

A Study on Effect of Serum bilirubin Levels on Maternal Fetal Outcome in Jaundice Complicating Pregnancy

Dr. S. Geetha Lakshmi¹. Dr. V. Bhavani². Dr.C.Bindu Reddy³

^{1,2,3}Department of Obstetrics and Gynaecology,
Government Maternity Hospital, S. V. Medical College, Tirupati.

Abstract

Context: Jaundice during pregnancy had serious effects on mother, fetus. Pre-eclampsia, viral hepatitis associated anaemia contributes major causes, common in IIIrd trimester. Disseminated intravascular coagulation (DIC), postpartum haemorrhage (PPH) with multi organ failure are the causes of mortality. Immediate delivery for better outcomes leads prematurity compromises perinatal outcome.

Aim: To study the effect of serum bilirubin levels on mother, fetus in jaundice complicating pregnancy

Materials and methods: Jaundiced pregnant women 46, Prospective study, Government maternity hospital, Tirupati

Statistical analysis: M.S. Excel, Epi-info

Results: Incidence of jaundice 0.16% and 1.61 per 1000 pregnant women. Common in women of primi gravida, III trimester, rural illiterate, low socioeconomic. Commonest factors preeclampsia, HELLP Syndrome, Hepatitis B infection, associated anaemia. Maternal complications 39.2% - PPH, DIC, abruption, hepatorenal failure. Maternal mortality was 0.021% among jaundiced women 13.04%. Prematurity 45.65%, perinatal mortality was 26.08%

Conclusion: Low socioeconomic status, low hygiene, lack of health awareness was influencing factors. Serum bilirubin levels raises 6 mg% presence of complications, fetomaternal morbidity, and mortality was significantly increased with 10 -14 mg%. The higher serum bilirubin levels had significant effect on maternal outcome as morbidity value is 0.0166, mortality with p value 0.035, fetal outcome p value 0.0021.

Recommendations: Serum bilirubin level ensures significant effect on fetomaternal outcome. Early diagnosis, timely treatment reduces maternal, fetal morbidity and mortality

Key words: hyperbilirubemia, jaundice, mortality, morbidity

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I. Introduction

Jaundice is defined as yellowish discoloration of skin and mucous membranes due to increase in serum bilirubin levels¹. The incidence of jaundice in pregnancy is 1 out of every 1500 pregnancies (0.067%)². The incidence in India is 0.92% to 1.46%³, Hepatitis B infection 1 in 425 pregnancies (0.245%)³. The actual incidence is high, nausea, vomiting, anorexia mislead as hyperemesis gravidarum.

Jaundice is prevalent in developing countries due to low hygienic conditions, anaemia, poor nutritional status and inadequate treatment facilities.⁴

During pregnancy causes of jaundice are particular to the pregnancy-toxaemia of pregnancy, HELLP Syndrome (Hemolysis, Elevated liver enzymes, low platelet count), obstetric cholestasis and acute fatty liver. Intercurrent Jaundice in pregnancy is viral Hepatitis A, B, C, D, E, and infections- Leptospirosis, Malaria, Typhoid, Herpes viruses etc¹.

Coexisting reasons like viral hepatitis or due to gall stones, pre-existing liver diseases like cirrhosis, portal hypertension, familial non haemolytic Jaundice (e.g.: Gilbert's disease) and miscellaneous causes are haemolysis, hepatotoxic drugs (chlorpromazine, phenylbutazone, etc.), gall bladder diseases (bile duct obstruction due to gall stones, primary biliary cholangitis, primary sclerosing cholangitis etc.)¹.

In India major sources of Jaundice during pregnancy are Preeclampsia (HELLP syndrome), viral hepatitis⁵.

The course of the jaundice and the fetal-maternal outcome will be directly effects on each other⁶. The maternal complications are abruptio placenta, puerperal pyrexia, pulmonary edema, acute fulminant hepatic failure, hepatic encephalopathy, hepatic failure, hepatic coma, Disseminated Intravascular Coagulation, Post-Partum Haemorrhage, hepatorenal failure and death⁶.

Prognosis is good in intrahepatic cholestasis of pregnancy, malaria, typhoid, viral hepatitis, Gilbert's disease, but poor in Acute Fatty Liver in Pregnancy (AFLP), some cases of HELLP syndrome⁶. Jaundice in

pregnancy causes 10% of maternal mortality in India^{7,8}. Maternal mortality was 30-60 % of cases of HELLP, 50-70% in AFLP, 2.8% with viral hepatitis⁶. Herpes simplex have grave prognosis, mortality exceeds 90% even with treatment⁶.

