Original Article

"The Pregnant's Itch"- A Conglomeration of Clinically Significant Cases of Intrahepatic Cholestasis of Pregnancy

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ABSTRACT

Introduction: Intrahepatic cholestasis of pregnancy (IHCP) is a multifactorial disorder characterised primarily with pruritus and raised serum random bile acid level.Diagnosis of IHCP is of prime importance in reducing stillbirth rates. The stillbirth rate, according to the Royal College of Obstetricians and Gynaecology guidelines, varies from 0.18% to 0.72%.1

With an Out Patient Department (OPD) average of around 500-600 patients per month, 4-5% patients present with complaints of generalized itching all over the body. Out of it, 0.7-0.8% is the prevalence of intrahepatic cholestasis of pregnancy (IHCP) at our institute.

Aim: To review different cases of pruritus in pregnancy, thereby diagnosis and management of intrahepatic cholestasis of pregnancy.

Methods and Materials: A prospective observational study conducted at a tertiary care hospital over a duration of 6 months.

Conclusion: A prompt suspicion and an early diagnosis is the key for effective management of the patients with IHCP. Regular monitoring of fetal well being using daily fetal kick count, non-stress test and obstetric doppler, plays an important role in management of these patients.

Key words: Itching, Intrahepatic cholestasis, Pruritis in Pregnancy, Bile acid, IHCP, Still birth

INTRODUCTION

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With an Out Patient Department (OPD) average of around 500-600 patients per month, 4-5% patients present with complaints of generalized itching all over the body. Out of it, 0.7-0.8% is the prevalence of intrahepatic cholestasis of pregnancy (IHCP) at our institute.

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CASES

Case 1

A 34-year-old, G2P1L1, previous vaginal delivery, at 34+3 weeks of gestation presented in OPD with complaints of itching all over body. Her serum random bile acid was 25 micromol/L. A complete workup was done with investigations as mentioned in Table 1. The patient was started on T. Udiliv 300mg twice a day. Biophysical profile including Non stress test and Obstetric Doppler sonography was performed at regular intervals and fetal well being monitored. Repeat bile acid after a week was 17 micromol/L and the patient continued the same dose till delivery.Elective induction of labour was performed at 40 weeks of gestation. The patient delivered a healthy male child of 2.9 kg.

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Case 2

A 35-year-old Primigravida,referred from a maternity hospital for deranged bile acid level. The patient presented to us at 24 weeks of gestation with generalised itching all over the body. Serum random bile acid level was 32 micomol/L. After a complete workup, the patient was started on T. Udiliv 300 mg twice a day. Growth scan demonstrated a normal interval growth. Steroid cover completed at 28 weeks and non stress test was repeated every fortnightly from 32 weeks. Repeat random bile acid at 36 weeks of gestation was 8 micromol/L. Obstetric Doppler suggested normal fetal growth and normal flows at 37 weeks of gestation. The patient went into spontaneous labour at 38+2 weeks of gestation. Intrapartum monitoring continued and artificial rupture of membranes was done at cervical dilatation of 4 cm, which revealed thick meconium stained amniotic fluid. An emergency cesarean section was done in view of meconium stained amniotic fluid with variable decelerations. The patient delivered a female child of 2.5 kg, with an APGAR of 8/10 at 1 minute of life and 9/10 at 5 minutes of life.

Case 3

A 25-year-old, Primigravida, was admitted from OPD at 35 weeks of gestation in view of itching all over body. Her serum random bile acid level was 20 micromol/L. After a complete blood investigation, obstetric doppler study revealed the presence of internal echoes in amniotic fluid. Also, the non stress test showed a non-reassuring tracing. Thereby, an emergency cesarean section was done in view of a non-reassuring non stress test in a case of intrahepatic cholestasis of pregnancy with internal echoes ?meconium flakes with poor BISHOP score. A single dose of betamethasone 12mg intramuscular was given to the mother 6 hours prior to delivery. The patient delivered a male child of 2.1 kg with APGAR of 8/10. Bag and mask ventilation was initiated by neonatologists in view of delayed cry and persistent intercostal retractions. The baby was shifted to NICU for observation and management. The patient and a healthy baby were discharged on day 10 of cesarean section.

