ORIGINAL ARTICLE

DIAGNOSIS AND NEONATAL OUTCOME IN OBSTETRIC CHOLESTASIS

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Background: Gestational cholestasis can cause preterm delivery, meconium staining of liquor, foetal distress, intrauterine foetal death, Respiratory Distress Syndrome and NICU admission. Fetomaternal surveillance can be done by serial assessments of serum bile acid (SBA) levels, liver function tests, foetal kick count chart, foetal cardio-tocography and serial ultrasound assessments along with routine antinatal care. This retrospective study was conducted to find alternative methods of foetal surveillance in case of non availability of SBA assessment. **Method:** This study was conducted at AERO Hospital, Hasanabdal from Jan 2013 to Jul 2015, and 69 patients aged 18–40 years with gestational cholestasis and singleton pregnancy after excluding other causes of pruritis and deranged liver function tests were included in study and above mentioned parameters assessed. All patients were administered Ursodeoxycholic acid and Dexamethasone 12 mg, two doses 12 hours apart. **Results:** Twenty-five percent patients underwent preterm delivery, 25% had meconium stained liquor, 2.8% had intrauterine death, and 1.4% had early neonatal death. Greater the grade of pruritis and higher the abnormality of ALT were, the higher the incidence of foetal complication was. **Conclusion:** Pregnancies with getational cholestasis monitored in this way have reasonably good foetal outcome even in the absence of SBA monitoring but required more frequent visits by mothers and vigilance of obstetrician.

Keywords: Gestational Cholestasis, Pruritis, Liver function test, Foetal Outcome
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INTRODUCTION

Gestational cholestasis is a multifactorial pregnancy associated reversible condition presenting mainly in late 2nd or 3rd trimester; characterized by pruritis, deranged liver function tests (LFTs) and elevated Serum Bile Acid levels (SBA) which resolve after delivery.[1,2] It causes maternal morbidity but foetal consequences are more devastating. It can cause preterm labour, meconium aspiration syndrome, intrauterine foetal death, and respiratory distress syndrome.[3] Gestational cholestasis leading to intrauterine foetal death is a major issue in management of these patients. It is a sudden event and generally there is no evidence of placental insufficiency.[4,5] Women with severe and prolonged biochemical abnormalities are more likely to have poor foetal outcome.[4]

Different techniques like Foetal Kick Count chart, Cardio-tocography (CTG), serial obstetrical ultrasounds, amniocentesis, transcervical amnioscopy for meconium identification after 36 weeks of gestation are used to prevent foetal complications.[4] None of these alone is of absolute significance in making decision about foetal outcome.

Gestational cholestasis affects 1.2–1.5% of Pakistani/Asian women during pregnancy. The most accurate diagnostic biochemical parameter is total SBA above upper normal value of 11 μmol/L.[6] For more precise diagnosis lithocholic acid (LCA) and ursodeoxycholic acid (UDCA)/LCA ratio is used. In our set-up, diagnosis is mainly based on clinical picture, i.e., pruritis (severity and distribution) dark coloured urine, steatorrhoea and deranged LFTs.[7] Amongst LFTs transaminases specially Alanine Transaminase (ALT) measurement is of prime importance. Transminase activity can rise up to 20 times normal.[8,9] The upper normal limit of transaminase (ALT) throughout normal pregnancy is 20% lower than the non-pregnant range.[4,5] Increased alkaline phosphatase during pregnancy is of placental origin, so it is not significant for the assessment in patients with gestational cholestasis.[11] Serum bilirubin usually remains within normal limits but may be raised in 10–22% cases.[10–12] Clinical jaundice is rare.[8]

