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Original Research Article

Prevalence of gestational diabetes mellitus in intrahepatic cholestasis of pregnancy

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ABSTRACT

Background: Incidence of IHCP in Indian population is 0.02%-2.4% and that of GDM is 3.8%-17.9%. Frequent co-existence of both has raised the question of any association. There exists only few studies to prove or disprove any association. Objective of current study was to determine the prevalence of GDM in women with IHCP and to compare the feto-maternal outcome in women with GDM with or without IHCP.
Methods: The study was conducted in the Department of Obstetrics and Gynaecology, VMMC and SJH, New Delhi. Women with singleton pregnancy ≥28wks were recruited for the study and further categorized as women with IHCP and women without IHCP according to their diagnosis of IHCP by the RCOG guidelines. OGTT with 75g glucose was done to make the diagnosis of GDM. Management was as per obstetrics protocol and feto-maternal outcomes recorded till delivery.
Results: No statistically significant difference in the prevalence of GDM observed in both groups (5.4% in women with IHCP and 8.2% in women without IHCP, p=0.220). Significantly higher number of preterm deliveries (21%, p<0.001), induced labour (53.6%, p<0.001), women undergoing LSCS (46.3%, p<0.001) in women with IHCP. No association of FGR, MSL, Fetal maturity, labour onset, mode of delivery, stillbirth, low APGAR score, NICU admission, or PPH in women with GDM with or without IHCP.
Conclusions: The prevalence of GDM is not higher in women with IHCP but significantly higher incidence of preterm delivery, induced labour, and Caesarean sections in women with IHCP. No significant difference in feto-maternal outcome in women with GDM with or without IHCP.

Keywords: Gestational diabetes mellitus, Intrahepatic cholestasis, Pregnancy

INTRODUCTION

Intrahepatic cholestasis of pregnancy (IHCP), originally described in 1883 by Ahlfeld is the second most common liver disease associated with pregnancy after viral hepatitis.[1] IHCP usually manifests in the later pregnancy and resolves after delivery. Incidence of IHCP in Indian population is 0.02% to 2.4% of all pregnancies and 70% of them present usually in third Trimester.[2] Incidence is affected by geographical location and ethnicity (Chile and Bolivia have an incidence rate of 15% and that of Europe is 1%. In South Asian population it is 0.8-1.46%).[3] The etiology of IHCP is not clear, yet the involvement of Genetic, Environmental and Hormonal factors, are suggestive of a Multi-factorial origin. Mutations of MDR-3 gene encoding canalicular Phosphatidylcholine Translocase is been said as one of it's genetic etiology and there are clinical evidences supporting the role of estrogen and progesterone in developing IHCP. Oral progesterone intake in pregnant women who are predisposed to IHCP have been seen developing IHCP at an earlier stage.[2-5] Low selenium levels and decreased glutathione peroxidase

activity (which are essential for anti-oxidation) make the anti-oxidative mechanism defective and thus takes part in the pathogenesis of IHCP. That is why low selenium levels during the winter season makes the incidence of IHCP higher.[6] Maternal complications are seldom in association with IHCP, but poor fetal outcomes are encountered many a time. Adverse pregnancy outcomes associated with IHCP are spontaneous pre-term delivery, fetal distress, still birth, meconium stained liquor, Caesarean section, PPH etc.[4] Gestational Diabetes Mellitus (GDM) is a disorder of carbohydrate intolerance that is diagnosed for the first time during current pregnancy. Incidence of GDM in India is 3.8%-17.9%.[7] It is said that four million women are affected by GDM in India at any given point of time.[6] GDM can lead to a wide range of fetomaternal complications. The maternal complications associated are miscarriage, preterm labour, polyhydramnios, infections, diabetic nephropathy, diabetic retinopathy, diabetic neuropathy, diabetic ketoacidosis etc. While fetal/ neonatal complications are macrosomia, fetal hypoglycemia, congenital malformations, birth injuries etc.[3-4,7-9] Studies have shown association of IHCP with GDM. FXR (Farsenoid X Receptor) is suggested to be the reason for this association.[3-4,7] High levels of Zonulin, a protein that regulates the tight junctions has been found in higher concentrations in patients with GDM and IHCP, both separately and in co-existence.[10] In normal physiology bile acids have significant role in gluconeogenesis by suppressing the key enzymes through FXR. They also stimulate the expression of Glucose transporter GLUT-4. Downregulation of FXR in IHCP causes disruption in this homeostasis. Enteric bile acids have the ability to stimulate TGR-5 receptor that follows GLP-1 release and further stimulation of endocrine pancreas leading to an increased insulin and decreased glucagon release.[11-13] Rise in GDM and IHCP has emanated recent interest in possible association between the two. Few studies available are on a small sample size and mostly retrospective and the controversy still persists. Hence, we have conducted a prospective cohort study to determine any association between gestational diabetes mellitus and intrahepatic cholestasis of pregnancy.

