

Original Research Article

The prevalence of pruritus gravidarum and its relation with intrahepatic cholestasis of pregnancy

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ABSTRACT

Background: Pruritus is a common complaint amongst pregnant woman, affecting 20% of them. This can be physiological or due to some specific dermatological conditions. Among them Intrahepatic cholestasis of pregnancy is most common cause and is characterized by pruritus with derranged liver enzymes and raised serum bile acid levels in the absence of any other liver pathology. It is associated with increased fetomaternal morbidity.

Methods: This was a prospective study, conducted at Bebe Nanki Mother and Child Care Centre, Government Medical College, Amritsar in the Department of Obstetrics and Gynaecology with collaboration of Dermatology Department, from March 2021 to Aug 2022. After taking ethical approval, informed consent, detailed history, clinical and biochemical assessment was done and fetomaternal outcome was recorded.

Results: Prevalance of pruritus was 20.8% amongst pregnant women, of which 24% patients were diagnosed having intrahepatic cholestasis of pregnancy (ICP) and 76% were labelled as NON ICP patients. Among NON ICP patients prevalence of pruritic urticarial papules and plaques of pregnancy was 32.10%. Majority intrahepatic cholestasis of pregnancy patients had moderately affected quality of life. Majority of pruritic patients had normal bilirubin levels and all intrahepatic cholestasis of pregnancy patients had raised serum Alanine transaminase, Aspartate transaminase, bile acids values. Meconium stained liquor, preterm delivery, Low birth weight, cesarean rates, NICU admissions rates were higher in intrahepatic cholestasis of pregnancy patients.

Conclusions: Pruritus in pregnancy is a common condition. Dermatological opinion along with liver function tests should be done to know about the cause and severity of pruritus. Intrahepatic cholestasis of pregnancy (ICP) affects perinatal outcomes. So patients should be closely monitored to improve the fetomaternal outcome.

Keywords: Fetomaternal outcomes, Intrahepatic cholestasis of pregnancy, Meconium stained liquor, Pruritus in pregnancy

INTRODUCTION

Pregnancy is a state of profound immunologic, endocrine, metabolic and vascular changes which are tolerated by the body.¹ Almost all pregnant women (90%) may develop both physiologic and pathologic changes in the skin, nails, and hair which should be recognized and appropriately managed. Pruritus is a common complaint among pregnant women, affecting upto 20% of them.

Causes are- Intrahepatic cholestasis of pregnancy (ICP), pruritic urticarial papules and plaques of pregnancy (PUPPP) / polymorphic eruption of pregnancy (PEP), herpes gestationis (HG), pemphigoid gestationis (PG), atopic eruption of pregnancy (AEP), scabies, insect bites, autoimmune causes, irritation and allergic reactions etc. Intrahepatic cholestasis of pregnancy (ICP) is the most common cause of pruritus of pregnancy. It is defined as pruritus with abnormal liver function tests (LFTs) in the

absence of any rash or any other liver pathology. Mostly it occurs in 2nd and 3rd trimester and it is associated with increased rates of Meconium stained liquor (MSL), preterm labour, intrauterine death (IUD).

Objectives was to study prevalence of pruritus in pregnant women, to assess intensity of pruritus using visual Analogue Score (VAS), to study pruritus in specific dermatoses of pregnancy, intrahepatic cholestasis of pregnancy (ICP), Pruritic urticarial papules and plaques of pregnancy (PUPPP)/ Polymorphic eruption of pregnancy (PEP), Atopic eruption of pregnancy (AEP), Pemphigoid gestationis (PG) etc, and to study impact of ICP on pregnancy outcome.

METHODS

This was a prospective study, conducted on 250 patients in the department of Obstetrics and Gynaecology, Bebe Nanki Mother and Child care Centre in collaboration with Dermatology Department, Government Medical College Amritsar, with permission of Institutional Ethics committee, Government Medical College, Amritsar from March 2021 to August 2022. Prior informed consent was taken from all the cases. Maternal demographic parameters followed by detailed history, clinical and biochemical examination were recorded.

Intensity of pruritus measured by Visual Analogue Scale (VAS) scale. Quality of life measured by Dermatological Life Quality Index (DLQI). Outcome was recorded as pregnancy complications like meconium stained liquor (MSL), preterm premature rupture of membranes (PPROM), preterm delivery, fetal growth restrictions (FGR), route of delivery. Fetal outcomes in view of gestational age at birth, weight at birth, APGAR score at 1 and 5 minutes of life, intrauterine death (IUD), neonatal intensive care unit (NICU) admissions were noted.