As gestational cholestasis can have serious foetal consequences, its proper diagnosis and management is important to improve foetal outcome. This study was conducted to find out correlation between pruritis, deranged LFTs, especially ALT, and foetal outcome. The main parameter studied was pruritis. Pruritis is defined as an unpleasant sensation that provokes scratching and this is a very subjective feature.[13] It is also a common feature of many pathologies involving hepatic, renal, dermatological and gynaecological systems. For its exact evaluation we need a definite scoring system. None has been exactly agreed upon till now as different aspects like duration, distribution, intensity need separate considerations. In this study, we used Verbal Rating Scale (VRS) for evaluation of pruritis. In VRS, patients verbally expressed degree of pruritis,

experienced. Phan *et al* described four point scale, another group proposed five point scale (none, mild, moderate, severe and very severe) which was used in this study.[13,14] Grade-1 or Mild described as intermittent, slight nocturnal pruritis, grade-2 or moderate as continuous diurnal slight to moderate pruritis, grade-3 or severe as more intense, and grade-4 or very severe pruritis as severe but with insomnia and itch lesions.[13] Patients with grade 1–4 pruritis were included in study. Patients in these four categories were assessed for steatorrhoea, dark colour urine, foetal movements, abnormal transaminases, CTG, gestation at delivery, presence or absence of meconium, APGAR score at five minutes, intra uterine deaths, NICU admission, early neonatal death. Results were compiled and analyzed.

MATERIAL AND METHODS

This retrospective observational study was conducted at AERO Hospital from Jan 2013 to Jul 2015. Sixty-nine patients with pruritis, deranged LFTs, aged between 18–40 years and with singleton pregnancy, with no co-morbidities were included in study irrespective of their parity.

Patients were thoroughly interviewed for present complaints, past medical, surgical and family history. Present complaints like severity of pruritis, colour of urine, steatorrhoea, foetal movements and bleeding tendencies were asked and noted. Blood CP, Urine R/E, Random blood sugar, HBS Ag/HCV, LFTs, Urea, Creatrine, Uric Acid, PT, APTT were done for all patients and recorded. Ultrasonography for liver and foetal assessment was done. Routine antenatal care and supplementation were provided. For foetal assessment Kick Count Chart, CTG, and Serial Growth Scan were done. Patients were advised to visit weekly and all tests except HBS Ag/HCV screening were repeated and findings of pruritis, steatorrhoea, high coloured urine and bleeding noted.

All patients were given injection dexamethasone 12 mg i/m (2 doses 12 hour apart) at 32 weeks. All aspects of disease were addressed against the pruritis score which was assessed by VRS. All diagnosed patients were given ursodeoxycholic acid 10–15 mg/Kg/day. Patients with grade-3 and 4 pruritis were given vitamin K 10 mg orally once daily, irrespective of value of PT. Foetal outcome was noted for all patients including gestation at delivery, meconium staining of liquor, APGAR score at 5 minutes, NICU requirement. Mode of delivery was not a parameter in study due to the fact that out of 69 patients, 21 patients underwent repeat elective caesarean section. None of the patients were allowed to go beyond 38 completed weeks of delivery.

All were offered LFTs after 2 weeks and 6 weeks of delivery. Patients were counselled for contraception and possibility of recurrence of symptoms during next pregnancy. All neonates were followed-up for 6 weeks after delivery.

RESULTS

Sixty-nine patients diagnosed with Gestational cholestasis were included in study according to our inclusion criteria. Fifty seven (82%) patients had steatorrhoea. It is obvious from table1 that with increasing pruritis grade abnormalities of LFTs especially ALT were increasing. In patients of grade-4 pruritis group ALT levels reached up to 1,200 mg/dl.

Twenty-one (30%) patients presented with complaint of reduced foetal movements. Out of these, 1 (6.5%) was of grade-1 pruritis, 5 (17%) of grade 2 pruritis, 7 (50%) of grade 3 pruritis and 8 (80%) of grade 4 pruritis group.

Fourteen (20%) patients presented with abnormal CTG before delivery. No CTG abnormality was detected in patients with grade-1 pruritis. one (3.4%) had abnormal CTG in grade 2 pruritis group,six (48%) had abnormal CTG in grade-3 group, seven (70%) patients in grade 4 group.

Out of 69 patients 17 (25%) patients presented with meconium stained liquor during labour or at delivery; 1 (6%) patient in grade-1, 3 (10%) patients in grade-2, 7 (50%) in grade-3 and 6 (60%) in grade-4 pruritis groups.Ten babies were born with 5 minute APGAR score of <7/10; 5 babies (36%) of grade-3 and 5 (50%) of grade-4 group.