METHODS

This prospective cohort study was conducted in the department of obstetrics and gyanecology, Safdarjung Hospital over a period of 18 months (November 2020 to April 2022). Women who attended the ANC clinics and admitted in Obstetric wards of Safdarjung Hospital who fulfilled the inclusion criteria were recruited for the study.

Inclusion criteria

Inclusion criteria for current study were; pregnant women with period of gestation ≥ 28 weeks who were diagnosed with IHCP as per RCOG criteria were recruited for the study group. Pregnant women with period of gestation ≥28 weeks who were not diagnosed with IHCP were recruited for the control group.

Exclusion criteria

Exclusion criteria for current study were; women with multifetal pregnancy, women with overt diabetes mellitus, HELLP Syndrome, Acute Fatty Liver of Pregnancy, Viral hepatitis, Biliary tract obstruction by stones and Hepatic and Biliary tumors.

Diagnosis of IHCP was made according to the RCOG definition; unexplained pruritus, elevated liver function tests and/or raised serum bile acids.[14] Diagnosis of GDM was made according to the Maternal Health Division, Ministry of Health and Family Welfare Government of India Guidelines, that was a blood sugar level ≥140 mg/dl post 2hr 75g oral glucose was managed as GDM. Negative result test repeated at 32-34 weeks.[15]

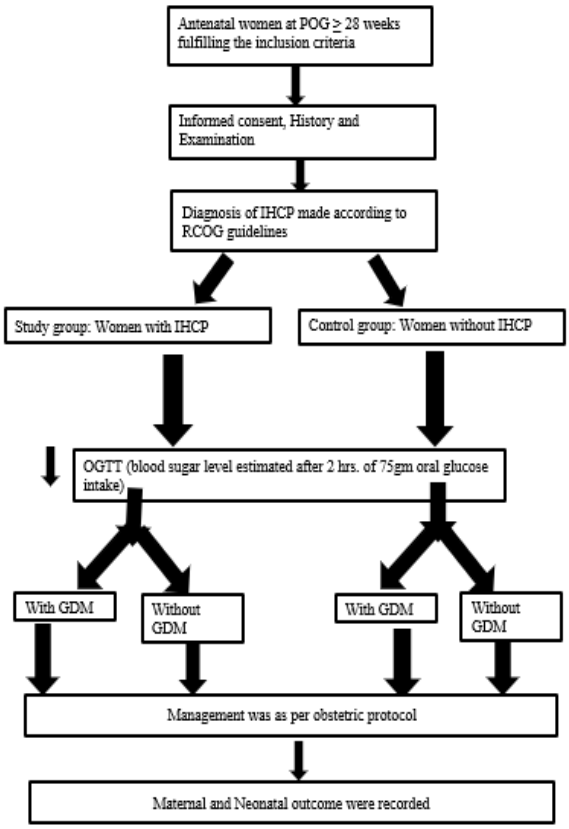

Figure 1: Study flowchart.

Outcome measures

Primary outcome: Number of women diagnosed with gestational diabetes mellitus with or without IHCP, Secondary outcome: Fetal outcomes; Neonatal APGAR score (1 minute and 5 minutes), Birth weight, Neonatal Hypoglycemia, Neonatal Hypocalcemia, Neonatal Respiratory distress syndrome, Congenital malformations, Still birth. Maternal outcomes; Term/Preterm delivery, Still birth, Meconium stained liquor, Post-partum hemorrhage and mode of delivery.

