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ORIGINAL ARTICLE

An Observational Study to Evaluate the Maternal and Foetal Outcomes in Pregnancies Complicated with Jaundice

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Abstract

Background Incidence of jaundice in pregnancy, including underlying chronic liver diseases, is 3–5%. However, the maternal mortality rate in some conditions can be as high as 18% in acute fatty liver of pregnancy and 22% in hepatitis E in pregnancy.

Objectives This is an observational study of the demographics, obstetrical profile, aetiology, maternal morbidity, mortality and neonatal outcomes in pregnancies complicated with jaundice.

Materials and Methods This is an observational study conducted in Department of Obstetrics and Gynaecology of a tertiary care hospital, situated amidst the biggest urban slum in Mumbai spanning over 1 year from January 2016 to December 2016. All registered, unregistered and transferred patients with abnormal liver function tests excluding patients with chronic liver diseases were included in this study.

Results Most of the cases of jaundice in pregnancy were seen in primigravida (51%) and age group of 20–30 years (58%). Fifty-three percentage of cases were referred or transferred from periphery hospitals. Hepatitis E was the

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most common cause (42%) of jaundice in pregnancy. Complications like disseminated intravenous coagulopathy, postpartum haemorrhage, hepatic encephalopathy and hepatoportal hypertension were seen in 65% of cases. Maternal mortality rate and perinatal mortality rate were as high as 40 and 37%, respectively, in our study.

Conclusion Incidence of jaundice in pregnancy, mainly due to viral hepatitis, is very high in lower socio-economic, densely populated urban slums. Special efforts should be made to counsel and educate the mothers about initial symptoms and preventive measures for viral hepatitis. Patients along with the relatives should be informed about the severe features of pre-eclampsia to combat these preventable causes of maternal mortality.

Keywords Jaundice · Hepatitis E · Maternal mortality · Preventable

Introduction

ICD 10 CM defines jaundice (R 17) as a clinical manifestation of hyperbilirubinemia which consists of deposition of bile pigments in the skin, resulting in yellowish staining of the skin and mucous membranes [1]. The normal serum bilirubin concentration in adults is less than 1 mg/dL; however, clinical jaundice is not manifested until the serum bilirubin is greater than 2 mg/dL. Liver function tests remain largely unchanged during pregnancy except the increased levels of alkaline phosphatase (ALP). ALP is physiologically produced by placenta at the brush border membranes of the syncytiotrophoblast [2]. Incidence of jaundice in pregnancy including the underlying chronic liver diseases is 3–5% [3]. However, the incidence and the aetiology of abnormal liver function tests varies in different parts of the world.

Jaundice during pregnancy can be attributed to liver diseases unique to pregnancy, pre-hepatic causes, hepatic causes and post-hepatic causes of jaundice. Liver dysfunctions unique to pregnancy are pre-eclampsia, HELLP syndrome, acute fatty liver of pregnancy, intrahepatic cholestasis of pregnancy and hyperemesis gravidarum. Pre-hepatic conditions including haemolytic anaemia, hepatic pathologies like acute viral hepatitis, drug-induced hepatitis, Budd–Chiari syndrome, Wilson's disease cause clinical hyperbilirubinemia. Post-hepatic pathologies like CBD obstructions, gall stones, choledochal cyst, pancreatitis can also lead to clinical jaundice in pregnancy. Pre-eclampsia-related liver dysfunctions and viral hepatitis are the most commonly encountered causes of jaundice in pregnancy.

India is hyperendemic for hepatitis A and E [4]. Viral hepatitis particularly faeco-oral hepatitis E infection is fairly common in lower socio-economic, densely populated areas of urban slums lacking basic hygiene with seasonal increase in incidence during summer and monsoon seasons [5]. Fulminant hepatitis E has the highest mortality rate of 22% followed by acute fatty liver of pregnancy 18% [6, 7].