Fetal complications like abortions, Intrauterine Growth Retardation (IUGR), Intra Uterine Death (IUD) and perinatal mortality are high⁶. Poor fetal outcomes due to meconium stained amniotic fluid (25%), preterm labour (20%), fetal distress (22-33%) and still birth (1-2%)⁹ The perinatal mortality rate in cirrhotic patients is 10-38%¹⁰

Course of Jaundice is not affected by pregnancy in most of the cases^{4,6}. Aggravation of jaundice is seen in conditions with pre-existing liver disorders like cirrhosis of liver, Gilbert's liver disease etc⁴

Early diagnosis, timely treatment, planned delivery in health care facility minimise the maternal and fetal complications⁶. Administration of immunoglobulin and vaccine (immune prophylaxis) to neonate will minimize perinatal transmission¹¹.

This study was undertaken to analyse aetiology, course of disease, effect of hyperbilirubemia on maternal, fetal outcome in jaundiced pregnant women. Present study will help in future forearly detection, treatment to reduce the morbidity and mortality in jaundiced pregnant women.

II. Aims And Objectives

1. To determine the incidence of jaundice during pregnancy
2. To assess the effect of jaundice on pregnancy, maternal and fetal outcome.
3. To explore the effect of serum bilirubin levels on mother, fetus as morbidity and mortality

III. Materials And Methods

Study design: Prospective observational study was conducted from April 2015 to November 2016 in department of Obstetrics and Gynaecology, Government maternity hospital (GMH), Sri Venkateswara Medical College, Tirupati,

Study Subjects: Jaundiced pregnant women 46 admitted, in department of obstetrics and Gynaecology, GMH, Tirupati

Inclusion Criteria: Antenatal women with the signs and symptoms of jaundice admitted and willing.

Exclusion Criteria: Women with malignancies like carcinoma liver, secondaries in liver.

Study Methods: Jaundiced pregnant women willing were registered after taking written consent in a standardised proforma, demographic profile, LMP, EDD, menstrual history, previous obstetric history was noted. Detailed present history, past history and family history of jaundice, history of injections, blood transfusions, and intravenous drug abuse were renowned. General, systemic, vital data examination were carried out, evidence for anaemia, hepatomegaly, splenomegaly ascites and purpuric spots documented.

Investigations included complete urine examination, complete haemogram, platelet count, coagulation profile, peripheral smear, VDRL, widal, liver function tests, renal function tests, viral markers for hepatitis B and HIV conducted.

Ultrasound scan directed for complete abdomen was done in all patients to know the hepatosplenomegaly, kidneys, for the fetus-viability, gestational age, liquor status, details of placenta, Doppler studies and biophysical profile.

Followed up all patients till the time of delivery, recovery, discharge and fetomaternal outcome assessed.

Analysis: Analysed in M.S Excel and Epi-info

IV. Results

A prospective study of women with jaundice during pregnancy at GMH, Tirupati from April 2015 to November 2016 was undertaken. The incidence of jaundice complicating pregnancy in our hospital was 0.16% i.e. 46 cases among 28,520 admissions, 1.61% per 1000 population.

The jaundice patients 46 in present study, 97.83 % between 20-35 years, remain below 19 years. Rural area patients were 33 (71.74%) and 13 (28.26%) urban sector. Most of the women 39 (84.78%) were illiterates, 7 (15.22%) literates. Jaundiced women with low socioeconomic status was 34 (73.91%), middle class people 10 (21.74%), two members (4.35%) belong to higher socioeconomic status.

Present study shows 36 (78.26%) cases unbooked, 10 (21.74%) booked. The maximum number of cases 30 (65.2%) were primi gravida, 9 (19.56%) stayed second gravida, 6 (13.04%) cases existed of third gravida and one (2.18%) fourth gravida.

Majority of patients 34 out of 46 (73.91%) were in 3rd trimester, 10 (21.74%) in 2nd trimester, 2 (4.35%) patients during postpartum.