RESULTS

A total of 514 women were recruited in the study (257 in women with IHCP group and 257 in women without IHCP group). There was no difference in age distribution in both the groups (Figure 2) and no difference in the mean age of subjects in both the groups (Table 1).

Table 1: Comparison of the 2 groups in terms of age (years) (n=514).

Age (years)	Group		Wilcoxon-Mann-Whitney U test	
	Women with IHCP	Women without IHCP	W	P value
Mean (SD)	25.80 (3.68)	25.36 (4.05)		
Median (IQR)	25 (23-28)	25 (22-28)	36027.500	0.074
Range	18-40	19-35		

No significant difference between the groups in terms of age (years) (W=36027.500, p=0.074), no effect of age on IHCP.

Table 2: Association between group and GDM (n=514).

GDM	Group			Chi-Squared test	
	Women with IHCP (Study Group), N (%)	Women without IHCP (Control), N (%)	Total	χ2	P value
Yes	14 (5.4)	21 (8.2)	35 (6.8)		
No	243 (94.6)	236 (91.8)	479 (93.2)	1.502	0.220
Total	257 (100.0)	257 (100.0)	514 (100.0)		

There was no significant difference between the various the group of Women with IHCP and that of Women without IHCP in terms of occurrence of GDM ($\chi2 = 1.502$, p=0.220), no association of GDM and IHCP observed.

Table 3: Association between group and fetal maturity (n=514).

Fetal maturity	Group			Chi-Squared test	
	Women with IHCP (Study Group), N (%)	Women without IHCP (Control), N (%)	Total	χ2	P value
Term	203 (79.0)	233 (90.7)	436 (84.8)		
Preterm	54 (21.0)	24 (9.3)	78 (15.2)	13.603	<0.001
Total	257 (100.0)	257 (100.0)	514 (100.0)		

There was a significant difference between the various groups in terms of distribution of Fetal Maturity ($\chi2=13.603$, p=<0.001). Women without IHCP had the larger proportion of Fetal maturity Term and Women without IHCP had the larger proportion of Fetal Maturity Preterm.

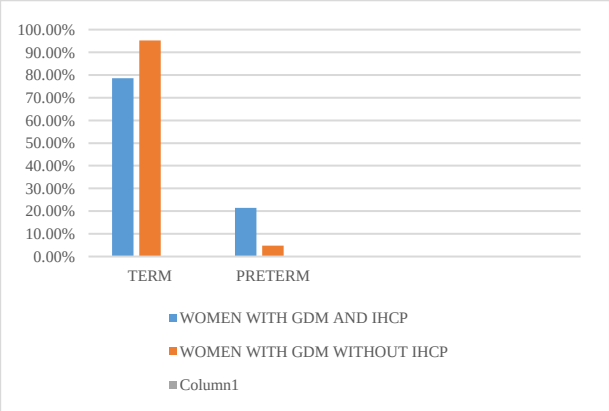

Figure 2: Comparison of women with GDM with or without IHCP in terms of fetal maturity.

No association with parity was also observed. Out of 257 women in study group 14 and 21 out of 257 subjects in women without IHCP group presented with GDM, according to these findings depicted in (Table 2), no significant association of GDM with IHCP was observed (p=1.502).

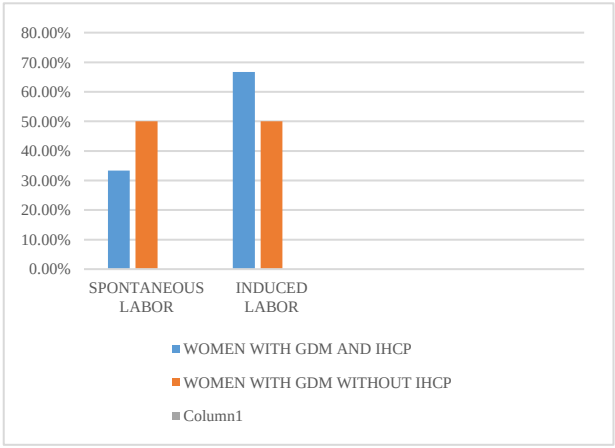

Figure 3: Comparison of Women with GDM with or without IHCP in terms of Labour onset.