Table 1 Demographic classification

Characteristics	No of cases	Percentage %
Age		
< 20 years	7	16
20–30 years	25	58
> 30 years	11	26
Residence		
Urban	34	80
Rural	9	20
Socio-economic status		
Lower middle class	15	35
Upper lower class	18	42
Lower class	10	23

Materials and Methods

Place of study The study was conducted in the Department of Obstetrics and Gynecology at Lokmanya Tilak Municipal Medical College and General Hospital, Sion, Mumbai 400022, a tertiary care hospital from January 2016 to December 2016.

Study design: Retrospective observational study.

Inclusion criteria: All registered, unregistered and transferred patients with abnormal liver functions were included in this study.

Exclusion criteria: Patients with chronic liver disease and drug-induced hepatitis.

Methodology: Demographics (age, residence, socio-economic status), obstetrical profile (gravida, ANC visits, nature of admission), aetiology, complications, maternal morbidity, mortality and neonatal outcomes of pregnancies complicated with jaundice were studied and compared with similar studies.

Results

Forty-three cases were studied during 1-year study. Most of the cases belonged to the age group of 20–30 years (58%) and resided in the urban slums (80%). All the enrolled patients were classified according to Kuppuswamy scale. Forty-two percentage of population belonged to upper lower class, followed by lower middle class (35%) and lower class (23%) (Table 1).

Table 2 Distribution according to nature of admission

Nature of admission	No of cases	Percentage %
Registered in LTMMC	11	26
Referral	23	53
Emergency	9	21
Total	43	100

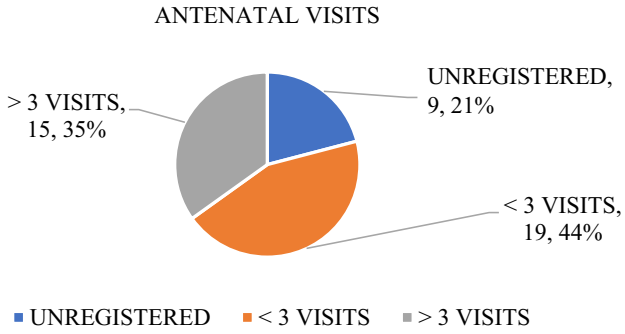

Fig. 1 Distribution according to ANC visits

Table 3 Aetiology of jaundice in pregnancy

Aetiology	No of cases	Percentage %
Hepatitis E	18	42.4
Pre-eclampsia	7	16.2
Cholestasis of pregnancy	4	9.2
Haemolytic anaemia	3	6.9
Malaria	2	4.6
Hepatitis B	2	4.6
Leptospirosis	1	2.3
Hepatitis A	1	2.3
Acute fatty liver of pregnancy	1	2.3
Undetected	4	9.2
Total	43	100

Twenty-one were primigravida (51%), 13 (32%) were 2nd gravida, and 8 (18%) were multigravida. In the present study, though most of the cases were ANC registered, only 35% had > 3 visits, 44% had < 3 ANC visits, and 21% were unregistered (Fig. 1). Fifty-three percentage of cases were referred or transferred from periphery hospitals (Table 2).

Hepatitis E (42.4%) was the most common cause of jaundice in pregnancy followed by pre-eclampsia (16.2%), cholestasis of pregnancy (9.2%) and haemolytic anaemia (6.9%) (Table 3). Sixty-seven percentage of cases had normal delivery, 14% LSCS, 5% forceps and 14% undelivered. Five normal deliveries and 1 LSCS were complicated with postpartum haemorrhage. Most common complications seen were disseminated intravascular coagulopathy (DIC) in 12 cases (28%), followed by postpartum haemorrhage in 6 cases (14%) and hepatic encephalopathy in 5 cases (11.5%). There were no complications in 15 patients (35%), giving a high maternal morbidity rate of 65% (Table 4).

