International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622
Indexing: Embase
Impact Factor (RJIF): 6.71

www.gynaecologyjournal.com
2025; 9(6): 1146-1150
Received: 18-10-2025
Accepted: 22-11-2025

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Maternal liver disease and perinatal outcomes: A retrospective cohort study from a tertiary care hospital

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DOI: https://www.doi.org/10.33545/gynae.2025.v9.i6f.1777

Abstract
Background: Liver disorders complicate 3%of all pregnancies, yet it takes a major toll on health of both mother and fetus especially in developing countries like India. It is responsible for about 60%of perinatal mortality and about 14%of maternal mortality. The aim of this study was to find out the effect of jaundice on maternal health in pregnancy and assess the complications of jaundice in pregnancy. To evaluate the outcome in labour and to study the maternal mortality, and to acknowledge the effect of jaundice on fetus and perinatal mortality rates.
Methods: Pregnant women with jaundice during pregnancy, attending the Amrita Institue of Medical Sciences and Research centre between 2017 to 2024 were included in the study.
Results: 50 patients had jaundice during pregnancy. The incidence of jaundice was 0.5%. Maximum age group of the patients with liver diseases was found to be between 31-35yr. 60% cases were seen in Primigravida and the rest were in multipara. The most common cause of jaundice was intrahepatic cholestasis of pregnancy (40%). The common maternal complications were atonic PPH were 10% followed by sepsis in 6%. Perinatal mortality was 6%. There was no maternal mortality.

Keywords: Liver disorders, fetomaternal outcome, hemolysis, elevated liver enzymes, and low platelet count syndrome

Introduction
Pregnancy is associated with several remarkable physiological adaptations and alterations many of which influence the functioning of liver [1]. The metabolic and excretory functions of liver are affected in pregnancy due to the increased production of estrogen and progesterone [2]. Physical findings such as palmer erythema, spider angiomas which may suggest liver disease, may be found normally during pregnancy [1, 3]. Liver diseases in pregnancies may be specific to gestation or coincidental and diagnosis of maternal and fetal situations and interventions in emergencies are crucial for maternal and fetal survival. Viral hepatitis is the most common cause of jaundice world-wide [4].
Liver diseases are broadly classified as pregnancy related and unrelated. The pregnancy related and unrelated common diseases of liver are listed in Table 1.
Pregnancy associated liver diseases affect upto 3%-10% of pregnant women. Diagnostic and therapeutic decisions must consider implications for both mother and fetus, and rapid diagnosis is indispensable for severe cases because decision of immediate delivery is important for maternal and fetal outcome. Hence liver disease is a serious complication of pregnancy and poses a challenge for the Gynaecologist and Hepatologist [5]. The main objective of the present study is to investigate the feto-maternal outcome due to various causes of liver diseases in pregnancy.

Methodology
The present work is a retrospective study on pregnant patients with liver diseases admitted in the department of OBG, Amrita Institute of Medical Sciences and Research Centre, Kochi during 2017-2023. Informed consent from patients were taken at time of admission. Using the patient data from the hospital records, this study was conducted after getting clearance from the Institutional Ethics Committee. A detailed history, clinical examination findings, and investigations done were collected. Age, parity index, symptoms and signs were assessed.

Liver function tests like total, direct, indirect serum bilirubin, total protein, albumin and globulin, serum transaminases, serum alkaline phosphatase, clotting time, bleeding time and ultasonogram, complete hemogram, coagulation profile, viral markers study such as HBsAg, Anti HAV IgM, Anti HCVab, Anti HEV IgM antibodies were done depending on clinical situation. IgM (ELISA) antibodies were done for leptospirosis.

Expert opinion was sought for all patients from the department of Gastroenterology and our management was modified accordingly. Data were analysed to find out percentage distribution of cases, course of pregnancy, and method of termination, maternal and fetal complications. Maternal outcomes analyzed include PPH (postpartum haemorrhage), Abruptio placenta, Hypertrophic choroidopathy, AKI (acute kidney injury), Sepsis. Fetal outcomes include Hyperbilirubinemia, Respiratory distress syndrome, Coagulopathy, prematurity, IUD (intra uterine death).