Table 4: Association between group and labour onset (n=459).

Labor onset	Group			Chi-Squared test	
	Women with IHCP (Study Group), N (%)	Women without IHCP (Control), N (%)	Total	χ2	P value
Spontaneous	104 (46.4)	144 (61.3)	248 (54.0)		
Induced	120 (53.6)	91 (38.7)	211 (46.0)	10.180	0.001
Total	224 (100.0)	235 (100.0)	459 (100.0)		

There was a significant difference between the various groups in terms of distribution of Labor Onset (χ2=10.180, p=0.001). Statistically significant no. of women in the Women without IHCP group delivered spontaneously (61.3%) and statistically significant number in the Women with IHCP went into Induced labour (53.6%).

Though this study could not observe any significant association between GDM and IHCP, it was found that a statistically significant number of preterm babies were born to the women with IHCP (p<0.001) (Table 3). Similarly, the incidence of induction of labour (p=0.001) and women undergoing caeserian section (p<0.001) also found to be significantly higher in women with IHCP (Table 5).

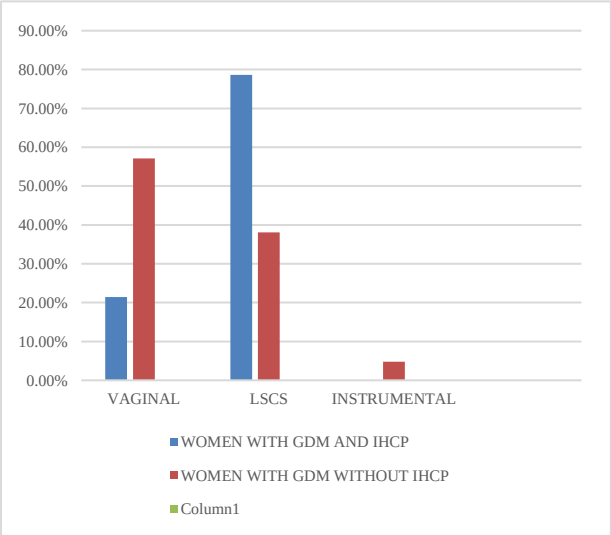

Figure 4: Comparison of women with GDM with or without IHCP in terms of mode of delivery.

The study also observed no association of occurrence of fetal growth restriction (p=0.254), meconium-stained liquor (p=0.578), perinatal outcome (p=0.373), low birthweight (p=848), low APGAR score at 1 and 5 minutes (p=0.971 and p=0.427), NICU admission (p=0.258) and occurrence of PPH (p=0.095) with IHCP (Table 5). The difference in occurrence of hypertensive disorders (p=0.215) and hypothyroidism (p=0.673) among the women with IHCP group and women without IHCP group could not draw any statistically significant association with IHCP. Further in women with GDM with or without IHCP, no effect of age (p=0.989) and gravidity (p=1.000) observed. Also there was no association of hypertensive disorders (p=0.853), hypothyroidism (p=1.000), FGR (p=1.000), MSL (p=1.000), Fetal maturity (p=0.419) (Figure 2), labour onset (p=0.551) (Figure 3), mode of delivery (p=0.060) (Figure 4), stillbirth (p=1.000), low APGAR score (at 1minute p=0.801, at 5 minutes p=1.000), NICU admission (p=0.059), or PPH (p=0.443) with GDM with or without IHCP (Table 6).

DISCUSSION

The present prospective cohort study was conducted in 514 women with singleton pregnancy at or above 28weeks POG who were attending ANC OPD or/and admitted in ANC ward. They were further divided into two groups according to the Diagnosis of IHCP as Women with IHCP and Women without IHCP.