Table 4 Complications in jaundice in pregnancy

Complications	No of cases	Percentage %
DIC	12	28
PPH	6	14
Hepatic encephalopathy	5	11.5
Hepatoportal tension	2	4.6
Abruption	2	4.6
Hepatorenal failure	1	2.3
Uncomplicated	15	35
Total	43	100

Table 5 Mortality in jaundice in pregnancy

Cause of death	No of cases	Percentage %
DIC	8	47.05
HELLP	4	23.52
Hepatic encephalopathy	4	23.52
Acute fatty of liver	1	5.88
Total no. of mortalities	17	100

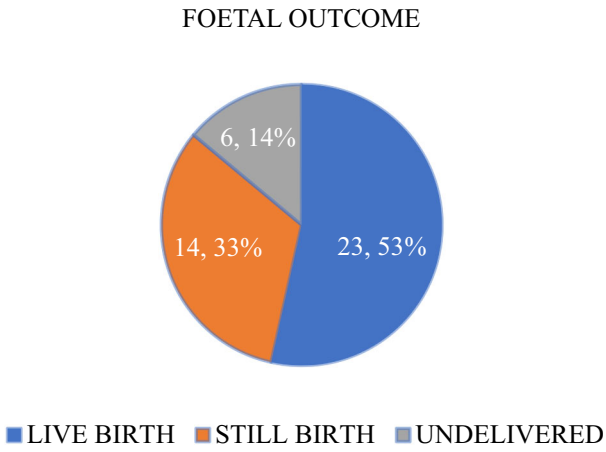

Fig. 2 Foetal outcome of jaundice in pregnancy

In our study, 17 maternal mortalities were reported with an extremely high fatality rate of 40% (Table 5). Maternal mortality was seen in most cases of hepatitis E succumbing to DIC and hepatic encephalopathy. Eleven cases of hepatitis E expired, 4 succumbed to hepatic encephalopathy, and 7 died of DIC.

Fifty-three percentage cases had live birth, out of which 7 were preterm. Intrauterine foetal demise were reported in 14 cases (33%), and 6 were undelivered (14%) (Fig. 2).