Table 1: Preganacy related and unrelated common diseases of liver

SI. No.	Pregnancy related liver diseases	Pregnancy unrelated	
		Pre-existing	Co-incident
1	Hyperemesis Gravidarum	Hepatitis	Acute Viral Hepatitis
2	Intrahepatic cholestasis of pregnancy	Cirrhosis & Portal Hypertension	Biliary Disease
3	Acute fatty liver of pregnancy	Autoimmune Liver Disease	Vascular-Budd Chiari
4	HELLP (Hemolysis, Elevated Liver Enzymes and Low Platelets)	WILSON'S DISEASE	Liver Tumors
5	---------	Post Liver Transplant	Drug Induced

Results

The total number of deliveries during this period was 9939. The number of cases with liver diseases complicating pregnancies was 50. The incidence of liver diseases complicating pregnancies was thus only about 0.5%. From figure 1, it can be seen that there are out of the 50 cases of liver diseases complicating pregnancy, 20 (40%) were found to be due to intrahepatic cholestasis of pregnancy. HELLP was the second common cause and was found in 11 cases. Hepatitis-A, B and C, was the next in the etiology.

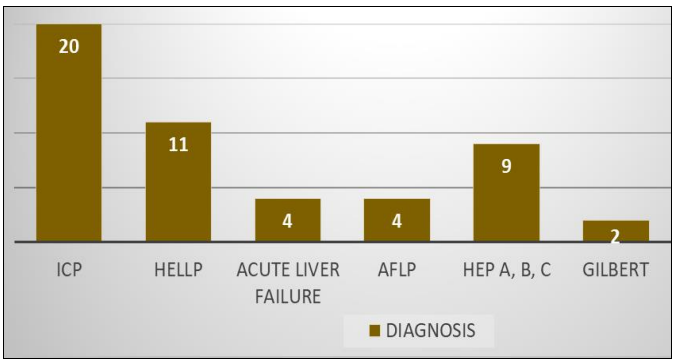

Fig 1: Etiology of the liver diseases complicating pregnancy

Results of the biochemical and pathological investigations of the patients

Maximum age group of the patients with liver diseases was found to be between 31-35yr. The age and parity index of the patients are depicted in figures 2.and 3. 60% cases were seen in Primigravida and the rest were in multipara.

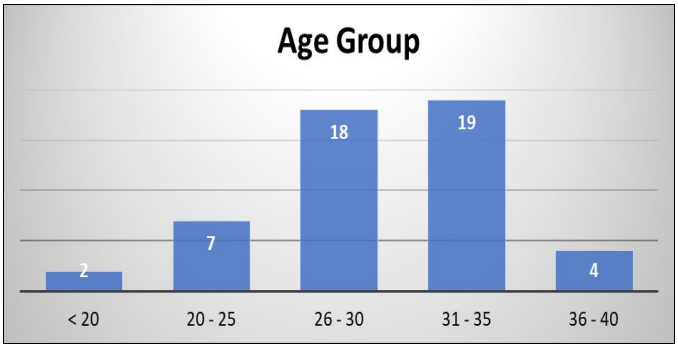

Fig 2: Age of the patients under this study

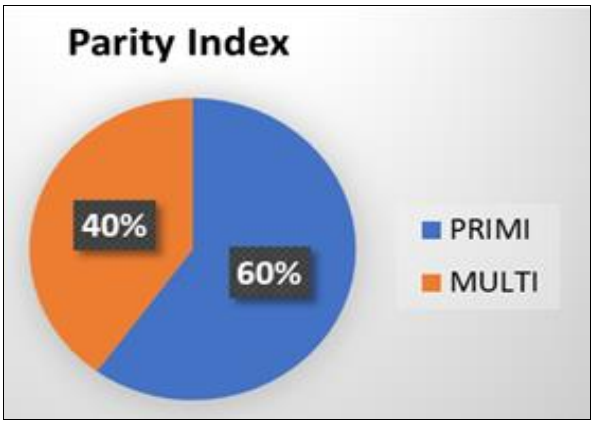

Fig 3: The Parity index of the patients investigated

Clinical Symptoms and signs noticed in the patients

Symptoms presented by patients include pruritus in 22 cases as can be seen in table 2. Other symptoms include nausea and vomiting, fever, pain abdomen, yellowish discoloration of urine, headache, fever. Icterus was seen in 16% of the cases. Other signs elicited include hepatomegaly, hypertension, ascites, pedal edema.