Statistical tool

The data was entered into computer and statistical analysis of the results was obtained by using windows based computer software devised with Statistical Packages for Social Sciences (SPSS-22) (SPSS Inc, Chicago, IL, USA).

Inclusion criteria include all antenatal women attending antenatal clinic, Bebe Nanki Mother and Child Care Centre, with complaint of pruritus were included in the study.

Exclusion criteria include the pregnant women with positive serology for Hepatitis A, B, C. and women with autoimmune diseases like primary biliary cirrhosis, women with pre-existing gall bladder diseases and ultrasonographic evidence of gall bladder diseases like gall stones, cholangitis etc.

RESULTS

Mean age of ICP patients and NON ICP was 26.20 ± 4.25 and 25.94 ± 4.67 respectively with p value 0.658, majority of patients were residing in rural area in both the groups ($p=0.274$). Majority of ICP and NON ICP patients were primigravida ($p=0.875$). Majority of patients were having singleton pregnancy (93.33% ICP vs 95.79% NON ICP). Maximum patients presented in their third trimester with insignificant p value= 0.640 . Among multigravida ICP patients, 24% had history of pruritus in previous pregnancy. Mean VAS and DLQI among ICP vs NON ICP was 4.91 ± 1.72 vs 1.29 ± 0.80 and 7.33 ± 2.13 vs 6.03 ± 1.43 respectively with $p=0.001$. Excoriation marks were there in 86.67% ICP vs 88.95% NON ICP patients. Abdominal area was involved in 91.67% ICP patients and 75.79% NON ICP patients ($p=0.008$). Palms and Soles were involved in all ICP patients (Table 1).

Table 1: Demographic profile.

	ICP	NON ICP	P - value
Mean Age	26.20 ± 4.25	25.94 ± 4.67	0.658
Rural Area	73.33%	80%	0.274
Urban area	26.67%	20.00%	
Primigravida	58.33%	59.47%	0.875
Type of pregnancy-			
Singleton	93.33%	95.79%	0.438
Twin	6.67%	4.21%	
Trimester-2nd	38.33%	45.26%	
3rd	61.67%	54.74%	0.64
History of pruritus in previous pregnancy	24%	0%	0.001
Mean VAS	4.91 ± 1.72	1.29 ± 0.80	0.001
Mean DLQI	7.33 ± 2.13	6.03 ± 1.43	0.001
Excoriation marks	86.67%	88.95%	0.631
Area involvement			
Upper limb	21.67%	55.79%	0.001
Abdominal	91.67%	75.79%	0.008
Lower limb	38.33%	60.00%	0.003
Palms and Soles	100%	0.00%	0.001

Serum bilirubin levels were normal in all the NON ICP patients where as 11.67% ICP patients had raised levels (1-3md/dl). 31.67% and 68.33% ICP patients had ALT levels between 45-100U/L and 101-200U/L respectively whereas all NON ICP patients had normal values ($p=0.001$). 35% and 65% ICP patients had AST levels between 45-100U/L and 101-200U/L respectively whereas all NON ICP patients had normal values ($p=0.001$).

Serum bile acids were raised in all ICP patients whereas NON ICP had normal values (Table 2). PPRM was seen in 10% of ICP vs 1.58% NON ICP patients (p=0.002). MSL was found in 43.33% ICP vs 5.79% NON ICP patients (p=0.001). FGR was seen in 16.67% and 1.57% of ICP and NON ICP patients respectively (p=0.001). Preterm delivery was seen in 40% ICP vs 9.47% NON ICP patients (p=0.001) (Table 3).

Table 2: Liver function tests.

	ICP	NON-ICP	P value
Serum bilirubin			
<1mg/dl	88.33%	100%	
1-3mg/dl	11.67%	0%	
Mean	0.96±0.51	0.78±0.12	0.002
ALT (IU/L)			
<44	0%	100%	
45-100	31.67%	0%	
101-200	68.33%	0%	
Mean	132.63±38.21	29.40±7.97	0.001
AST (IU/L)			
<44	0%	100%	
45-100	35%	0%	
101-200	65%	0%	
Mean	149.32±43.02	25.50±6.68	0.001
Serum bile acid (µmol/L)			
<10	0%	100%	
10-40	93.33%	0%	
41-50	6.67%	0%	
Mean	32.71±7.40	3.21±1.01	0.001

Table 3: Fetomaternal complications in pruritic patients.