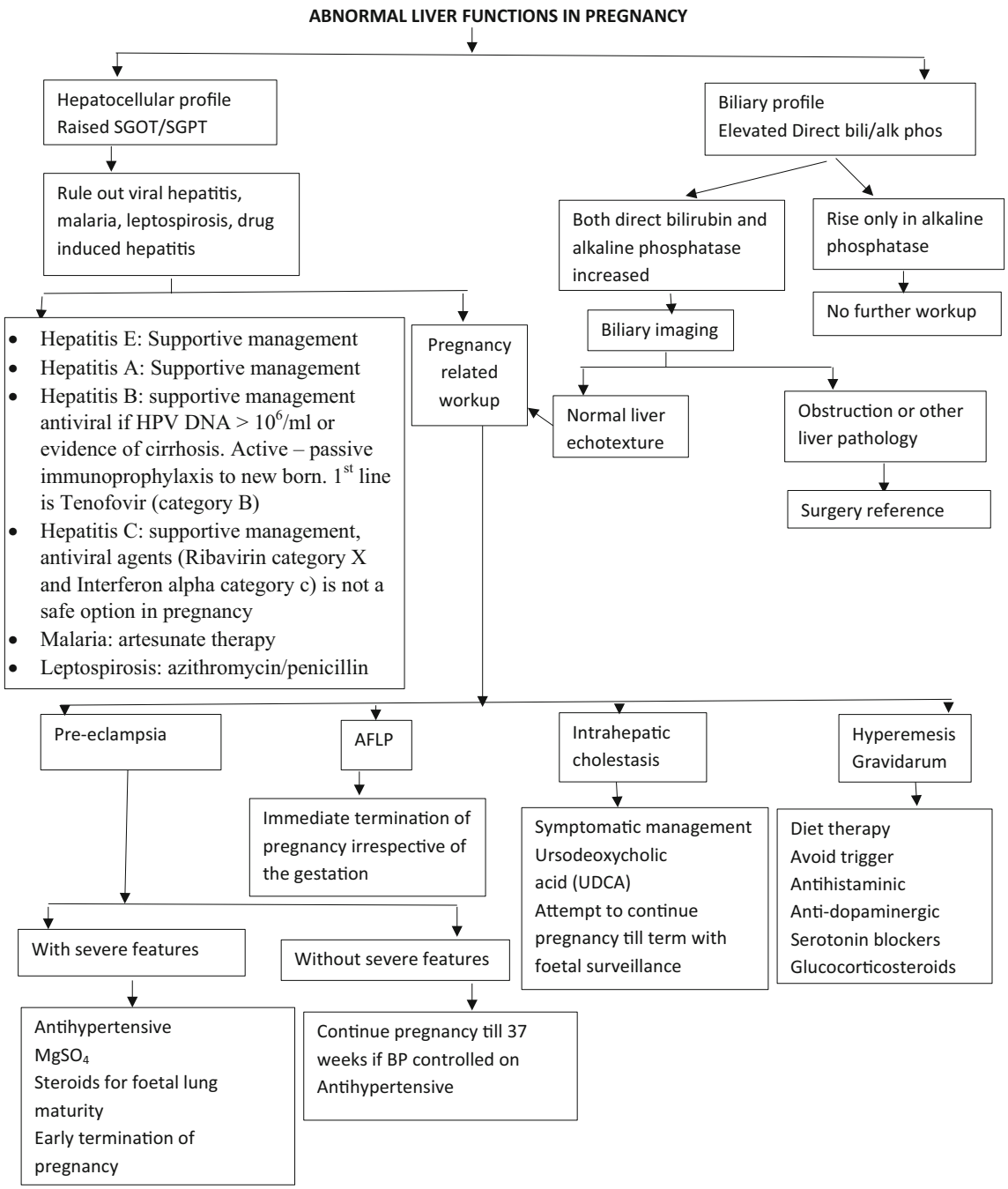

Fig. 3 Management protocol for jaundice in pregnancy

Two babies died in within 7 days of delivery. Hence, perinatal mortality rate was 37%.

Discussion

Liver dysfunction in pregnancy is associated with various pathologies including viral hepatitis, leptospirosis, malaria, increased haemolysis and pregnancy-related conditions like pre-eclampsia, HELLP, acute fatty liver, cholestasis of pregnancy and hyperemesis gravidarum. Though the incidence of pre-eclampsia in pregnancy remains uniform worldwide (2–8%) [8], there is a major geographical variation in other hepatic conditions encountered during pregnancy. In developed countries like USA, gall stones and pre-eclampsia are the commonest cause of abnormal liver function [9]. In subdeveloped countries like India where sanitation and safe drinking water are still major

social issues, viral hepatitis especially hepatitis E is on a rising trend. In many contemporary studies including the present study, hepatitis E was found to be the most common cause of jaundice in pregnancy even surpassing pregnancy-related liver dysfunctions [10].

Most of the cases of jaundice were seen in primigravida (51%), age group of 20–30 years (58%) and upper lower class (42%). Similar findings were reported by other parallel studies [10, 11]. Pre-eclampsia is more common in primigravida with a relative risk of 2.91 [12]. Overcrowding, contaminated drinking water, lack of sewage management and unawareness of basic hygiene habits predispose the lower socio-economic group to infectious cause of hepatitis like hepatitis E, hepatitis A, leptospirosis and malaria.

