver enzymes including AST, ALT, ALP, GGT, and LDH were found to be elevated. Surprisingly these parameters were highest in subjects with moderate severity of IHCP. Further while all other parameters were significantly different, GGT failed to reach the significance[14].

Present study was also contrary to various other studies done by Geenes et al where no significant difference was found to exist between parity of IHCP subjects and control subjects[9].

Gestational age at delivery was found to be 36.63±2.57 weeks in IHCP subjects and was significantly less compared to controls 37.24±1.9 in a study by Shobailli et al[10].

In this study, 76.47% of IHCP cases and 23.53% of controls had preterm delivery. 70.83% of IHCP cases and 29.17% of control had low birth weight babies. It was statistically significant (p-values 0.02% and 0.02% respectively).

In a study by Shemer et al though maximum pregnancies were terminated only after achieving full term, significantly higher frequency of moderate preterm births were noted compared to non IHCP group[13].

Preterm delivery frequency was also significantly higher in a study by Arbinder et al[15]. Shobaili et al noted significantly higher rate of meconium stained liquor in IHCP subjects similar to present study while no significant difference was noted in rate of IUD[10].

Geenes et al noted significantly higher rate of stillbirth in IHCP group, their findings regarding 5 min APGAR score were in this present study the findings were not significant (p-values 0.15% and 0.24% respectively), while neonatal unit admission were found to be higher than controls[9].

Shemer et al found no significant difference in two groups regarding frequency of neonatal death or meconium aspiration, rather contrary to most studies they noted increased rate of large for gestational age babies[13].

Arbinder et al noted significantly higher rate of meconium stained liquor while no significant increase in IUGR or fetal distress was noted[15].

Comparison of biochemical marker levels was performed in two study groups significantly higher levels were noted in IHCP subjects. Bile acid has been noted as one of the most sensitive markers for IHCP by many authors and has also been performed and observed to be raised in ICP subjects compared to control subjects[10,15,16,17].

Further levels of bile acids are said to be indicative of severity of ICP with increasing levels suggesting higher associated risk[10].

The mechanism for poor perinatal outcome remains unclear. Because high bile salt levels were found to be associated with more frequent occurrence of fetal distress, this might be of great relevance for fetal prognosis. Autopsies show signs of acute, lethal anoxia with petechial bleeding in pleura, pericardium and adrenal glands, but no signs of chronic anoxia[18-19].

Fetuses of women with ICP have adequate birth weights for gestational age and normal Doppler umbilical artery velocimetry, suggesting that chronic placental insufficiency is not the primary cause of fetal death. Bile acids have been shown to induce vasoconstriction of human placental chorionic veins, and myometrial sensitivity to oxytocin[20,21].

As per Brouwers et al, postpartum hemorrhage was present in 7.4% of all cases[22].

None of present study subjects showed post-partum hemorrhage or placental abruption.

The maternal complication associated with IHCP are increased risks of post-partum haemorrhage, operative delivery, severe pruritus with dyslipidemia and deranged coagulation profile, preterm prelabour rupture of membrane[23].

In some studies, perinatal mortality including stillbirths were reduced to 3.5% or less with more recent active management, which includes treatment with UDCA, intensified fetal monitoring and planned deliveries at gestation 37-38 weeks[24,25].

TABLE 1:- Obstetrics and Neonatal parameters in this study.

		IHCP (n=65)		Non-IHCP (N=65)		Total (n=130)		p-Value
Delivery	NVD	19	42.22%	26	57.78%	45	100.00%	
	LSCS	46	54.12%	39	45.88%	85	100.00%	0.2
Maternal Outcome	GDM	8	72.73%	3	27.27%	11	100.00%	0.12
	PIH	14	73.68%	5	26.32%	19		**0.02**
	Transaminase	32	78.05%	9	21.95%	41	100.00%	**<0.001**
Fetal Outcome	Preterm	13	76.47%	4	23.53%	17	100.00%	**0.02**
	Meconium	17	65.38%	9	34.62%	26	100.00%	0.08
	LBW	17	70.83%	7	29.17%	24	100.00%	**0.02**
	IUD	2	100.00%	0	0.00%	2	100.00%	0.15
	Low APGAR	5	71.43%	2	28.57%	7	100.00%	0.24
	NICU	18	64.29%	10	35.71%	28	100.00%	0.09
	Neonatal Jaundice	8	72.73%	3	27.27%	11	100.00%	0.12

IV. Conclusion:-

It is concluded that IHCP mothers are at risk for obstetrical complication like gestational hypertension and various fetal complications like preterm delivery, low birth weight babies. Though intra-partum complications such as fetal heart rate changes, meconium stained liquor are higher there is no significant increase in postpartum complications.

Fetus is at higher risk ofmeconium stained liquor, NICU admisssion and lower APGAR score but not statistically significant.

Significant association between elevated T. bilirubin, AST, ALT and ALP was noted with IHCP. Thus, IHCP is associated with higher risk of complications in infants and to lesser extent in mothers.

In this study categorization into mild, moderate and severe IHCP was not done as well as long term follow up is needed usually to reach a conclusion.

As IHCP is associated with obstetrics and various fetal complications, woman must be counselled early to ensure a healthy maternal and fetal outcomes.

The findings of this study would facilitate pre-conceptional, antenatal counselling and management of these pregnant women.

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Ethical approval: The study was approved by the Institutional Ethics Committee of Zonal Military Hospital.