Case 4

A 35-year-old, married for 17 years, Primigravida, at 32+2 weeks of gestation was referred from a maternity hospital in view of a deranged liver function test, as mentioned in Table 1. The patient presented with complaints of generalized itching with yellowish discoloration of sclera. The patient was a known case of Hepatitis B reactive status. On investigations, Hepatitis B viral load was above the linear line, Total bilirubin 3.4, SGOT- 459 U/L, SGPT-194U/L, serum random bile acid level was >200 micromol/L. Patient and relatives counselled regarding the high risk status of her pregnancy. Steroid cover completed. Strict daily fetal kick count monitoring done. Ultrasound obstetric doppler study revealed appropriate for gestational age (AGA) fetus with normal flows. Twice a week non stress tests were done and noted to be reactive. Gastromedicine reference was taken and required investigations were done. The patient was started on T. Udiliv 300 mg thrice a day. The plan was to terminate the pregnancy at 35-36 weeks of gestation. But at 33+4 weeks of gestation, the patient complained of decreased fetal movements. An Intrauterine fetal demise was noted on ultrasound. Induction of labour was done and the patient delivered a fresh stillborn male of 2.7 kg. Intrapartum 4 pint Fresh frozen plasma were transfused in view of INR of 3.6. Post delivery, liver function tests normalized subsequently.

Table 1: Investigation chart

	Case 1	Case 2	Case 3	Case 4
Hemoglobin (g/dL)	11.2	10.4	9.6	12.1
WBC count (number/cumm)	7630	9820	10730	9260
Platelet (number/cumm)	167000	205000	255000	128000
PT (secs)	14.3	12.4	13.0	17.1
INR	1.2	1.03	1.08	1.49
Total bilirubin (mg/dL)	0.7	0.5	0.8	3.4
Direct bilirubin (mg/dL)	0.3	0.2	0.3	2.8
SGOT (IU/L)	28	22	35	459
SGPT (IU/L)	30	15	40	194
Total protein (g/dL)	6.3	5.8	6.4	4.7
Albumin (g/dL)	3.6	3.3	3.8	2.5
BUN (mg/dL)	9	7	8	10
Creatinine (mg/dL)	0.7	0.6	0.9	0.8
Anti HIV	Non reactive	Non reactive	Non reactive	Non reactive
Anti HBsAg	Non reactive	Non reactive	Non reactive	Reactive
Anti HCV	Non reactive	Non reactive	Non reactive	Non reactive
Anti HAV	Non reactive	Non reactive	Non reactive	Non reactive
Anti HEV	Non reactive	Non reactive	Non reactive	Non reactive
Ultrasonography (Abdomen + Pelvis)	No abnormality detected	No abnormality detected	No abnormality detected	Altered liver echotexture

DISCUSSION

Intrahepatic cholestasis of pregnancy (IHCP) is a multifactorial disorder, requiring a comprehensive management protocol. There are a conundrum of clinical features that mimic IHCP. Pruritus is the hallmark feature of IHCP and when associated with raised serum random bile acid levels confirms the diagnosis. It mostly presents in the third trimester, but can even present in early trimesters. Some differentials of IHCP include Urticaria, Pruritus of Pregnancy, or any other specific dermatological conditions. Thereby, we must seek a dermatology opinion to exclude the differentials. Intrahepatic cholestasis of pregnancy is often associated with slight derangement of liver enzyme levels and hence liver function tests

must be carried out in all patients with IHCP. A gastromedicine reference must be sought in cases of severe IHCP and very early or atypical presentation of IHCP. Based on serum random bile acid levels, IHCP is divided into 3 classes as shown in Table 2.

Table 2: Classification of intrahepatic cholestasis of pregnancy (adopted from Girling J, Knight CL, Chappell L; on behalf of the Royal College of Obstetricians and Gynaecologists. Intrahepatic cholestasis of pregnancy. BJOG. 2022)

Diagnosis	Clinical features
Gestational pruritus	Itching and peak bile acid concentrations <19 micromol/L[a]
Mild ICP	Itching and raised peak bile acid concentrations 19–39 micromol/L
Moderate ICP	Itching and raised peak bile acid concentrations 40–99 micromol/L
Severe ICP	Itching and raised peak bile acid concentrations ≥100 micromol/L

Note: Peak bile acid concentrations refer to the highest bile acid concentration recorded during a woman's pregnancy. Thus a woman's diagnosis may progress in severity during pregnancy.

[a]The upper limit of normal bile acid concentrations in pregnancy is 18 micromol/L.[10]