A tremendously high maternal morbidity (65%) and mortality (40%) was seen in our study which is accounted to fulminant nature of hepatitis E infection and the fact that majority of enrolled patients (53%) were cases referred with poor prognosis requiring intensive management. Mortality from fulminant hepatic failure secondary to hepatitis E virus (HEV) infection can be as high as 50% [13, 14]. Hepatitis E infection during pregnancy (especially in the third trimester), with genotype 1 of hepatitis E virus, is associated with more severe infection and might lead to fulminant hepatic failure and maternal death [15]. Amongst the 4 genotypes of hepatitis E virus, genotype 1 is most prevalent in India, accounting for high incidence of fulminant hepatitis.

As 65% of cases in our study had severe morbidity, most of these cases were managed in intensive care setting with consultation with medicine and gastroenterology departments. Acute viral hepatitis is managed conservatively. Antiviral therapy for hepatitis B in pregnancy depends upon the presence or absence of cirrhosis, HBeAg and hepatitis B e antibody (anti- HBe), as well as the HBV DNA and aminotransferase levels [16]. Gastroenterologists generally defer antiviral therapy until delivery provided there is no evidence of cirrhosis. However, if there is HBV DNA (i.e. $> 2 \times 10^5$ int. units/mL or $> 10^6$ copies/mL) tenofovir disoproxil fumarate (300 mg daily) or lamivudine (100 mg daily) should be started in third trimester to prevent mother-to-child transmission [16]. In our institute, all newborns receive 1st dose of hepatitis b vaccine and HBIG (hepatitis B immunoglobulin) within 12 h of birth. Antiviral therapies for hepatitis C is contraindicated in pregnancy as both first-line therapies ribavirin (category X) and interferon (category C) have detrimental effects on foetus [17].

Pre-eclampsia was the second most common aetiology for abnormal liver functions in our study (16.2%). If pre-eclampsia is complicated with severe features like visual disturbances, severe headache, HELLP, thrombocytopenia, renal abnormality, pulmonary oedema or uncontrolled hypertension, it is prudent to terminate the pregnancy immediately [18]. Mild pre-eclamptic pregnancies should be terminated after 37 weeks with weekly pre-eclampsia profile and foetal assessment.

In our present study, we had only one case of acute fatty liver of pregnancy (AFLP) who expired at 18 weeks of gestation. AFLP is an obstetric emergency presenting as fulminant hepatitis or hepatic encephalopathy with grave prognosis. AFLP has been linked with deficiency of long chain 3-hydroxyacyl coenzyme A dehydrogenase (LCHAD) in foetus. Mothers of neonates with LCHAD deficiency have 79% chance of developing AFLP and HELLP [19]. Management of AFLP is maternal stabilisation and prompt delivery irrespective of gestation age. The route of delivery is individualised according to maternal and foetal status. Unlike AFLP, intrahepatic cholestasis during pregnancy has a very milder course which can be managed conservatively with ursodeoxycholic acid (UDCA) and does not warrant premature termination of pregnancy [20]. A detailed description of management of jaundice in pregnancy is provided in Fig. 3.

In addition to high MMR associated with jaundice in pregnancy, neonatal mortality was also reported to be exorbitantly high (43%). High neonatal mortality is specifically seen in hepatitis E, AFLP and HELLP.

Conclusion

Liver disease unique to pregnancy and pregnancy with liver disease might constitute a small cohort of complicated pregnancies but requires meticulous attention by both obstetricians and physicians owing to the high maternal and neonatal morbidity and mortality. Unlike the Western countries, where gall bladder and pre-eclampsia constitute the major causes of jaundice, communicable diseases like hepatitis E, malaria and leptospirosis account to majority of cases of jaundice in India. ANC visits provide an excellent opportunity for early diagnosis of pre-eclampsia and can also encompass awareness on basic hygiene and other preventive measures against hepatitis E.

Compliance with Ethical Standards

Conflict of interest None.

Ethical Standards All procedures performed were with the standard of institutional research ethical committee and the 1964 Helsinki declaration and its later amendments.

References

1. www.cdc.gov/nchs/icd/icd10cm.htm. Assessed 28 Sept 2017.

