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Original Research Article

A prospective study on pregnancy complicated with jaundice with special emphasis on fetomaternal outcome

Neha Choudhary*, Sangeeta Sen, Varalakshmi K.

Department of Obstetrics and Gynecology, Panna Dhaya Zanana Hospital, RNT Medical College, Udaipur, Rajasthan, India

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***Correspondence:**

Dr. Neha Choudhary,

E-mail: nehachoudhary1710@gmail.com

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ABSTRACT

Background: Jaundice defined as yellow discolouration of skin, sclera and mucus membrane resulting from increased serum bilirubin concentration. It is usually clinical visible when plasma bilirubin exceeds 3mg/dl. This study aimed at determining maternal and foetal outcome in women with jaundice complicating pregnancy.

Methods: This prospective study was conducted on 58 cases of pregnant women with jaundice (serum bilirubin ≥ 3 mg%) admitted at Panna Dhaya Zanana Hospital (PDZH), RNT Medical College, Udaipur, Rajasthan from January 2016 December 2016.

Results: The incidence observed in this study was 0.28%. 77.59% cases in this study were in third trimester of pregnancy. Serum bilirubin was >20 mg% in 5.18% cases. Haemolysis, elevated liver enzymes, low platelets (HELLP) syndrome, acute fatty liver of pregnancy, intrahepatic cholestasis of pregnancy, viral hepatitis and malaria were the causes of jaundice. HELLP syndrome was the most common cause of jaundice. Of 58 women 38 delivered vaginally and 12 were LSCS for obstetrical indication and 8 were undelivered. The disease is associated with high incidence of preterm labour, IUGR, birth asphyxia and foetal distress. Perinatal mortality was 38%. Maternal mortality in 11 cases i.e. 18.96%. Main causes of maternal mortality were hepatic encephalopathy, DIC followed by shock due to PPH, DIC followed by multiple organ dysfunction syndrome.

Conclusion: Jaundice and pregnancy having a grave prognosis, resulting in a very high perinatal as well as maternal morbidity and mortality, and requires an early diagnosis and careful management.

Keywords: Jaundice, Pregnancy with jaundice, Serum bilirubin

INTRODUCTION

Jaundice is defined as yellow discoloration of skin, sclera and mucous membrane resulting from increased serum bilirubin concentration. It is usually clinically visible when plasma bilirubin exceeds 3mg/dl.¹

The normal physiological changes in pregnancy e.g. palmar erythema, spider naevus, cherry angiomas, lithogenic bile, cholestasis etc. may mimic liver disease, but can be attributed to increase serum estrogen and progesterone.²

Physiological changes during pregnancy leads to increase in alkaline phosphatase levels 3 to 4-fold and no change in liver transaminase levels (AST, ALT), GGT, Bilirubin level, prothrombin time, blood flow to the liver.³

Pregnancy with jaundice is considered as high-risk pregnancy carrying grave prognosis for both mother and foetus. Up to 3% of all pregnancies are complicated by liver disorders.⁴ Incidence of jaundice in pregnancy is 0.4-0.9/1000 in India. Jaundice in pregnancy carries adverse fetomaternal outcome and accounts for 60% of perinatal and 14% of maternal mortality.⁵

Table 1: Clinical features of the most common liver disease that occurs in pregnancy.

Condition	Main symptoms	Trimester	bilirubin	Transaminases	Platelet count	Other features
Hyperemesis gravidarum (HG)	Prolong nausea, vomiting, weight loss and nutritional deficiency	1st trimester	↑	Normal to mild rise upto ≤ 250 IU/L	Normal levels	Ketonuria
Intrahepatic cholestasis of pregnancy (ICP)	Pruritus, steatorrhea, abdominal pain	2 nd -3 rd trimester	↑↑↑	Normal to mild rise upto ≤ 250 IU/L	Normal levels	Bilirubinuria
Acute fatty liver of pregnancy (AFLP)	Epigastric /right upper quadrant pain, nausea, vomiting, malaise, fatigue	3 rd trimester	↑	Markedly high	Normal levels	Associated with pre-eclampsia in about 50%
Pre-eclampsia/eclampsia	Hypertension, edema, epigastric /right upper quadrant pain, neurological deficit (headache, seizures, blurring of vision, coma)	2 nd -3 rd trimester and postpartum	↑	Markedly High	Normal levels or ↓	High uric acid levels, proteinuria
Syndrome of haemolysis, elevated liver enzymes and low platelets (HELLP)	Hypertension, edema, epigastric /right upper quadrant pain, neurological deficit (headache, seizures, blurring of vision, coma)	2 nd -3 rd trimester and postpartum	↑	Markedly high	Low levels	Haemolysis, high uric acid levels, proteinuria