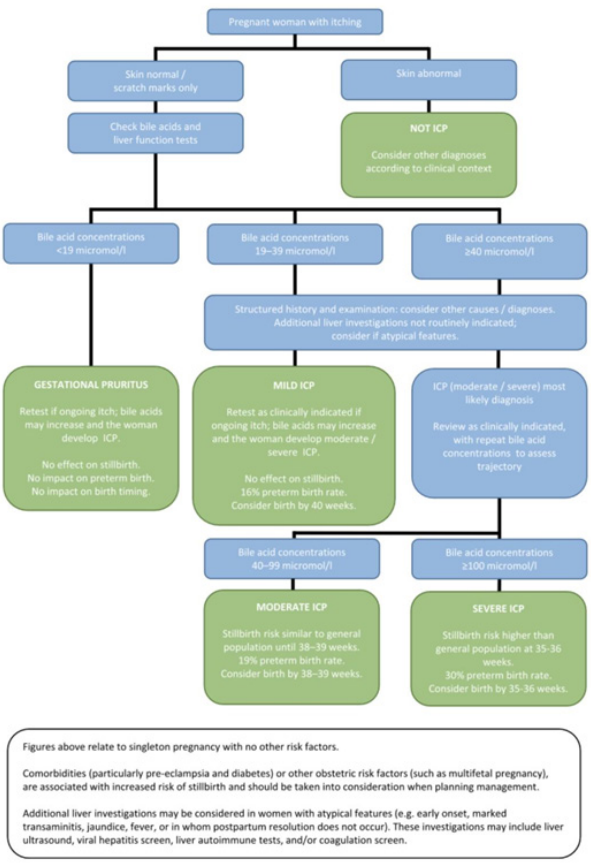

Figure 1: Management of Intrahepatic cholestasis of pregnancy (adopted from Girling J, Knight CL, Chappell L; on behalf of the Royal College of Obstetricians and Gynaecologists. Intrahepatic cholestasis of pregnancy. BJOG. 2022)

There is no evidence that routine medical treatment improves maternal raised bile acid concentrations or perinatal outcomes. Topical emollients, antihistaminics and ursodeoxycholic acid (Udiliv) can be used but evidence does not support a strong indication for administering the following drugs.[2]

The most dreaded complication of IHCP is stillbirth. The exact pathophysiology of stillbirth is uncertain but could be due to sudden raised bile acids leading to sudden fetal arrhythmia and fetal anoxia or acute placental vessel spasm.[3] There is an increased chance of meconium stained amniotic fluid in cases of IHCP.[4] The Management of the condition is based on bile acid level and weeks of gestation, as outlined in Figure 1.

The following case series is documented over a period of 6 months at a tertiary care hospital in India with an average footfall of 500-600 OPD antenatal patients in a month. Out of which, 28 patients presented with generalised itching. However, when serum bile acid levels were checked in these patients, only 4 patients had clinically significant IHCP i.e. serum random bile acid level >19 micromol/L. Out of the 4 cases, 2 had meconium stained amniotic fluid while one patient had a sudden intrauterine fetal demise. Although, the patient with intrauterine fetal demise was diagnosed with acute-on-chronic viral hepatitis with features of liver cell failure. (Figure 2 and 3). Therefore, maternal and neonatal outcomes depend largely on timely diagnosis, fetal well-being monitoring, associated comorbidities and termination at specific weeks of gestation.

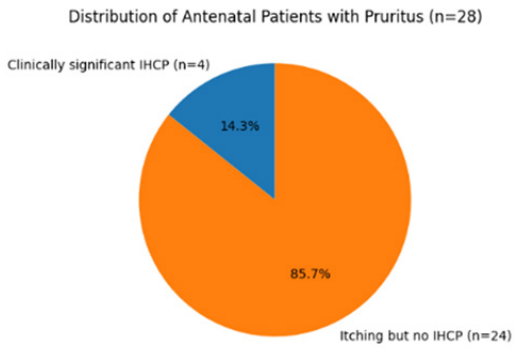

Figure 2: Distribution of antenatal patients with pruritis.

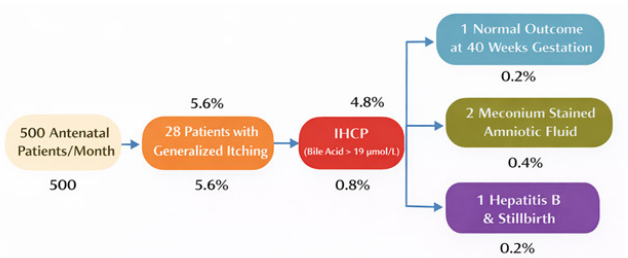

Figure 3: Outcomes of patients with generalised itching attending the antenatal OPD in a tertiary care hospital over a period of 6 months.

CONCLUSION

IHCP constitutes a small proportion of patients, but diagnosing the condition upholds greater importance for both maternal and fetal

well being. A prompt suspicion with early diagnosis can reduce risk of associated stillbirth. Fetal well being monitoring using daily fetal kick count measurement by mother along with non-stress test and obstetric doppler studies at regular intervals plays an important role in determining perinatal outcomes. Antenatal counselling of patients and relatives regarding adverse outcomes in cases of IHCP is a must. Finally, IHCP must be dealt with in a multidisciplinary manner with intense monitoring to provide optimum maternal and neonatal outcomes.

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