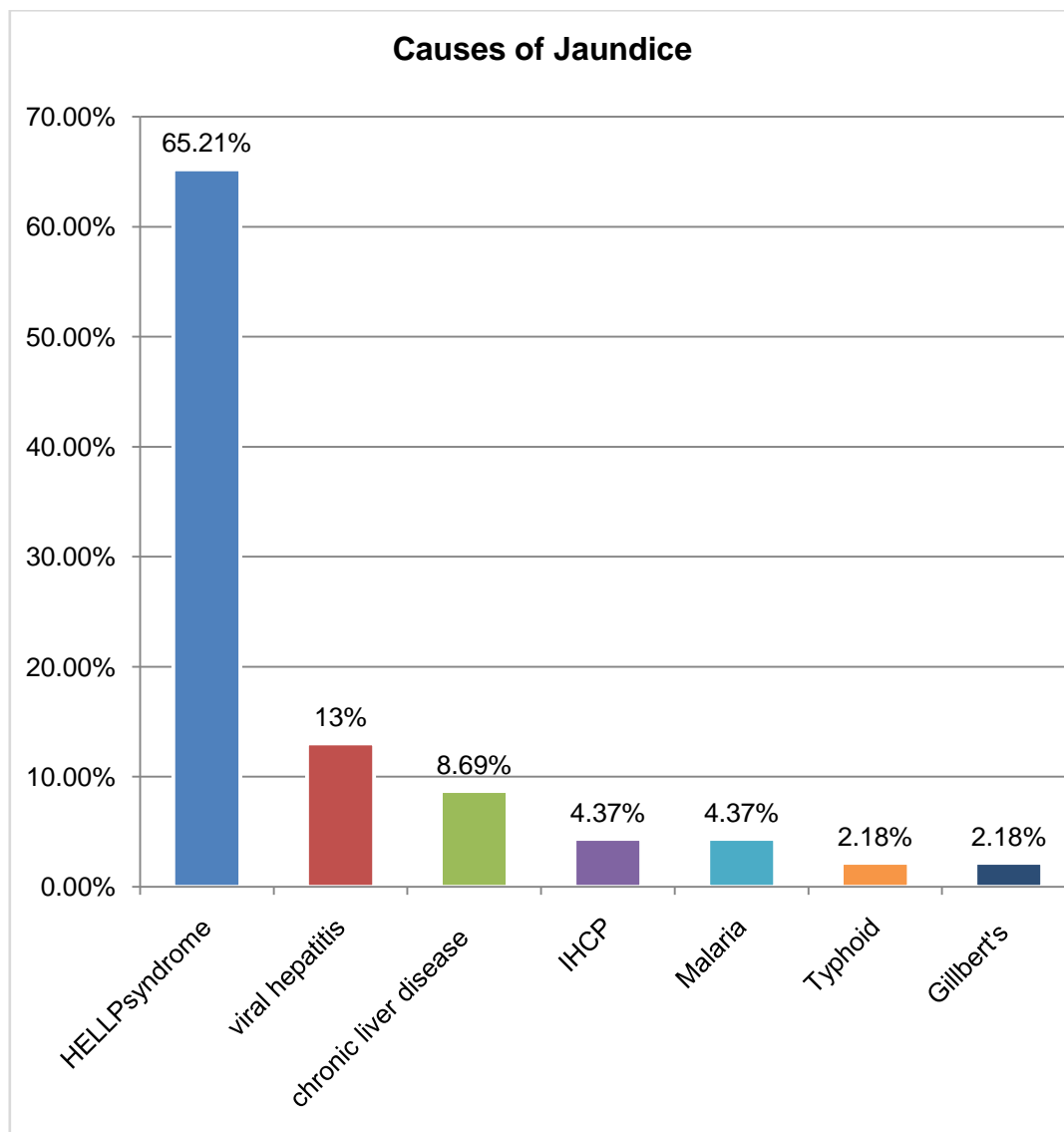


Fig - 1 Different Causes of Jaundice in Pregnancy

The "Fig-1" reveals out of 46 patients, 30 (65.21 %) cases were due to HELLP Syndrome. Six (13%) remained viral hepatitis B, chronic liver disease with portal hypertension were four (8.69%), two (4.37%) cases each malaria, intrahepatic cholestasis of pregnancy, and one case each (2.18%) typhoid and Gilbert's disease. Jaundice associated with anaemia seen in 26.09%.

Out of 46 cases two (4.3%) spontaneous abortions, 36 (78.3%) cases delivered normally and 8 (17.4%) underwent caesarean section. 25(54.3 %) cases were induced labour and 19(41.3%) cases went into spontaneous labour. Among 46 jaundice cases, 16 (34.80%) had the level of serum bilirubin range of 2-4mg%, 18 members (39.1%) revealed 4-6 mg%, six members (13.0%) presented with 6-10 mg%, four members (8.7%) shown 10-14%, two (4.3%) exhibited level above 14mg%, none above 20mg%.

Table - 1 MATERNAL OUTCOME WITH HYPER BILIRUBINEMIA

Maternal out come	Serum Bilirubin levels mg/dl					Total
	2-4mg%	4-6mg%	6-10%	10-14%	>14%	
Without complications	11	14	3	0	0	28
PPH	4	2	1	2	1	10
DIC	0	0	2	1	2	5
abruption	0	1	1	1	1	4
Hepatorenal failure	0	1	0	0	0	1
Hepatic coma	1	0	0	0	0	1
Maternal deaths	1	1	1	2	1	6

Present study reveals 28 (60.8%) out of 46 jaundiced women presented without complications. PPH was observed in 10, maternal deaths - 6, DIC - 5, abruption - 4 and hepatorenal failure, hepatic coma each one shown in "Table-1". The effect of serum bilirubin levels over maternal outcome confirms statistical significance with *p* value of 0.0166.