Socio-demographic data

Age and parity: In the present study there was no significant difference between women with IHCP and women without IHCP in terms of age (years) (p=0.074). The mean age in women with IHCP was found to be 25.80 (3.68) and that in women without IHCP was 25.36 (4.05), the highest percent (50.6%) women in the IHCP group were in the 18-25 yrs age group (p=0.051). These findings were similar to that of a Case-Control Study conducted in Ankara, Turkey by GG Turkmen et al, where the mean age in IHCP group was 27.6 (5.0) and in Non-IHCP group 27.2 (5.2) (p=0.62).[16] Indian study by Sangeeta Parihar et al observed significantly older population of women with IHCP. 35.48% women in the IHCP group were >35 years (p=0.0099).[17] No significant difference was found between women with IHCP and women without IHCP in terms of distribution of gravidity (p=0.556). In concordance with the observations of present study Martineau et al (p=0.54), Turkmen et al (p=0.44), Aftab et al (p=0.594), and Liu et al (p=0.559) also observed no association with gravidity of IHCP.[4,16-18]

Associated morbidities

Gestational diabetes mellitus: In the present study there was no significant difference between women with IHCP and women without IHCP in terms of occurrence of GDM (p=0.220). 5.4% women with IHCP and 8.2% women without IHCP had GDM. The mean blood glucose level (OGTT-2) was not significantly different in both the groups, 93.59 (17.43%) in women with IHCP and 96.21 (24.02%) in women without IHCP (P=0.572). These

Observations were similar to the findings of GG Turkmen et al. who observed no association of GDM with IHCP (11.25% GDM in IHCP group and 6.25% in non-IHCP group, p≥0.187).[16]

Table 5: Association between group and parameters (n=257).

Parameters	Group		P value
	Women with IHCP (Study Group), N (%)	Women without IHCP (Control), N (%)	
Parity			1.000
Primigravida	118 (45.9)	118 (45.9)	
Multigravida	139 (54.1)	139 (54.1)	
POG (Weeks) (mean±SD)	37.85±1.77	38.64±1.29	<0.001
Morbidity: GDM (Yes)	14 (5.4)	21 (8.2)	0.220
Morbidity: HDP (Yes)	43 (16.7)	54 (21.0)	0.215
Morbidity: Hypothyroidism (Yes)	30 (11.7)	27 (10.5)	0.673
Morbidity: FGR (Yes)	17 (6.6)	24 (9.3)	0.254
Morbidity: MSL (Yes)	17 (6.6)	14 (5.4)	0.578
Morbidity: Others (Yes)	56 (21.8)	83 (32.3)	0.007
POG of IHCP Diagnosis (Weeks)	34.03±1.99	-	-
POG of GDM Diagnosis (Weeks)	31.86±3.43	32.84±2.60	0.448
Age (years)	25.80±3.68	25.36±4.05	0.074
Age groups (years)			0.051
18-25	130 (50.6)	141 (54.9)	
26-30	103 (40.1)	82 (31.9)	
31-35	22 (8.6)	34 (13.2)	
36-40	2 (0.8)	0 (0.0)	
Fetal maturity			<0.001
Term	203 (79.0)	233 (90.7)	
Preterm	54 (21.0)	24 (9.3)	
Labor onset			0.001
Spontaneous	103 (46.2)	144 (61.3)	
Induced	120 (53.8)	91 (38.7)	
Mode of delivery			<0.001
Vaginal	135 (52.7)	187 (72.8)	
LSCS	119 (46.5)	67 (26.1)	
AVD	2 (0.8)	3 (1.2)	
Delivery outcome			0.373
Live	253 (98.4)	256 (99.6)	
Fetal demise	4 (1.6)	1 (0.4)	
Birth weight (Kg)			0.408
<1.5	1 (0.4)	0 (0.0)	
1.5-2.5	65 (25.3)	57 (22.2)	
≥2.5	191 (74.3)	200 (77.8)	
APGAR (1 minute)	7.52±0.86	7.50±0.81	0.621
APGAR (5 minutes)	8.69±0.69	8.65±0.72	0.418
Low APGAR (1 minute) (Yes)	36 (14.0)	36 (14.1)	0.971
Low APGAR (5 Minutes) (Yes)	6 (2.3)	9 (3.5)	0.427
NICU admission (Yes)	53 (20.6)	43 (16.7)	0.258
Maternal outcome			0.095
Uneventful	237 (92.2)	246 (95.7)	
Eventful	20 (7.8)	11 (4.3)	

Table 6: Association between diagnosis and parameters.