Table 2: Clinical Symptoms noticed in the patients

Symptoms	Number	Percentage (%)
Pruritus	22	44
Nausea & Vomiting	7	14
Pain Abdomen	5	10
Yellowish Urine	4	8
Fever	3	6
Headache	2	4

Table 3: Clinical signs elicited in the patients

Signs	Number	Percentage
Icterus	8	16
Hepatomegaly	4	8
High BP	3	6
Ascites	1	2
Pedal EDEMA	1	2

Investigations on liver function

Liver function tests were assessed in each and every patient. The level of serum bilirubin varied widely between 0.2-11.5 mg/dl. Total bilirubin level showed mild elevation (1.5-5mg/dl) in 10%.

2%of patients had high serum bilirubin more than 10 mg/dl. The serum transaminase level was below 75 IU/L in 47% of patients, 13.7% of patients had the enzyme level more than 500 IU/L. The figure 4 depicts the data on the number of patients exhibiting different levels of transaminase.

Transaminase IU/L

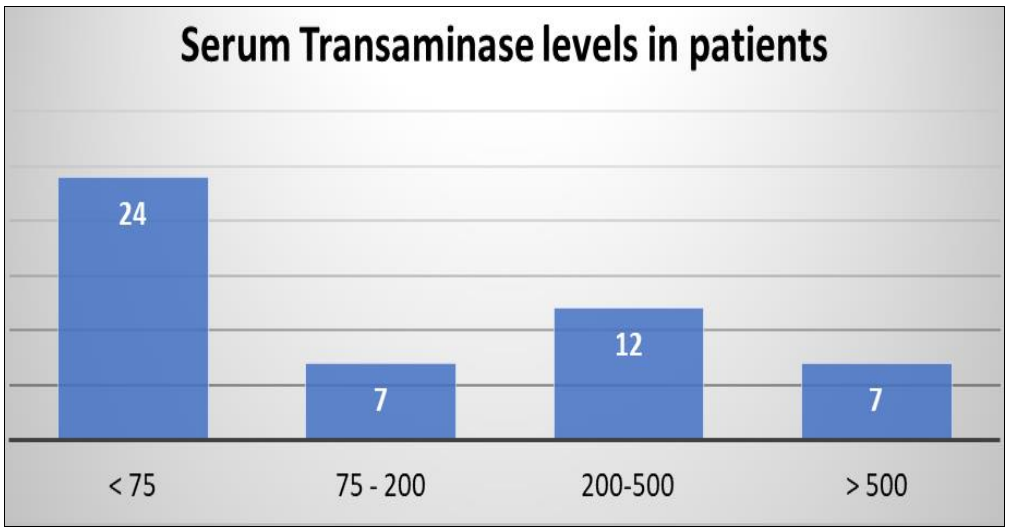

Fig 4: Investigations on liver function

Mode of delivery

Out of total cases, 68% underwent caesarean section and 32% had vaginal delivery and the results are presented in figure 5.

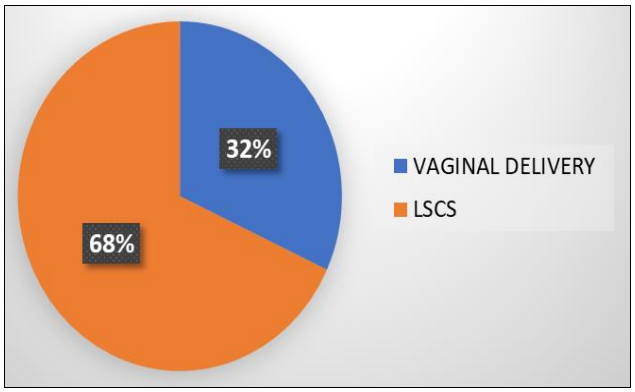

Fig 5: Mode of Delivery

Vaginal delivery

Out of 18 vaginal deliveries, 3 were instrumental deliveries and 3 were IUD expulsion. 2 deliveries occurred as preterm at 32 and 34 weeks.

Caesarean delivery

Out of 32 caesarean sections, 11 cases were due to previous Caesarean. 8 cases due to HELLP with worsening of lab parameters, 1 case due to eclampsia. 2 cases due to liver failure with maternal deterioration. Other cases constituting 11 were due to obstetrical indications like fetal distress, failure to progress, DCDA with unfavorable cervix, MCDA, Triplets.