	ICP	NON-ICP	P value
PPROM	10%	1.58%	0.002
MSL	43.33%	5.79%	0.001
FGR	16.67%	1.57%	0.001
Preterm delivery	40%	9.47%	0.001

(PPROM-preterm premature rupture of membrane, HDP-hypertensive disorder of pregnancy, NPOL-non progress of labour, MSL-meconium stained liquor, FGR-fetal growth restriction).

Table 4: Indication of LSCS in pruritic patients.

Indication of LSCS	ICP(35)		NON-ICP(43)		p-value
	No.	%	No.	%	
Fetal distress with MSL	13	37.14	7	16.28	0.036
Previous 1 LSCS	8	22.86	12	27.91	0.611
Previous 2 LSCS	7	20.00	8	18.60	0.876

Cesarean sections rate was higher in ICP than NON ICP patients (58.33% vs 22.63%) with a significant p value of 0.002. Fetal distress with MSL was the most common indication of cesarean section among ICP patients (37.14% ICP vs 16.28%NON ICP,p=0.036). Cesarean section rate due to previous 1 LSCS was (22.86%ICP vs 27.91%NON ICP,p=0.611),followed by that due to previous 2 LSCS(20% vs 18.60%,p=0.876) (Table 4).

Table 5: Perinatal outcome in pruritic patients.

Perinatal outcome	ICP (60)		NON-ICP (190)		p-value
	N o.	%	No.	%	
Live birth	49	81.67	187	98.42	0.007
Low birth weight babies	28	46.67	10	5.26	0.008
NICU admission	21	35.00	9	4.74	0.001
IUD	11	18.33	3	1.58	0.001
Mean Apgar score at 5 minutes of life	6.31±3.10		7.92±0.64		0.001

Live birth seen among 81.67% ICP patients as compared to 98.42% in NON-ICP patients with p value of 0.007.IUD was seen in 18.33% ICP vs 1.58% NON ICP patients (p=0.001). NICU admissions were more common among ICP patients (35% vs 4.74%,p=0.001),LBW babies were common among ICP patients than NON ICP patients (46.67% vs 5.26%,p=0.008). Mean Apgar score was 6.31±3.10 among ICP than 7.92±0.64 NON ICP patients (p=0.001) (Table 5).

DISCUSSION

Prevalence of pruritus amongst pregnant women in our study was 20.8% which is in consistence with a study done by Szczech J et al 2017 and Kenyon AP et al 2010 showing it as 20.2% and 23% respectively.3,4 Prevalence reported in the literature varies from 14 to 23%.

All pruritic pregnant patients were subjected to liver function tests (LFTs), of which 24% patients had derranged LFTs without any liver pathology and were labelled as ICP patients, as per definition of ICP, depicting ICP as the common cause of pruritus in pregnancy. Nair AS et al 2017, has reported the prevalence of ICP as 18.18% while Chander R et al 2011, has reported 54.2% which is quite high from the above two studies.^{5,6}

In our study, overall prevalence of ICP in all pregnant patients with or without pruritus is 5% Different authors have given different prevalence as 4.08%, 3.3%, 3.34% and 2.81% by Arora S et al 2021, Bassi R et al 2012, Uniyal S et al 2019 and Mitra B et al 2020 respectively.⁷⁻

¹⁰ Authors have given different incidences of different types of dermatoses of pregnancy as shown in the Table 6. In our study, most common area involved was

abdominal area in 91.67% ICP and 75.79% NON ICP patients. Szczech J et al 2017 also reports that abdominal area was involved in 88.10% of pruritic patients.³

Table 6: Incidences of type of dermatoses of pregnancy by different authors.

Authors name	PUPPP	AEP (prurigo)	PG	Tinea corporis	Scabies
Nair AS et al 2017 ⁵	63.60%	16.60%	1.50	-	-
Uniyal S et al 2019 ⁹	28.4%	18.34%	9.17%	17.27%	20.48
Chander R et al 2011 ⁶	7.1%	38.5%	0%	-	-
Kabir MH et al 2022 ²³	44.82%	21.53%	0%	-	-
Chopra D et al 2017 ²⁴	7%	13%	1%	-	-
Our study	32.11%	11.58%	0.53%	14.74%	17.89%

Table 7: Incidence of MSL and Preterm delivery in ICP patients by different authors.

Fetomaternal outcome	Mitra B et al 2020 ¹⁰	Gupta S et al 2022 ¹⁹	Arthuis C et al 2022 ²²	Alsulyman et al 1996 ²⁵	Jhirwal M et al 2022 ¹³	Our study
MSL	29.93%	18.37%	18.6%	25.3%	12.5%	43.33%
Preterm delivery	20.44%	31.12%	15.7%	14%	-	24%

Table 8: Fetal outcomes in ICP patients by different authors.

