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Research Article

Pruritus In Pregnancy and Its Relation to Development of Obstetrics Cholestasis with Co-Relation to Mode of Delivery: A Hospital Based Observational Study

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ABSTRACT

Aim: The aim was to study different causes of pruritus in pregnancy and its relation to development of intrahepatic cholestasis of pregnancy (IHCP) with co-relation to mode of delivery in these patients.
Materials and Methods: This was a hospital-based prospective observational study conducted in a tertiary care hospital by analysing a prospectively maintained database over a period of 1.5 years. Data from 3523 pregnant females was analysed out of which 352 pregnant females were found to be suffering from pruritus and 42 were found to be having IHCP.
Results: Prevalence of pruritus amongst pregnant women in our study was 9.99%. Serum bile acid levels were increased in all the patients of IHCP. Most of these patients underwent Caesarean section ($p = 0.081$).
Conclusion: Pruritus in pregnancy is a relatively common symptom, affecting nearly 10% of pregnant women in our study. A significant subset of these patients was diagnosed with intrahepatic cholestasis of pregnancy (IHCP), which was consistently associated with elevated serum bile acid levels. Although not statistically significant, a higher rate of Caesarean section was observed among patients with IHCP. Early recognition and monitoring of pruritus in pregnancy are therefore crucial to ensure timely diagnosis of IHCP and to optimize maternal and fetal outcomes.

Keywords*: Pruritus in pregnancy, Intrahepatic cholestasis of pregnancy (IHCP), Serum bile acids, Caesarean section, Maternal outcomes, Obstetric complications*

INTRODUCTION

During pregnancy, many symptoms and signs related to skin are common, most of which are believed to be physiological due to hormonal changes. Pruritus is one of these common skin symptoms during pregnancy and is said to affect about 10 to 20% of pregnant women although there is great variation according to the authors. [1-3] Many pregnant women complain about intense itching and seek medical advice, rarely leading to early delivery. [4] Pruritus is chronic if symptoms last longer than 6 weeks. Chronic pruritus is an overlooked symptom but is responsible for impairment of quality of life.

Pruritus of pregnancy may be idiopathic or may be associated with pregnancy-specific conditions such as Atopic Eruption of Pregnancy [AEP], Polymorphic Eruption of Pregnancy [PEP], Pemphigoid Gestationis [PG] and Intrahepatic Cholestasis of Pregnancy [IHCP]. Pruritus may also arise from dermatoses that coincidently develop during pregnancy, exacerbation of pre-existing dermatoses, and physiological skin changes in pregnancy. [5]

Atopic Eruption of Pregnancy includes both patients with exacerbation of pre-existing atopic dermatitis (about 20% of patients) and patients experiencing skin manifestations for the first time during pregnancy. [6,7] Polymorphic Eruption of Pregnancy is a benign self-limiting pruritic inflammatory disorder which usually occurs in the third trimester or immediately postpartum (in about 15% of cases). [8-9] Pemphigoid Gestationis is a rare self-limiting bullous autoimmune disease which also usually occurs in the late third trimester, related to HLA-DR3 and DR4. [10-11]

Intrahepatic Cholestasis of Pregnancy (IHCP), also known as obstetric cholestasis (OC) is the most common liver disease related to pregnancy [12] which occurs in the late second and early third trimester and is characterized by pruritus with increased serum bile acids and deranged liver function tests.

IHCP is associated with an increased risk of adverse obstetrical outcomes which include stillbirth, respiratory distress syndrome, meconium passage and foetal asphyxia [13]. A higher incidence of IHCP is observed with a prior history of IHCP, chronic liver disease, chronic hepatitis C, multifetal pregnancy and advanced maternal age. The aetiology of IHCP is poorly understood and is thought to be complicated and multifactorial. There appears to be a relation between cholesterogenic properties of reproductive hormones in genetically susceptible women and IHCP.

Clinical triad of the disease includes - severe pruritus, jaundice starting 2–4 weeks after the onset of pruritus and elevated maternal bile acids (>19micromol/L). Pruritus classically begins on the palms and soles which may become generalized and more intense with progression of pregnancy. However, there are classically no primary skin lesions. Maternal complications associated with IHCP include- increased risk of dyslipidaemia, coagulopathy, Premature Rupture of Membranes (PROM), Preterm Premature Rupture (PPROM), caesarean section and post-partum haemorrhage.