Maternal complications

Table 3, presents the data on maternal complications during delivery. There were 5 cases of PPH that occurred during CS mainly due to HELLP. 1 case of PPH was seen in triplets. There was 1 case of Abruptio placenta in HELLP that ultimately lead to IUD expulsion. 3 cases of sepsis, 1 was in Hepatitis C and other 2 in AFLP.

Fetal outcome

60% cases were term deliveries and of these 57% babies born were females. The data on Gestational age classifications are presented in Fig 6 and the data on sex distribution of the babies are presented in Figure 7.

Table 4: Maternal complications during delivery

PPH	5
SEPSIS	3
Acute Kidney Injury	1
Abruptio Placenta	1
Hypertensive Choroidopathy	1

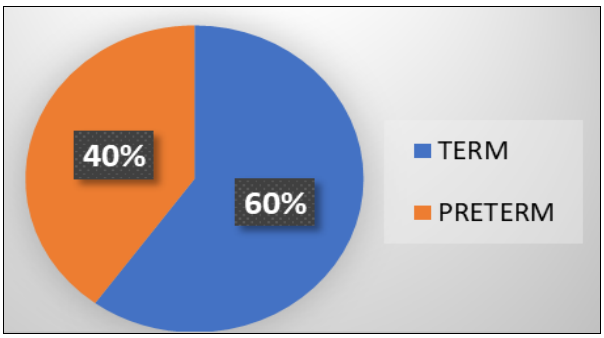

Fig 6: Gestational age classifications

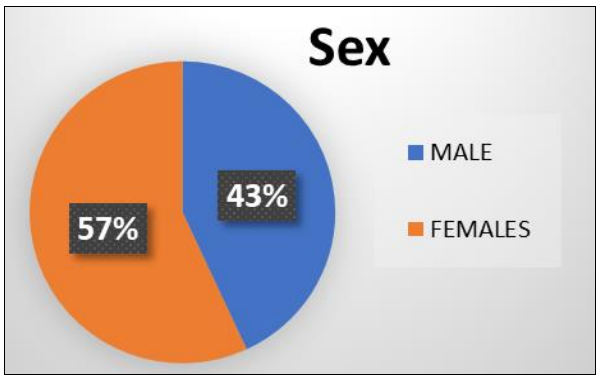

Fig 7: Sex distribution of babies

Birth weight distribution

The data on birth weight distribution of the babies, both term and preterm, are presented in Fig 8. 18 babies had weight of 2.1-2.5 kg.

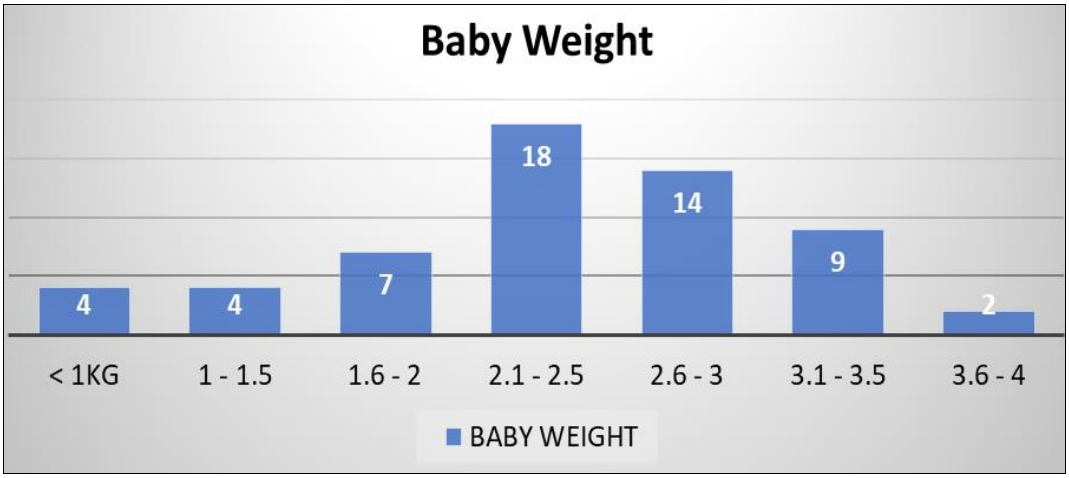

Fig 8: Number of baby's and their birth weight distribution

Fetal complications

Neonatal hyperbilirubinemia requiring phototherapy was seen in 18 babies. 14 babies had Respiratory distress syndrome and 5 babies required Bipap 3 were in ventilator. 3 fetus had stage 3 FGR which was seen in mother with HELLP. 3 babies had sepsis and 3 had metabolic acidosis. There was 3 perinatal mortality due to HELLP and acute liver failure.