2. Celik H, Tosun M, Cetinkaya MB, et al. Markedly elevated serum alkaline phosphatase level in an uncomplicated pregnancy. J Matern Fetal Neonatal Med. 2009;22(8):705–7. https://doi.org/10.1080/14767050802702323.
3. Hay JE. Liver disease in pregnancy. Hepatology. 2008;47(3):1067–76. https://doi.org/10.1002/hep.22130.
4. Nandi B, Hadimani P, Arunachalam R, et al. Spectrum of acute viral hepatitis in Southern India. Med J Armed Forces India. 2009;65(1):7–9. https://doi.org/10.1016/S0377-1237(09)80044-0.
5. Fares A. Seasonality of hepatitis: a review update. J Fam Med Prim Care. 2015;4(1):96–100. https://doi.org/10.4103/2249-4863.152263.
6. Chaudhry SA, Verma N, Koren G. Hepatitis E infection during pregnancy. Can Fam Physician. 2015;61(7):607–8.
7. Zhang Y-P, Kong W-Q, Zhou S-P, et al. Acute fatty liver of pregnancy: a retrospective analysis of 56 cases. Chin Med J. 2016;129(10):1208–14. https://doi.org/10.4103/0366-6999.181963.
8. Jeyabalan A. Epidemiology of preeclampsia: impact of obesity. Nutr Rev. 2013. https://doi.org/10.1111/nure.12055.
9. Ellington SR, Flowers L, Legardy-Williams JK, et al. Recent trends in hepatic diseases during pregnancy in the United States, 2002–2010. Am J Obstet Gynecol. 2015;212(4):524.e1-7. https://doi.org/10.1016/j.ajog.2014.10.1093.
10. Krishnamoorthy J, Murugesan A. Jaundice during pregnancy-maternal and fetal outcome. Int J Reprod Contracept Obstet Gynecol. 2016;5:2541–5.
11. Aparajita D. Maternal and fetal outcome in liver diseases of pregnancy—a tertiary hospital experience. Int J Sci Res Publ. 2015;5(9):1–4.
12. English FA, Kenny LC, McCarthy FP. Risk factors and effective management of preeclampsia. Integr Blood Press Control. 2015;8:7–12. https://doi.org/10.2147/IBPC.S50641.
13. Westbrook RH, Dusheiko G, Williamson C. Pregnancy and liver disease. J Hepatol. 2016;64(4):933–45. https://doi.org/10.1016/j.jhep.2015.11.030.
14. Devarbhavi H, Kremers WK, Dierkhising R, et al. Pregnancy associated acute liver disease and acute viral hepatitis: differentiation, course and outcome. J Hepatol. 2008;49:930–5.
15. Devi SG, Kumar A, Kar P, et al. Association of pregnancy outcome with cytokine gene polymorphisms in HEV infection during pregnancy. J Med Virol. 2014;86(8):1366–76.
16. Society for Maternal-Fetal Medicine (SMFM), Dionne-Odom J, Tita AT, Silverman NS. #38: hepatitis B in pregnancy screening, treatment, and prevention of vertical transmission. Am J Obstet Gynecol. 2016;214:6.
17. Ghany MG, Strader DB, Thomas DL, et al. Diagnosis, management, and treatment of hepatitis C: an update. Hepatology. 2009;49:1335–74.
18. American College of Obstetricians and Gynecologists. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' task force on hypertension in pregnancy. Obstet Gynecol. 2013;122:1122.
19. Eskelin PM, Laitinen KA, Tyni TA. Elevated hydroxyacylcarnitines in a carrier of LCHAD deficiency during acute liver disease of pregnancy—a common feature of the pregnancy complication? Mol Genet Metab. 2010;100(2):204–6.
20. Kremer AE, Oude Elferink RP, Beuers U. Pathophysiology and current management of pruritus in liver disease. Clin Res Hepatol Gastroenterol. 2011;35:89.