Liver disorders in pregnancy is multifactorial in origin. Jaundice in pregnancy can be classified in 3 categories:

- Jaundice specific to pregnancy such as Hyperemesis gravidarum, intrahepatic cholestasis of pregnancy, acute fatty liver of pregnancy, preeclampsia/eclampsia, and HELLP syndrome. These occur in patients with previously healthy liver and usually resolve spontaneously in puerperium
- Pregnancy in preexisting chronic liver disease, e.g. cirrhosis of liver, chronic viral hepatitis, Wilson's disease

- Pregnancy with acute viral hepatitis which may lead to fulminant hepatic failure, e.g. hepatitis E, hepatitis B, hepatitis A, HSV etc. and drug induced hepatitis.

Viral hepatitis is the most common cause of jaundice in pregnancy.^{6,7} HEV and HBV were most frequent cause of fulminant hepatic failure in pregnancy.^{1,8,9} In developing countries as India, Hepatitis E is the most common cause of fulminant hepatic failure.¹⁰⁻¹² In viral hepatitis patient presents with prodromal symptoms like vomiting, fatigue, malaise, arthralgia, myalgia and headache. Liver becomes enlarged and tender leading to abdominal pain.² Intrahepatic cholestasis is found to be the second most common cause of jaundice in pregnancy.⁶

In the present study, aim is to determine the fetomaternal outcome in pregnancy complicated by jaundice at Panna Dhay Zanana hospital, Udaipur. This includes:

- Incidence of jaundice in pregnancy in Panna Dhay Zanana Hospital, Udaipur.
- Etiological factors for jaundice in pregnancy.
- Clinical presentations in pregnant women with jaundice.
- Maternal and fetal morbidity and mortality in pregnancies complicated with jaundice.

METHODS

Present study was a prospective study. The study was conducted on 58 cases of pregnant women with jaundice (serum bilirubin ≥ 3 mg%) admitted at Panna Dhay Zanana Hospital (PDZH), RNT Medical College, Udaipur, Rajasthan from January 2016 to December 2016.

The diagnosis of each case of jaundice in pregnant women was based on clinical evaluation, biochemical and hematological parameters and in all cases foetomaternal outcome analysed in detail as follows:

History

A detailed history of present illness including origin, duration and progress of following symptoms like yellow colored urine, anorexia, nausea, vomiting, fever, epigastric pain and pain in abdomen, constipation/diarrhea, irritability and weakness.

General physical examination

A thorough general examination was carried out with special attention to:

- The evidence of yellow discoloration of sclera, skin and mucus membrane and yellow urine
- Level of consciousness
- Built and nutrition
- Pulse, temperature, respiration and blood pressure
- Presence of anemia and fever
- Edema of face, feet, abdomen wall, vulva and may involve whole body
- Enlargement of lymph nodes.

Systemic examination

Abdomen was examined for any lump including liver and spleen. Ascites and tender areas were looked for.

A thorough obstetrical examination in each case was carried out in detail. It included

- Per abdomen examination in each and every case
- Per speculum and per vaginal examination whenever it was necessary.

Investigations

Every patient was investigated as follows.

- Routine examination for CBC and PBF for hemoglobin, total and differential white cell count, platelet counts, blood group, TSH, blood sugar, blood urea, HIV, VDRL, malaria.
- Urine examination was carried out for presence of albumin, sugar, bile salts, bile pigments, urobilinogen and microscopical abnormalities.
- Liver function tests included-
 - a) Serum bilirubin
 - b) Plasma proteins
 - c) Serum transaminases enzymes (SGOT, SGPT) exceed more than 400IU/L indicates liver injury.
 - d) Alkaline phosphatase (ALP)
 - e) Gamma glutamyl transferase
 - f) Coagulation profile including bleeding time, clotting time and prothrombin time (BT, CT, PT/INR).
- Serological tests for viral markers
 - a) IgM anti-HAV antibody
 - b) HBV (HBsAg, HBeAg, IgM anti HBV core antigen)
 - c) IgM anti-HCV antibody
 - d) IgM anti-HEV antibody
 - e) Herpes simplex virus PCR.