Parameters	Diagnosis				P value
	IHCP with GDM, N (%)	IHCP without GDM, N (%)	Control with GDM, N (%)	Control without GDM, N (%)	
Parity					
Nulliparous	10 (71.4)	137 (56.4)	9 (42.9)	124 (52.5)	0.605
Primiparous	4 (28.6)	87 (35.8)	9 (42.9)	92 (39.0)	
Multiparous	0 (0.0)	19 (7.8)	3 (14.3)	20 (8.5)	
Gravidity					
Primigravida	5 (35.7)	113 (46.5)	7 (33.3)	111 (47.0)	0.556
Multigravida	9 (64.3)	130 (53.5)	14 (66.7)	125 (53.0)	
Labor onset					
Spontaneous	4 (33.3)	100 (47.2)	8 (50.0)	136 (62.1)	0.008
Induced	8 (66.7)	112 (52.8)	8 (50.0)	83 (37.9)	
Mode of delivery					
Vaginal	3 (21.4)	133 (54.7)	12 (57.1)	175 (74.2)	<0.001
LSCS	11 (78.6)	108 (44.4)	8 (38.1)	59 (25.0)	
AVD	0 (0.0)	2 (0.8)	1 (4.8)	2 (0.8)	
Route of delivery					
Vaginal	3 (21.4)	135 (55.6)	13 (61.9)	177 (75.0)	<0.001
LSCS	11 (78.6)	108 (44.4)	8 (38.1)	59 (25.0)	
Birth weight (kg)					
<1.5	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0.824
1.5-2.5	4 (28.6)	61 (25.1)	0 (0.0)	57 (24.2)	
2.5-3	7 (50.0)	115 (47.3)	13 (61.9)	111 (47.0)	
3-3.5	3 (21.4)	59 (24.3)	7 (33.3)	60 (25.4)	
3.5-4	0 (0.0)	7 (2.9)	1 (4.8)	7 (3.0)	
>4	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	

The following variables were significantly associated ($p<0.05$) with the variable 'Diagnosis': labor onset, mode of delivery, route of delivery

A study by Marcus Martinaeu et al in a London population revealed higher levels of post-parandial sugar in IHCP group by using CGMS ($p\leq0.005$) and 30% incidence of GDM in IHCP group (by GTT, $p\leq0.005$).[4] The Retrospective Cohort Study performed by Liu et al in China saw a significantly higher prevalence of GDM in IHCP group (17.1%) as compared to the non-IHCP group (12.4%) with $p<0.001$. The women in both these studies had a higher mean age as compared to the present study.[18] Study by Nigat Aftab et al in a tertiary hospital in Dubai in women with a mean age higher than the present study revealed that the risk of GDM in women with IHCP to be 2 times in comparison to non-IHCP group ($p<0.05$).[17] This difference can be attributable to the difference in ethnicity, higher mean age of the study population as compared to the current study. These studies differ with the present in terms of the ethnicity and size of the study population, retrospective nature of the study and diagnostic tests used.

A systemic Meta-analytical study by Ahamed Arafa et al established that women with IHCP are more likely to develop GDM (pooled OR=2.19, 95% CI: 1.58, 3.03, I^2=88.25%).[19] Another Meta-analytical study by Mohan et al found the risk of development of GDM in patients with IHCP to be double as compared to the Non-IHCP patients.[20] However, most of the studies in these analysis were also retrospective in nature. The present study also observed no significant association between the POG at GDM diagnosis and IHCP. Hypertensive disorders of pregnancy: no significant difference between women with IHCP and women without IHCP in terms occurrence of hypertensive disorders of pregnancy ($p=0.215$). Present study observed an incidence of 16.7% of HDP in Women with IHCP and 21.0% incidence in Women without IHCP ($p=0.215$). Study by Liu et al reported a much lower incidence of pre-eclampsia, 5.5% in IHCP group and 2.4% in non-IHCP group ($p<0.001$).[18] Another retrospective study by Axelsen et al in a population in Denmark, observed an incidence of pre-eclampsia in IHCP group to be 23.9% and that in Non-IHCP group as 7.6% with $p=0.003$.[21] This difference could be due to the difference in ethnicity of the study population. Hypothyroidism: No significant association was established between women with and without IHCP in terms of the occurrence of hypothyroidism ($p = 0.673$) in the current study. The proportion of women diagnosed with Hypothyroidism was found to be higher in IHCP with GDM group. However, the number of patients in the subgroup was small (14 patients in Women with IHCP with GDM), hence this study is not powered to draw any statistically significant correlation.