References:-

[1]. Van Wettere AJ. Histologic patterns of hepatotoxic injury. Comprehensive Toxicol. 2018;2:97-136.
[2]. Kenyon AP, Piercy CN, Girling J, Williamson C, Tribe RM, Shennan AH. Pruritus may precede abnormal liver function tests in pregnant women with obstetric cholestasis: a longitudinal analysis. BJOG. 2001;108(11):1190-2.
[3]. Ghosh S, Chaudhuri S. Intra-hepatic cholestasis of pregnancy: a comprehensive review. Indian J Dermatol. 2013;58(4):327.
[4]. Reyes H. Intrahepatic cholestasis. A puzzling disorder of pregnancy. J Gastroenterol Hepatol. 1997;12:211-6.
[5]. Davidson KM. Intrahepatic cholestasis of pregnancy. Semin Perinatol. 1998;22:104-11.
[6]. Reyes H, Ribalta J, Gonzalez MC, Segovia N, Oberhauser E. Sulfobromophthalein clearance tests before and after ethinyl estradiol administration, in women and men with familial history of intrahepatic cholestasis of pregnancy. Gastroenterol. 1981;81:226-31.
[7]. Webb GJ, Elsharkawy AM, Hirschfield G: Editorial: the etiology of intrahepatic cholestasis of pregnancy: towards solving a monkey puzzle. Am J Gastroenterol. 2014;109:85.
[8]. Lammert F, Marschall HU, Glantz A, Matern S. Intrahepatic cholestasis of pregnancy: molecular pathogenesis, diagnosis and management. J Hepatol. 2000;33:1012-21.
[9]. Geenes V, Chappell L, Seed P, Steer P, Knight M, Williamson C. Association of severe intrahepatic cholestasis of pregnancy with adverse pregnancy outcomes: A prospective population-based case-control study. Hepatol. 2014;59(4):1482-91
[10]. Al Shobaili H, Hamed H, Al Robaee A, Alzolibani A, Amin A, Ahmad S. Obstetrical and fetal outcomes of a new management strategy in patients with intra-hepatic cholestasis of pregnancy. Arch Gynecol Obstet. 2010;283(6):1219-25.
[11]. Reyes H. Review: intrahepatic cholestasis. A puzzling disorder of pregnancy. J Gastroenterol Hepatol. 1997;12:212-6.
[12]. Bacq Y, Sapey T, Bréchot MC, Pierre F, Fignon A, Dubois F. Intrahepatic cholestasis of pregnancy: a French prospective study. Hepatol. 1997;26(2):358-64.
[13]. Wikström Shemer E, Marschall H, Ludvigsson J, Stephansson O. Intrahepatic cholestasis of pregnancy and associated adverse pregnancy and fetal outcomes: a 12-year population-based cohort study. BJOG. 2013;120(6):717-23.
[14]. Brouwers L, Koster M, Page-Christiaens G, Kemperman H, Boon J, Evers I, et al. Intrahepatic cholestasis of pregnancy: maternal and fetal outcomes associated with elevated bile acid levels. Am J Obstet Gynecol. 2015;212(1):100.e1-7.
[15]. Dang A, Agarwal N, Bathla S, Sharma N, Balani S. Prevalence of liver disease in pregnancy and its outcome with emphasis on obstetric cholestasis: An Indian scenario. J Obstet Gynecol India. 2010;60(5):413.
[16]. Wikström Shemer E, Thorsell M, Marschall H, Kaijser M. Risks of emergency cesarean section and fetal asphyxia after induction of labor in intrahepatic cholestasis of pregnancy: A hospital-based retrospective cohort study. Sexual Reproductive Healthcare. 2013;4(1):17-22.
[17]. Geenes V, Chambers J, Khurana R, Shemer E, Sia W, Mandair D, et al. Rifampicin in the treatment of severe intrahepatic cholestasis of pregnancy. Eur J Obstet Gynecol Reprod Bio. 2015;189:59-63.
[18]. Heinonen S, Kirkinen P. Pregnancy outcome with intrahepatic cholestasis. Obstet Gynecol. 1999;94(2):189-93.
[19]. Laatikainen T, Tulenheimo A. Maternal serum bile acid levels and fetal distress in cholestasis of pregnancy. Int J Gynaecol Obstet. 1984;22:91-4.
[20]. Zimmermann P, Koskinen J, Vaalamo P, Ranta T. Doppler umbilical artery velocimetry in pregnancies complicated by intrahepatic cholestasis. J Perinat Med. 1991;19:351-5.
[21]. Simpson LL. Maternal medical disease: risk of antepartum fetal death. Semin Perinatol. 2002;26:42-50.
[22]. Brouwers L, Koster MP, Page-Christiaens GC, Kemperman H, Boon J, Evers IM, et al. Intrahepatic cholestasis of pregnancy: maternal and fetal outcomes associated with elevated bile acid levels. Am J Obstet Gynecol. 2014;105:75
[23]. Mays JK. The active management of intrahepatic cholestasis of pregnancy. Current Opinion Obstet Gynecol. 2010;22(2):100-3
[24]. Geenes V, Williamson C. Intrahepatic cholestasis of pregnancy. World J Gastroenterol. 2009;15:2049-66.
[25]. Glantz A, Reilly SJ, Benthin L, Lammert F, Mattsson LA, Marschall HU. Intrahepatic cholestasis of pregnancy: amelioration of pruritus by UDCA is associated with decreased progesterone desulphated in urine. Hepatol. 2008;47:544-51.

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