Discussion

This study on Liver diseases in pregnancy was conducted retrospectively from collecting data from 2017-2023 in the Department of Obstetrics and Gynacology, Amrita Institute of Medical Sciences and Research Centre, Kochi. Women confirmed with liver diseases were included in this study. The total number of cases over this time period was 50 out of 9939 deliveries. Incidence of liver diseases varies. Developing countries reported a higher incidence than developed ones. In this study, incidence of liver diseases complicating pregnancy was found to be 0.5%. In study of Krishnamoorthy *et al.* [6], incidence of liver diseases in pregnanacy was 0.29%. In another study conducted in 2017 in Government medical college, Calicut incidence was almost same of 0.2% [5]. But in a study conducted in Seth Gordhandas Medical College, the incidence reported was 0.81% [7]. Neema Acharya [8] reported an incidence of 4% in her 6 year study. Thus incidence varies from region to region. In this study, intrahepatic cholestasis of pregnancy was the commonest cause of liver diseases in pregnancy followed by HELLP. Out of 50 cases, 20 were ICP. This was followed by 11 HELLP cases. 9 cases of Hepatitis were seen, of which 4 due to Hepatitis A, 3 due to Hepatitis B and 2 due to Hepatitis C and 1 chronic hepatitis. 5 hepatitis cases comes under low socioeconomic status [9]. Study on seroprevalence of subclinical HEV infection in pregnant women by Begum M, *et al*. reported of increased prevalanve of Hepatitis E in lower socio economic classes 4 cases were due to AFLP and same number of cases were referred to our institution due to liver failure. 2 cases were due to Gilbert syndrome diagnosed pre pregnancy. HELLP as the most common cause (34.6%)in the study by Vinayachandran *et al.* and Krishnamoorthy *et al.* [5, 6] reported an incidence of 51% cases of hepatitis and 5.8% of ICP, 13.72% HELLP. Shukla *et al.* [10] observed an incidence of 57% and Harshad *et al.* [11] reported 47%cases of viral hepatitis in their study. Rathi U *et al.* [12] reported 52.3% cases with liver dysfunction due to preclampsia and HELLP.A decrease in incidence of hepatitis is noted in recent years. This may be due to increased awareness about personal and community hygiene. There were few Hbs Ag cases that were carrier or chronic state, none of them were in active stage and hence was excluded from the study. There were 2 cases of chronic liver diseases during our study period. Agarwal *et al.* [13] studied 50 pregnant patients with NCPH and reported that in 56% patients, NCPH was detected first during pregnancy. Maximum number of cases were seen in primigravida, 60%. Majority of cases presented in third trimester. On analysing the presenting symptoms, 22 had pruritus. Other predominant symptoms were nausea and vomiting, pain in abdomen, yellowish discoloration of urine, fever and headache. Icterus was seen in 8 cases clinically. Other signs include hepatomegaly, ascites, hypertension, pedal edema.

Total bilirubin level showed mild elevation (2-5mg/dl) in 20% cases and that was in AFLP. A higher level of 10-19.9 mg/dl bilirubin was found in 2% of cases. Bilirubin level showed mild elevation (2-5mg/dl) in 69.2% cases by Vinayachandran *et al.* [5]. SGOT/SGPT values were higher (> 500) in 14% and 24% (200-500) according to our study. Similar results were seen in study conducted by Krishnamoorthy *et al.* [6] were 93% had enzymes less than 500. t Marked elevation of transaminases (10 fold) was seen in viral hepatitis, whereas pregnancy asssociated liver disease like HELLP, Intra hepatic cholestasis of pregnancy and hyperemesis had only 2-3 fold rise in transaminases.[11]. Coagulation parameters were deranged in 2 patients.