RESULTS

The incidence observed in this study is 2.8 pregnant women with jaundice/1000 pregnancies (0.28%) recorded at Panna Dhay Zanana Hospital, Udaipur (Rajasthan, India) in the duration from January 2016 to December 2016 (Table 2).

Table 2: Incidence of pregnancy complicated with jaundice.

Period of study	Total no. of deliveries	Total no. of abortion	Total no. of pregnancies	Total no. of cases of jaundice with pregnancy	Incidence (%)
January 2016 to December 2016	19494	1288	20782	58	0.28%

Of those 58 women, 68.97% (40/58) were unbooked and 72.42% (42/58) were from rural area. The incidence of jaundice in pregnancy were highest in primigravida i.e. 50%. In this study the disease was found to be more common in younger age group, highest (56.89%) in the age group of 21-29 years. It may be due to the fact that higher no. of pregnancies was in this age group. Most of cases were in 3rd trimester that is 77.59% followed by 2nd trimester and least no. of cases presented in 1st trimester.

Clinical picture of pregnant women with jaundice was extremely variable from the stage of slight malaise in early stage which can be neglected easily by many to a very severe form culminating into hepatic coma and eventual death.

In all patients more than one symptom was present. Chief symptoms that were observed are nausea, vomiting, loss of appetite, epigastric pain and dark or yellow colored urine.

In this study most common presenting symptom were nausea and vomiting that were 56.90% and 44.83% followed by Loss of appetite and yellow colored urine were as presenting feature in 41.38%. Epigastric pain or pain in right hypochondrium was presenting symptoms in 34.48%. Pruritus is presenting symptom in 13.79% cases of jaundice in pregnancy. Only one patient had complaint of hematemesis. All 58 patients i.e.100% had icterus at the time of admission (Table 3).

Table 3: Clinical findings observed in this study.

Symptoms	No. of patients	Percentage
Icterus	58	100
Yellow/dark colored urine	53	91.38
Fever	33	56.90
Pallor	31	53.45
Nausea	33	56.90
Vomiting	26	44.83
Edema	27	46.55
Loss of appetite	24	41.38
Yellow/dark colored urine	24	41.38
Epigastric pain/pain in abdomen	20	34.48
Tenderness in right hypochondrium/ epigastric region	13	22.41
Unconsciousness /coma	11	18.96
Hepatomegaly	11	18.96
Itching (pruritus)	8	13.79

53.45% of cases showed positive for bile pigments and bile salts in urine. 27 (46.55%) cases showed positive for protein in their urine.

Serum bilirubin level varied widely between 3 mg% to 24.15 mg% in group.

The serum transaminase level was raised in majority of cases of jaundice in pregnancy. Serum alkaline phosphatase was ≤ 400 IU/L in 68.97% cases and ≥ 800 IU/L in 12.07% cases. Raised serum transaminases are due to hepatocellular injury and raised alkaline phosphatase reflects degree of cholestasis in cases of jaundice (Table 4).

Table 4: Distribution according to liver enzymes serum transaminase level and serum alkaline phosphatase.

SGOT (IU/L)	No. of patient	Percentage
≤ 200	37	63.79
200-500	17	29.31
≥ 500	4	6.90
SGPT (IU/L)		
≤ 200	35	60.34
200-500	17	29.31
≥ 500	6	10.35
Alkaline phosphatase (U/L)		
≤ 400	40	68.97
400-800	11	18.96
≥ 800	7	12.07

Coagulation parameters found altered in 21 patients. Out of which 13 patients went into DIC (Table 5). Among 58 cases 15 patients (25.86%) received blood transfusion of various component to maintain their vitals haemodynamically stable. Two patients with HELLP syndrome with DIC transfused 8 Packed cells, 12 FFP and 12 platelets.

Table 5: Coagulation parameters.

Test	Level	No. of patients (n=58)	Percentage
PT/INR	Normal	37	63.79
	Raised	21	36.20
FDP (Fibrin degradation product)	Normal	47	81.04
	Raised	11	18.96
D-dimer	Normal	49	84.48
	Raised	9	15.52

In present study most common predominant cause of jaundice in pregnant women was pre-eclampsia, HELLP syndrome that was observed in 27 (46.55%) cases.