Pregnancies with grade-1 pruritis were delivered at 38 weeks. Those with grade-2 between 37 to 38 weeks, grade-3 between 36–37 weeks and grade-4 between 34–35^{+6} weeks gestation. All 17 (25%) preterm deliveries were in grade-3 and 4 group. Eight (47%) of these had pre PROM, 4 (27%) patients had spontaneous pre term labour, 3 (18%) had iatrogenic pre term labour. Two (2.8%) patients had intrauterine foetal deaths at 35 weeks and 37 weeks respectively. One (1.4%) patient had early neonatal death due to RDS.

Out of 69 babies, 15 (22%) required NICU care; 1 (3.4%) from grade-2, 5 (35%) from grade-3, and 9 (90%) of grade-4 group. Out of these 15 babies, 4 developed RDS and 7 aspired meconium.

Seventeen (25%) patients had preterm delivery, 2 (2.8%) patients suffered intrauterine foetal death, 1 (1.4%) had early neonatal death. Fifteen (22%) new born babies required NICU admission.

Seventeen (25%) patients had meconium staining of liquor, 21 (30%) patients complained of reduced foetal movements and 14 (20%) patients had abnormal CTG findings just before delivery.

Table-1: Effect of clinical and biochemical parameters on foetal outcome [n (%)]

VRS for pruritis	Pruritis	Steatorrhoea	Decreased foetal movements	Deranged ALT (mg/dl)	Abnormal CTG before delivery	Meconium Stained liquor	APGAR score <7/10 at 5 min	Gestational age at delivery (Weeks)	Preterm delivery	IUD	Early Neonatal death	NICU admission
Grade 1	16 (23)	9 (56)	1 (6.5)	40–150	-	1 (6)	-	38	-	-	-	-
Grade 2	29 (42)	24 (82)	5 (17)	150–300	1 (3.4)	3 (10)	-	37–38	-	-	-	1 (3.4)
Grade 3	14 (20)	14 (100)	7 (50)	300–600	6 (43)	7 (50)	5 (36)	36–37	7 (50)	1 (6)	-	5 (35)
Grade 4	10 (44)	10 (100)	8 (80)	600–1200	7 (70)	6 (60)	5 (50)	34–35+6	9 (90)	1 (10)	1 (10)	9 (90)
Total	69 (100)	57 (82)	21 (30)	-	14 (20)	17 (25)	10 (14.4)	-	17 (25)	2 (2.8)	1 (1.4)	15 (22)

DISCUSSION

Gestational cholestasis has profound foetal implications. It is obvious from table 1 that all these complications were more common in patients with grade 3 and 4 pruritis indicating that greater was the severity of pruritis, higher was abnormality of liver transamenases especially ALT, and higher was incidence of foetal complications.

In a study conducted by Ruqqia Sultana and colleagues, meconium staining of liquor was seen in 20% patient, pre-term labour in 10% and intrauterine foetal death in 6% patients.[3] The difference in rate of intrauterine foetal death is due to the fact that they also included un-booked patients while all our patients were on strict foeto-maternal surveillance. Difference in rate of preterm delivery might be due to the fact that they included patients with spontaneous preterm labour only while we included iatrogenic preterm deliveries as well. In another study conducted by Sangita and Soumik, rate of preterm labour was found to be 19–60%, meconium staining of liquor 27%, foetal loss 0.4–4.1%.[15]

Sebiha *et al*[2] reported incidence of meconium staining of liquor to be 25–45%, pre-term labour 44%, and intrauterinal foetal death 2–5%. Their mainstay of diagnosis and follow-up was Serum Bile Acid level measurement.

In all above mentioned studies Serum Bile Acid levels were used mainly along with LFTs especially ALT for follow-up. In this study grade of pruritis (VRS), levels of ALT, Foetal Kick Count Chart, CTG and ultrasound were used to address non availability of serum bile acid assessment. Foetal outcome assessed on clinical grounds and ALT was found comparable to that found in patients assessed with serum bile acid levels so in the absence of facility of serum Bile Acid level assessment ,clinical picture along with Liver Function tests serially is sufficiently helpful to achieve optimal foetal outcome but it requires more vigorous foeto-maternal monitoring.

CONCLUSION

Foeto-maternal surveillance in gestational cholestasis in the absence of facility for serum bile acid level assessment can be achieved with pruritis score, serial liver function tests are very useful parameters though it requires more frequent visits and more vigilance on part of mother. Dexamethasone administration improves foetal outcome.

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