Feto-maternal outcomes

Fetal growth restriction: The present study revealed no significant association between IHCP and FGR (p=0.254). The incidence was found to be 6.6% in Women with IHCP and 9.3% in Women without IHCP. Similar to this a retrospective Cohort study by Sarkar et al also observed no significant association of IHCP with FGR (p=0.96).[22] Meconium stained liquor: the difference between women with IHCP and women without IHCP in terms of distribution of MSL (p=0.578) in this study was not significant with an incidence of 6.6% in women with IHCP and 5.4% in women without IHCP. A case-control study performed by Anita Kant et al was found to be similar to the present study with the incidence of MSL in IHCP group to be 9.09% and that in non-IHCP group to be 2.7% (p=0.2).[23] Study by Sangeeta Parihar et al. observed significant association between Meconium stained liquor and IHCP with incidence of MSL in IHCP group 40.32% and that of Non-IHCP group 8.48% (p<0.001).[21] while Mitra et al observed a rate of 29.93% MSL in IHCP patients in their prospective observational and Asulum et al observed a rate of 44.3% of MSL in IHCP patients. [24,25] Fetal maturity: An incidence of 21% preterm births in Women with IHCP v/s 9.3% in Women without IHCP (p<0.001) observed in this study. The incidence of Preterm in the IHCP showed no significant difference, 21.4% in IHCP with GDM and 21% in IHCP without GDM. Kant et al observed an incidence of 25% Preterm in IHCP group and 11.36% in Non_IHCP group (p=0.4).[23] Similarly Parihar et al observed 40.32% preterm births in IHCP group v/s 29.09% in non-IHCP group (p=0.0602).[26] Case-Control study by Aftab et al revealed the incidence of Preterm delivery in IHCP group to be 36% and that in Control group 26.7% (p=0.116).[17] Labour onset: It has been established by different studies in the past that the Induction of labour is seen in greater numbers in women with IHCP. This study too observed a significant number in IHCP group having Induced labour (53.8%) while many in the non-IHCP group delivered spontaneously (p=0.001). Observation of present study was in concordance with the observation made by Aftab et al 53.8% Induced labour in IHCP group and 38.7% in non-IHCP group (p<0.001).[17] In contrast to this, the study by Liu et al observed 4.1% of Induced labour in IHCP group and 6.7% in non-IHCP group (p=0.001).[18] Mode of delivery: Present study observed that majority in the non-IHCP group delivered Vaginally (72.8%) while 46.5% in the IHCP group underwent LSCS (p<0.001). The proportion of women underwent instrumental delivery was found to be higher in non-IHCP group. The common indications of LSCS were MSL, failed IOL and FD. These observations were in concordance with the observations of Parihar et al and Liu et al 58.06% (p<0.001) and 74.3% (p<0.001) LSCS in IHCP group.[18,26] Present study findings were in contrast with the observations of Kant et al and Aftab et al where the incidence of LSCS was not significantly higher in IHCP group (43.48%, p=0.14 and 33.3% p=905) respectively.[17,23] Stillbirth: The present study revealed no significant difference between the various groups in terms of distribution of stillbirth, 1.6% stillbirth in women with IHCP and 0.4% stillbirth in the women without IHCP (p=0.373). Similar to this Liu et al observed 0.1% Stillbirth in IHCP group and 0.3% Stillbirth in non-IHCP group (p=0.259).[18] Birthweight: Though the present study observed no statically significant association between Birth-weight and IHCP, extremely low birth weight (<1.5kg) was seen only in IHCP group and the proportion of low birth weight (1.5-2.5kg) in IHCP group was higher (25.3% vs. 22.2%). These findings revealed in the present study were in concordance with the observations made by Sangeeta et al no significant association between IHCP and low birth weight (p=8128).