Fetal outcome	Arora S et al 2021 ⁷	Hablani K et al 2022 ¹⁶	Gupta S et al 2022 ¹⁹	Alsulyman et al 1996 ²⁵	Mitra B et al 2020 ¹⁰	Present study
NICU admissions	2%	3.8%	20.41%	41.5%	23.36%	35%
IUD	2%	10.00%	3.06%	2.7%	2.18%	18.33%

In our study palms and soles were involved in all ICP patients so it is suggested that it should be differentiated from scabies or any drug reactions. Kumar S et al 2018 also shows 100% involvement of palms and soles among ICP patients.¹¹

In our study, 11.67% of ICP patients had raised serum bilirubin level between 1-3mg/dl, whereas study done by Padmaja M et al 2010, Jhirwal M et al 2022 shows 18.4%, 7.24% respectively. All ICP patients had raised LFTs. similar to the study done by Arora S et al 2021 and Padmaja M et al 2010 showing liver transaminases raised in 100% and 97.8% of patients respectively. In our study, serum bile acid levels were increased in all the patients of ICP. Similar results were seen in a study done by Gupta V et al 2021 which shows all ICP patients had raised serum bile acid value. Arora S et al 2021 reports 89% patients had raised bile acid value >14µmol/l.¹²⁻¹⁵

In the present study, 10% ICP patients had preterm premature rupture of membrane (PPROM). This in consistence with a study done by Padmaja M et al 2010 and Hablani K et al 2022 which shows 8.9% and 11.3% of ICP patients had PPRM.^{12,16} Different studies gives different incidences of MSL and Preterm delivery as showing in Table 7.

In our study, cesarean rate was higher among ICP patients (58.33% vs 22.63% NON ICP patients), whereas studies done by Jhirwal M et al 2022, Arora S et al 2021,

Kant A et al 2018, Naga VK et al 2019, Gupta S et al 2022, Garg N et al 2020 shows cesarean rate of 31.58%, 41.7%, 56.81%, 34%, 36.22%, 37.50% respectively among ICP patients.^{13,14,17-20} The higher rate of cesarean section in our study may be explained as ours being a referral hospital catering nearby districts.

In the present study, cesarean sections done due to fetal distress with MSL seen in 37.14% of ICP patients vs 16.28% of NON ICP, (p=0.036), whereas study done by Gupta S et al 2022 show rate of cesarean sections due to MSL as 18.30% which is lower than our study.¹⁹

In our study, rate of cesarean sections due to previous 1 cesarean section and previous 2 cesarean section was 22.86% and 20% respectively vs 27.91% and 18.60% respectively in NON ICP patients (p value=0.611). A study done by Ghosh S et al 2013 shows a rate of cesarean sections due to previous cesarean section as 11.26%, which is lower than our study.²¹

In our study, low birth weight babies (LBW) were found in 46.67% in ICP vs 5.26% in NON ICP patients (p value=0.008), whereas study done by Jhirwal M et al 2022, Kant A et al 2018, Gupta S et al 2022, shows LBW rate of 15.79%, 22.72%, 14.29%, respectively in ICP patients.^{13,17,19}

Fetal outcomes in ICP patients by different authors is reported as showing in Table 8.

In the present study, mean Apgar score at 5 minutes of life of babies born to ICP patients is 6.31 ± 3.10 and that of NON ICP patients is 7.92 ± 0.64 , $p = 0.001$, 66.67% babies born to ICP patients had Apgar score more than 7, 15.00% had Apgar score 4-6 and 18.33% had Apgar score 0-3. Whereas study done by Jhirwal M et al 2022, Hablani K et al 2022, Gupta S et al 2022, Arthuis C et al 2020 shows Apgar score <7 in 1.33%, 6.3%, 10.20%, 2.9% respectively babies born to ICP patients.^{13,16,19,22}

Limitations

Out of 1200 antenatal women, 250 cases of pruritus was there. Of these 250 cases, 60 cases had ICP and 190 cases were of NON ICP with pruritus. Their fetomaternal outcomes were recorded. As the number of cases were less in our study so further studies needed to evaluate the results.

CONCLUSION

Pruritus in pregnancy is a common condition. Dermatological opinion along LFTs should be done to know about the cause and severity of pruritus. Intrahepatic cholestasis of pregnancy (ICP) though a benign maternal disease, affects perinatal outcomes. So patients should be closely monitored and treated to improve fetomaternal outcomes.

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