Analyzing the mode of delivery 32 (68%) underwent Caesarean section and 18 (32%) had vaginal delivery. Out of 18 deliveries, 3 were instrumental deliveries and 3 were IUD expulsion. 2 deliveries occurred as preterm at 32 and 34 weeks (11%). Mitta and Rao [14] in their study reported term delivery rate of 62.5% and preterm delivery rate of 35%Out of 32 caesarean sections, 11 cases were due to previous Caesarean. 8 cases due to HELLP with worsening of lab parameters, 1 case due to eclampsia. 2 cases due to liver failure with maternal deterioration. Other cases constituting 11 were due to obstetrical indications like fetal distress, failure to progress, DCDA with unfavorable cervix, MCDA, Triplets. In the study by Vinayachandran *et al.* [5], 55.7% delivered vaginally and 44.2% by Caesarean section. Krishnamoorthy *et al.* [6] reported 70% vaginal delivery rate in their study. Maternal outcome was studied in terms of complications, need for ICU admission, blood transfusion. 11

(22%) had various complications and 8 required ICU stay and 6 required massive transfusion. Most of the complications was associated with AFLP and HELLP. There were 5 cases of PPH that occurred during CS mainly due to HELLP. 1 case of PPH was seen in triplets. 5 cases of PPH were managed with medical methods and bilateral uterine artery ligation. There was 1 case of Abruptio placenta in HELLP that ultimately lead to IUD expulsion and DIC in mother. 3 cases of sepsis, 1 was in Hepatitis C and other 2 in AFLP. AKI was seen in a referred case of liver failure at 32 weeks and postoperatively patient was on inotropes for few days and improved with multidisciplinary approach. There was a single case of hypertensive choroidopathy in patient with HELLP.A much higher rate of complications was seen in study conducted by Krishnamoorthy *et al.* (35%) and by Satia *et al.* (55%) [6, 7]. Maternal morbidity is showing declining trend when comparing to earlier studies. With timely intervention and multidisciplinary approach there was no maternal mortality in our study. There was 1 case of maternal death due to hepatitis A in Vinayachandran *et al.* study and were reported in Krishnamoorthy *et al.* study [5, 6]. Most of the studies have shown increase in preterm birth, but our study had only 40%. Close monitoring of fetus and mother has helped us in reducing preterm births. A study by Kumar *et al.* showed incidence of 66.6% of preterm birth [15]. While analyzing sex of babies, majority were female babies. There was 6 twins and 1 triplets. 18 babies had weight of 2.1-2.5 kg. Only 4 babies born had weight below 1kg and 4 had between 1-1.5kg. Neonatal hyperbilirubinemia requiring phototherapy was seen in 18 babies. 14 babies had Respiratory distress syndrome and 5 babies required Bipap 3 were in ventilator. 3 fetus had stage 3 FGR which was seen in mother with HELLP. 3 babies had sepsis and 3 had metabolic acidosis. There was 3 perinatal mortality due to HELLP and acute liver failure. Perinatal mortality rate was 0.05 per 1000 births. This was much lower when compared to study conducted by Vinayachandran *et al.* was 122 per 1000 cases of liver diseases [5].

Conclusion

The incidence of liver diseases complicating pregnancy in this study was 0.5%. ICP was the commonest cause of liver diseases followed by HELLP and Hepatitis. Most of the women underwent Caesarean sections. Maternal complications were mainly due to HELLP and AFLP. Early detection of hypertension and timely management may help in reducing complications seen with HELLP. Perinatal mortality rate was 0.05 per 1000 births. With timely intervention and multidisciplinary approach there was no maternal mortality in our study. Liver diseases in pregnancy can be difficult to manage due to various presentations that range from subtle liver biochemical changes to hepatic failure. Early diagnosis and prompt management of cases have decreased the perinatal and maternal morbidity as well as mortality to a greater extent.

Acknowledgements

The authors would like to thank the Department of Obstetrics and Gynaecology and Department of Health Science Research of Amrita Institute of Medical Sciences and Research Centre, Kochi for providing facility to carry out this study.

Conflict of Interest

Not available

Financial Support

Not available

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How to Cite This Article

Murali V, Nair D, Kochumon SP, Radhamany K, Nair CKK. Maternal liver disease and perinatal outcomes: A retrospective cohort study from a tertiary care hospital. International Journal of Clinical Obstetrics and Gynaecology 2025;9(6):1146-1150.