2nd most common cause was viral hepatitis found in 11 (18.96%) cases followed by intrahepatic cholestasis of pregnancy that was found in 9 (15.52%) cases. Majority of cases of HELLP syndrome i.e.50% were in Mississippi Class 3 (Figure 1).

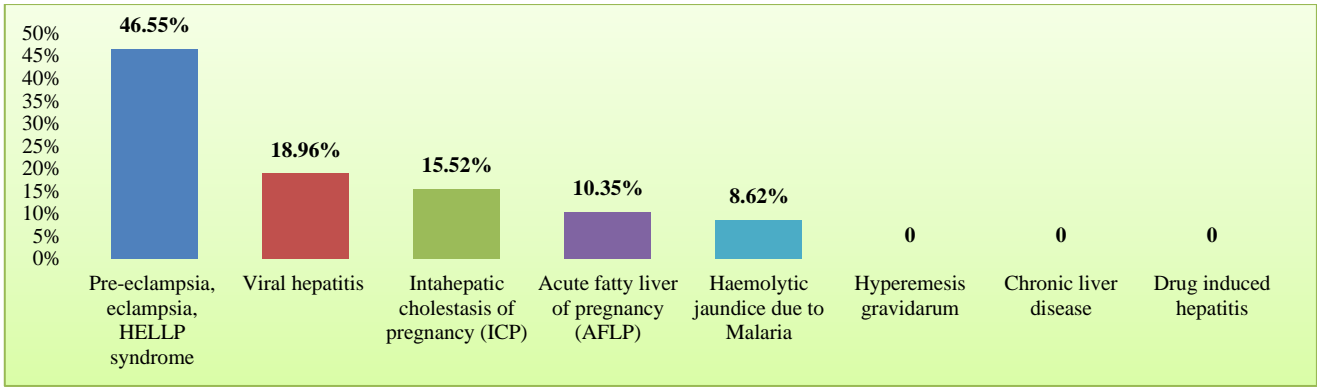


Figure 1: Distribution of cases according to etiological factors of jaundice in pregnant women.

Table 6: Obstetrical outcome.

Outcome	No. of patient	Percentage
Mode of delivery		
Vaginal	37	63.79%
Instrumental vaginal (forceps, ventouse)	1	1.72%
Caesarean section	12	20.67%
Undelivered		
Improved and discharged	3	5.18%
Left against medical advice	1	1.72%
Expired undelivered	2	3.45%
Aborted	2	3.45%

Obstetrical outcome

In this study out of total 58 pregnant women 50 patients delivered. Among 8 undelivered patients 2 were early pregnancy aborted, 3 patient improved condition and discharged, one patient left against medical advice and 2 patients expired undelivered (Table 6). The obstetrical outcome in delivered patients in terms of mode of delivery is shown in Table 6.

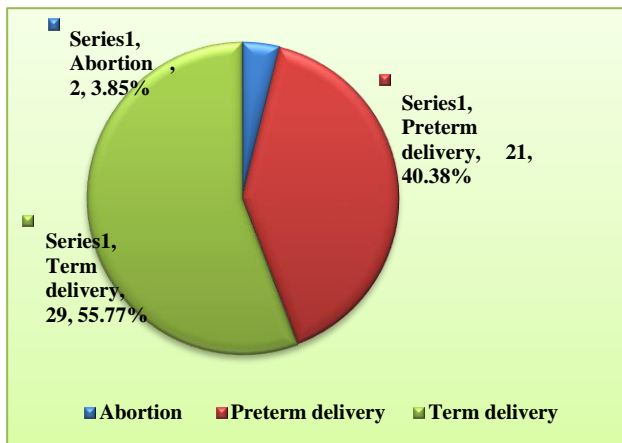


Figure 2: Pregnancy outcome of women who delivered (n = 52).

In this study 55.77% had term delivery, 40.38% had preterm delivery and 3.85% cases aborted among 52 patients. Among 21 cases of preterm delivery 66.67% were spontaneously occurred and rest of 33.33% were iatrogenically induced as when the risk of continuation of pregnancy was more for mother (Figure 2).

Table 7: Maternal morbidity and mortality.