[26] Other studies by Martinaeu et al (p=0.54), and Aftab et al (p=597) also observed statistically insignificant association between birth weight and IHCP.[4,17] However a statistically significant association between Birth-weight was observed by Turkmen et al, Mean Birth-weight was found to be higher in Non-IHCP group than that in IHCP group (p=0.001).[16] Low APGAR score: There was no significant difference between the various groups in terms of distribution of Low APGAR Score (1 Minute) (p=0.971) and low APGAR Score (5 Minutes) (p=0.666). These observations were similar to the observations made by Liu et al, Aftab et al and Concong Liu et al saw an Incidence of 0.7% in IHCP group and 0.6% in non-IHCP group (p=0.932).[18] Aftab et al observed an incidence of 8.2% in IHCP group and 9.8% in non-IHCP group (0.731), of low APGAR at 1 minute and 4.7% in IHCP group and 3.6% in non-IHCP group (0.736).[17] NICU Admissions: no significant difference between the various groups in NICU admissions (p=0.258) was observed inspite of higher incidence of preterm births in women with IHCP (20.6% v/s 16.7%). This observation was in concordance with the study by Anita et al whereas observed 6.8% NICU admissions in the IHCP group and 2.7% NICU admissions in the non-IHCP group (p=0.31).[23] Findings of the present study were in discordance with the studies by Liu et al (29.5% in IHCP group and 13.5% in Non-IHCP group, p<0.001) and Aftab et al (11.8% in IHCP group and 34.1% in Non-IHCP group, p=0.001).[17,18] Postpartum Hemorrhage: The occurrence of PPH in both the groups had no statistically significant difference (p=0.095). Similar to this Aftab et al observed no association between IHCP and PPH, 14.7% incidence of PPH in IHCP group and 9.3% in non-IHCP group (p=0.696).[17] However, Parihar et al saw 19.35% incidence in IHCP group and 9.44% in non-IHCP group of PPH (p<0.05).[26] Significantly high incidence of PPH was observed in IHCP group by Liu et al 3.3% incidence in IHCP group and 5.4% in Non-IHCP group of PPH (p=0.005).[18] Women with GDM with IHCP vs. without IHCP: The present study observed no effect of age (p=0.989) and gravidity (p=1.000) in women with GDM with or without IHCP. Also there was no association of hypertensive disorders (p=0.853), hypothyroidism (p=1.000), FGR (p=1.000), MSL (p=1.000), Fetal maturity (p=0.419), labour onset (p=0.551), mode of delivery (p=0.060), stillbirth (p=1.000), low APGAR score (at 1minute p=0.801, at 5 minutes p=1.000), NICU admission (p=0.059), or PPH

(p=0.443) with GDM in IHCP. Further studies are recommended to see the difference in effect on pregnancy, fetomaternal outcomes and the sequelae in patients with GDM and IHCP and those with GDM without IHCP. Serum bile acid levels could not be used for the diagnosis of IHCP as the Test was not available at the Institution's Lab. The number of women with GDM in IHCP group was very small in number, hence the conclusion drawn at the end of this subgroup analysis is not relevant enough.

CONCLUSION

This prospective cohort study was conducted to evaluate the prevalence of GDM in women with IHCP and to compare the feto-maternal outcomes in women with GDM with and without IHCP. We conclude our study in 514 singleton pregnant women that, the prevalence of GDM is not higher in women with IHCP. Significantly higher incidence of preterm delivery, induced labour, and caesarean sections are observed in women with IHCP. Women with GDM with or without IHCP was observed to have no association with any of the parameters such as age, gravidity, hypertensive disorders of pregnancy, hypothyroidism, FGR, MSL, fetal maturity, labour onset, mode of delivery, stillbirth, low APGAR score, and PPH. Since the number of patients in the subgroups women with GDM with IHCP (14) and women with GDM without IHCP (21) was small, further studies with larger sample size recommended to draw a more meaningful conclusion.

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