The severity of IHCP is categorised by the serum total bile acids levels (RCOG). The diagnosis of Intrahepatic Cholestasis of Pregnancy (IHCP) should be considered in pregnant women who have itching with normal appearance of skin and raised peak random total bile acid concentration of 19micromol/L or more (RCOG). [14]
Royal College of obstetricians and gynaecologists (RCOG) Green Top Guidelines No 43 (2022):-

Serum Bile Acid Level (micromol/L)	Category	Risk of Stillbirth	Delivery
<19	Gestational Pruritus	Normal risk	At term
19-39	Mild IHCP	Similar to background risk	At term (40wks)
40-99	Moderate IHCP	Similar to background risk	38-39wks
>100	Severe IHCP	Higher than background risk	35-36wks

Conventionally, the discussion of pruritus in pregnancy has been focused on pregnancy-specific dermatosis. However, coexistent dermatological disorders and underlying neurologic, psychological, and systemic conditions are also responsible for pruritus.

MATERIALS AND METHODS

It was a tertiary care hospital based prospective observational study done to find out relation of pruritus with Intrahepatic Cholestasis of Pregnancy and with mode of delivery in these patients conducted over a period of one and a half year. All the antenatal patients that presented to the hospital with the symptoms of pruritus were included in the study. Patients with primary skin lesions, diabetes, chronic kidney disease, other liver diseases, HIV positive and patients having history of OCPs intake were excluded from the study.

Total 3523 pregnant women were screened during the study period. Patients with pruritus were identified in maternity care units. A detailed history was taken in a pre-designed proforma including demography, patient's hygiene, chief complaints related to skin, presence of itching, pre-existing skin lesions and its onset, history of jaundice, fever, vaginal discharge, family history of similar lesions, exacerbating or relieving factors, associated medical or skin disorders etc. Complete cutaneous examination was carried out in all cases. The diagnosis of IHCP was based on clinical examination, generalized pruritus in the absence of any other dermatologic condition, laboratory results with serum bile acids greater than 19mmol/L and no evidence of viral hepatitis, negative assays for Hepatitis B surface antigen and Hepatitis A and C antibodies and normal ultrasonography of the liver and biliary tract. In case of any specific dermatoses, patient was reviewed in the outpatient clinic in the Department of Dermatology. For pre-existing skin conditions, any evidence of exacerbation or remission was recorded. Investigations were done as advised by dermatologist to confirm diagnosis. If required, skin biopsies were done in a few cases to confirm the diagnosis.

Assessment of pruritus remains a challenge due to its subjective character. Itch questionnaires were used to evaluate the severity of pruritus. The 12-Item Pruritus Severity Scale (12-PSS) [15] was used to differentiate between patients suffering from mild, moderate, and severe pruritus. The 12-PSS was indicated as covering several dimensions of itch characteristics: localization, frequency, intensity, scratch response, affective qualities, sleep disturb ances, and quality of life. The 12-PSS bands best define the categories of mild (3–6 points), moderate (7–12 points) and severe pruritus (13–22 points).

OBSERVATIONS AND RESULTS

Out of 3523 total pregnant females screened, 352 pregnant women were found to be suffering from pruritus. Among all the patients suffering from pruritus, 42 were found to have IHCP.

Mean age of patients presented were 28.11 years of age with majority being primigravida 224 cases (63.6%) than multigravida 128 cases (36.4%). Most of the patients were having singleton pregnancy with maximum patients presenting in their third trimester. Among multigravida, 24% had history of pruritus in previous pregnancy. The pruritus was mild in 119 cases (33.8%), moderate in 228 cases (64.8%), and severe pruritus in only 5 cases (1.4%) as assessed by 12-item Pruritus Severity Scale. Prevalence of pruritus amongst pregnant women in our study was 9.99%. All pruritic pregnant patients were subjected to liver function test (LFT). Caesarean section rate was higher among these patients with p value of 0.081 being statistically significant.

Table 1: Correlation of classification in relation to serum bile acid classification of patients studied

CLASSIFICATION	BILE ACIDS				Total
	Normal(<19mmol/L)	Mild Obstetric Cholestasis(19-39mmol/L)	MODERATE Obstetric Cholestasis(40-99mmol/L)	SEVERE Obstetric Cholestasis(>100 mmol/L)	
GESTATIONAL PRIRITUS	60(19.4%)	15(68.2%)	10(52.6%)	1(100%)	86(24.4%)
GESTATIONAL PRURITU(IHCOP)	1(0.3%)	10(45.5%)	9(47.4%)	1(100%)	21(6%)
NON-GESTATIONAL PRURITUS	250(80.6%)	7(31.8%)	9(47.4%)	0(0%)	266(75.6%)
Total	310(100%)	22(100%)	19(100%)	1(100%)	352(100%)

P≤0.001**, Significant, Chi-Square Test

Table 2: Bile acids- frequency distribution of patients studied in relation to initial presentation of pruritus.