Maternal complication	No. of patients	Percentage
Postpartum haemorrhage	21	36.21
DIC	13	22.41
Renal failure	13	22.41
Hepatic encephalopathy	12	20.67
Eclampsia	10	17.24
Abruptio placentae	6	10.35
Septicaemia	3	5.18
Oesophageal varices	1	1.72
Coma	9	15.52
Death	11	18.96

In present study most common maternal complication was atonic PPH which occurred in 36.21% cases followed by DIC and renal failure each in 22.41% cases. Hepatic encephalopathy found in 12 (20.67%) cases among them 9 (15.52%) cases had coma. Only one patient had oesophageal varices at time of hospital admission (Table 7).

Table 8: Causes of maternal mortality.

Cause of mortality	No. of patients (n=11)	Percentage
Multiple organ dysfunction syndrome	4	36.36
HELLP Syndrome with DIC with acute renal failure	2	18.18
Hepatic encephalopathy	2	18.18
Cerebral malaria	2	18.18
Septicaemia	1	9.09

In present study maternal mortality was 18.96%. In majority of cases cause of mortality was multiple organ dysfunction syndrome (MODS) accounting for 36.36% of all mortality followed by HELLP syndrome with DIC with acute renal failure, hepatic encephalopathy and cerebral malaria each for 18.18%. One case (9.09%) died as a result of septicemia (Table 8).

Perinatal outcome

Among 50 deliveries still birth was 30%, early neonatal death was 8% and baby discharged healthy were 62%. Perinatal mortality in this study was 38%.

Most common cause of neonatal mortality in present study was prematurity and low birth weight in 42.11% followed by birth asphyxia and foetal distress (Figure 3).

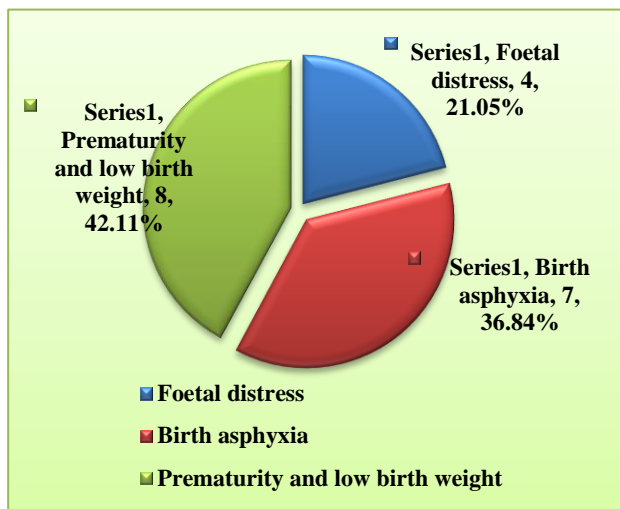


Figure 3: Causes of perinatal mortality (n = 19).

In the present study 31.43% out of 35 live born babies required NICU admission, leading cause was prematurity and low birth weight i.e.45.45% followed by birth asphyxia i.e. 27.27%, meconium aspiration syndrome i.e.18.28% and sepsis i.e. 9.09%.

DISCUSSION

The incidence of jaundice in India varies from 0.4 to 0.9/1000 deliveries. Present incidence is 0.28% deliveries. Krishnamoorthy J et al reported 0.29% incidence while Acharya N et al and Karegoudar D et al reported 0.4 % incidence. In the present study, most of the women 28 (75.68%) belonged to age group of 21 to 30 years.^{6,12,13}

HELLP is commonly encountered in the second or third trimester but can also arise after delivery.¹⁴ In the present study, the predominant cause of jaundice was found to be of pre-eclampsia, HELLP syndrome that was observed in 27 (46.55%) cases. 2nd most common cause was viral hepatitis found in 11 (18.96%) cases followed by

intrahepatic cholestasis of pregnancy that was found in 9 (15.52%) cases.

Comparable results cited by Reddy MG et al who noted hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome, acute fatty liver of pregnancy, intrahepatic cholestasis of pregnancy, viral hepatitis, malaria and sickle cell anemia were the causes of jaundice in their study. HELLP syndrome (33.3%) was the most common cause of jaundice followed by AFLP in 22.2% cases and Karegoudar D. et al observed that among 37 pregnant women with jaundice predominant cause of jaundice was HELLP 24 (64.86%) followed by acute viral hepatitis and Leptospirosis 5 (13.51%) of each.^{1,12}

HEV infection is the most prevalent and dangerous type of viral hepatitis in Asian and African continents. The incidence reported by a study done by ICMR is as high as 80-90% in cases of viral hepatitis in pregnancies. In present study Hep E virus found to be most common cause of viral hepatitis it accounts for 45.45% of cases of viral hepatitis. Other studies reported as Acharya N et al, Ambreen A et al and Parveen T et al noted HEV being the commonest with a high maternal and perinatal mortality.^{6,8,9} Reyes H and Simms HF et al studied the course of viral hepatitis in pregnancy and concluded that its course is unaltered in pregnancy, except in cases of HEV infected cases, in which cases hepatitis has more fulminant course.^{15,16}

However, Sharma S et al found Hepatitis B was the most common cause of acute hepatitis (26.7%) and incidence of hepatitis E was 13.3% in this study.¹⁷

Acute fatty liver during pregnancy usually occurs in the 3rd trimester. Preeclampsia is associated in 50-100% of cases. There is moderately increased liver enzyme level of <1000 IU/mL, bilirubin level of 1-10 mg% and hypoglycemia. The maternal mortality is 18% while preterm labor is increased and the perinatal mortality is 23%.¹⁸ In our observations AFLP was found as cause of jaundice in 6 (10.35%) cases, half of AFLP patients had preeclampsia.

Jaundice in pregnancy is associated with high maternal and perinatal mortality rates. We observed in this study that out of 50 delivered cases 62% babies were alive, 30% stillbirth and early neonatal death in 8% cases. Perinatal mortality in this study was 38%. Prematurity and low birth weight in 42.11% accounted for majority of the deaths. Higher perinatal mortality was also supported by these studies as Tripti N et al reported that perinatal mortality was 61.76% with 50% stillbirth and 11.76% early neonatal death.⁵

Perinatal mortality was observed as cited by Acharya N et al 16.6%, Karegoudar D et al 46.16%, Jayanti N et al 19% and Mitta P et al 30.76%.^{6,12,19,20} In the present study 31.43% out of 35 live born babies required NICU

admission, most common indication for NICU admission was prematurity and low birth weight that was in 45.45% of total NICU admissions. This was followed by birth asphyxia, meconium aspiration syndrome and sepsis.

Jaundice in pregnancy accounted for maternal mortality 18.96% that occurred in our department during the period of study. In majority of cases cause of mortality was multiple organ dysfunction syndrome (MODS) accounting for 36.36% of all mortality followed by HELLP syndrome with DIC with acute renal failure, hepatic encephalopathy and cerebral malaria each for 18.18%. One case (9.09%) died as a result of septicemia.

Various studies also report jaundice as one of the major indirect cause of maternal death. Similarly high maternal mortality observed by other studies. Tripti N et al noted maternal mortality was 24.4%. Cause of death was hepatic encephalopathy with renal failure in 60%, disseminated intravascular coagulation in 20%, postpartum hemorrhage and congestive cardiac failure associated with severe anemia in 10% each.⁵

Karegoudar D et al noted maternal mortality was 75.68%.¹² Reddy MG et al noted among 18 cases of jaundice in pregnancy maternal mortality in 3 (16.66%) cases.¹

Maternal mortality in other studies also comparable as Jayanti N et al 10%, Wani S et al noted 11% and Krishnamoorthy J et al noted 7.8%. Sharma S et al reported that maternal mortality was found in 1 out of 30 cases i.e. 3.33% due to hepatic encephalopathy and coagulopathy.^{10,13,17,19}

Maternal deaths were directly proportional to the level of the serum bilirubin. Tripti N et al and Trivedi et al also observed the same.⁵

CONCLUSION

By the present study we concluded that pregnancy complicated with jaundice have very poor maternal as well as foetal outcome. In this study most common predominant cause was pre-eclampsia, HELLP syndrome followed by viral hepatitis. However, the prevalence and aetiology of jaundice still remain debatable in developing and developed countries.

We observed maternal mortality was 18.96% and perinatal mortality was 38% this shows grave foeto maternal prognosis for pregnancy complicated with jaundice.

Poor fetomaternal outcome associated with poor nutrition, prevalence of anaemia, delay in seeking medical advice and delay in referral to the hospital. Many of the patients when brought to the hospital are already in moribund condition and often, do not respond to treatment. So health awareness, routine antenatal check-

ups and most important is early diagnosis and management is necessary to overcome burden of disease and to reduce high maternal and maternal mortality in jaundiced pregnant women.

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