BILE ACIDS	INITIAL PRESENTATION OF PRURITUS			Total
	1ST TRIMESTER	2ND TRIMESTER	3rd TRIMESTER	
<19	9(90%)	84(86.6%)	217(88.6%)	310(88.1%)
>19	1(10%)	13(13.4%)	28(11.4%)	42(11.9%)
Total	10(100%)	97(100%)	245(100%)	352(100%)

P=0.863, Not Significant, Chi-Square Test

Table 3: 12-item pruritus severity scale- frequency distribution of patients studied in relation to initial presentation of pruritus

12-ITEM PRURITUS SEVERITY SCALE	INITIAL PRESENTATION OF PRURITUS			Total
	1ST TRIMESTER	2ND TRIMESTER	3rd TRIMESTER	
3-6	5(50%)	30(30.9%)	84(34.3%)	119(33.8%)
7-11	5(50%)	64(66%)	159(64.9%)	228(64.8%)
12-22	0(0%)	3(3.1%)	2(0.8%)	5(1.4%)
Total	10(100%)	97(100%)	245(100%)	352(100%)

P=0.344, Not Significant, Fisher Exact Test

Table 4: Correlation of ALP, AST, ALT in relation to serum bile acid of patients studied

Variables	SERUM BILE ACIDS				Total	P Value
	Normal(<19mmol/L)	Mild Obstetric Cholestasis (19-39mmol/L)	MODERATE Obstetric Cholestasis (40-99mmol/L)	SEVERE Obstetric Cholestasis (>100 mmol/L)		
ALP						
<44	2(0.6%)	0(0%)	0(0%)	0(0%)	2(0.6%)	0.965
>44	308(99.4%)	22(100%)	19(100%)	1(100%)	350(99.4%)	
AST						
8-33	12(3.9%)	1(4.5%)	0(0%)	0(0%)	13(3.7%)	0.840
>33	298(96.1%)	21(95.5%)	19(100%)	1(100%)	339(96.3%)	
ALT						
4-36	17(5.5%)	2(9.1%)	1(5.3%)	0(0%)	20(5.7%)	0.904
>36	293(94.5%)	20(90.9%)	18(94.7%)	1(100%)	332(94.3%)	
Total	310(100%)	22(100%)	19(100%)	1(100%)	352(100%)	

Chi-Square Test/Fisher Exact Test

Table 5: Correlation between mode of delivery and serum bile acid levels

Mode of Delivery	BILE ACIDS				Total
	Normal(<19mmol/L)	Mild Obstetric Cholestasis (19-39mmol/L)	MODERATE Obstetric Cholestasis (40-99mmol/L)	SEVERE Obstetric Cholestasis (>100 mmol/L)	
LSCS	130(41.9%)	14(63.6%)	11(57.9%)	1(100%)	156(44.3%)
NVD	180(58.1%)	8(36.4%)	8(42.1%)	0(0%)	196(55.7%)
Total	310(100%)	22(100%)	19(100%)	1(100%)	352(100%)

P=0.081+, Significant, Chi-Square Test

DISCUSSION

Prevalence of pruritus amongst pregnant women in our study was 9.99% which was lower than the study done by Szczech J et al 2017 [16] and Kenyon AP et al 2010 showing it as 20.2% and 23% respectively. Prevalence reported in the literature

varies from 14 to 23%. [17] All pruritic pregnant patients were subjected to liver function tests. In our study, overall prevalence of IHCP in all pregnant patients with pruritus was about is 11.93 %. Most of IHCP 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. In our study, serum bile acid levels were increased in all the patients of IHCP. Similar results were seen in a study done by Gupta V et al 2021 which shows all IHCP patients had raised serum bile acid value. Arora 48 S et al 2021 reports 89% patients had raised bile acid value >19μmol/L. Most of these patients underwent caesarean section as the mode of delivery (57.33%) with p value of 0.081 being statistically significant 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 caesarean rate of 31.58%, 41.7%, 56.81%, 34%,36.22%,37.50% respectively among ICP patients. The higher rate of caesarean section in our study may be explained as the hospital being a tertiary referral centre catering high risk patients from the adjacent districts.

CONCLUSION

Our study revealed that Pruritus in Pregnancy is a common condition causing anxiety, stress and discomfort to the patient. Our study revealed that majority (88.06 %) of the cases were non-IHCP and therefore dermatological opinion should be sought out to rule out any primary skin disorders. Serum bile acids should be done to assess the severity of IHCP with caesarean section rate being higher among these patients.

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