Table -2 MATERNAL COMPLICATIONS WITH HYPER BILIRUBINEMIA

Sr.No.	Serum Bilirubin mg/dl	No. of Cases	Maternal complications
1.	2-4mg/dl	16	6
2.	4-6mg/dl	18	5
3.	6-10mg/dl	6	5
4.	10-14mg/dl	4	6
5.	>14mg/dl	2	5
	Total	46	27

The above "Table- 2" exhibits occurrence of complications appreciated in serum bilirubin levels lower than 6 mg%, further escalation seen in higher than 6mg%, increasing the maternal complications especially after 10-14 mg% and above. Maternal complications were high with hyper bilirubenemia recognized statistical significance with *p* value of 0.0166.

The present study period amongst 28520 admissions 25(0.09%) maternal deaths and six (0.021%) were due to jaundice. Pregnancy complicated with jaundice were 46, among them six (13.04%) died due to complications of jaundice. Among 25 maternal deaths, six (24%) were died due to jaundice.

Table-3 MATERNAL MORTALITY DUE TO JAUNDICE

Sl.No.	Serum Bilirubin mg/dl	No. of Cases	Maternal Mortality
1.	2-4mg/dl	16	1
2.	4-6mg/dl	18	1
3.	6-10mg/dl	6	1
4.	10-14mg/dl	4	2
5.	>14mg/dl	2	1
	Total	46	6

The "Table-3" represents six maternal deaths due to jaundice, two noted with bilirubin levels less than 6mg%, and four seen with more than 6mg%. Among the four deaths three observed with more than 10 mg% of serum bilirubin level. The effect of serum bilirubin levels over maternal mortality confirms statistical significance *p* value of 0.034.

Four maternal deaths were due to HELLP Syndrome, one each viral hepatitis, chronic liver disease. No mortality was seen in cases of intrahepatic cholestasis of pregnancy, typhoid, malaria and gilberts disease.

Raised serum transaminase levels 100 IU in 18(39.20%), levels 100-400 IU/L seen in 26(56.50%), two(4.3%) presented levels more than 400IU

Maternal deaths occurred in four cases out of six were observed with serum transaminase value between 100-400 IU, one death each with value less than 100IU and more than 400 IU/L. The relation between serum transaminases and maternal mortality does not show statistical significance as *p* value is 0.546

Normal values of prothrombin time in 41 (89.13%) and five (10.87%) cases raised levels, among six deaths three had the levels are more than 30 seconds.

In a total of 46 cases two (4.34%) were less than 500 grams, no baby weighed 500-1 kg, 31 (67.4%) between 1-2.5kg, 11(23.91%) in the middle of 2.5-3.5 kg and 2 (4.35%) above 3.5 kg

Table - 5 FETAL OUT COME WITH

Fetal out come	Serum Bilirubin levels in mg/dl					Total
	2-4mg%	4-6mg%	6-10%	10-14%	>14%	
Term deliveries	8	11	3	1	0	23
Pre term deliveries	8	6	2	3	2	21
abortions	0	1	1	0	0	2
Intra uterine deaths	0	0	1	2	1	4
Still birth	0	0	0	0	1	1

Neonatal deaths	3	2	1	1	0	7
Birth asphyxia	0	1	0	1	0	2
Meconium stained liquor	1	1	1	0	1	4
Intra uterine growth retardation	0	1	1	0	0	2

HYPER BILIRUBINEMIA

The above “Table-5“ discloses fetal outcome 21(45.65%) of preterm deliveries ,two(4.35%) abortions and 23(50%) term deliveries.

Out of 46 cases 34 had less than 6 mg% bilirubin levels amongst undesirable fetal outcome observed in 9 babies ,more than 6mg% were 12 , all had exclusively adverse fetal outcome with birth asphyxia, meconium stained liquor, IUGR, IUD, still birth and perinatal deaths. Maternal serum bilirubin had significant effect over fetal outcome as *p* value was 0.0021

V. Discussion

The present study of jaundice complicating pregnancy was conducted in GMH, Tirupati from April 2015 to November 2016.

The incidence of jaundice was 1.61 per 1000 population. Reddi Rani et al¹² study shows 1.57 nearly correlating, according to Bhaskar Rao⁸ incidence of jaundice was 0.26, according to Devinder Kaur et al¹³ 0.92 per 1000. . Our hospital incidence 1.61 per 1000 population was high because of greater incidence of malnutrition, poor sanitation and low socioeconomic status⁴, compared to Western countries where it was 1 in 1500 pregnancies⁶.

In the present study 97.83% jaundiced pregnant women were reproductive age coincides with Devinder Kaur et al¹³, Jeyaram K et al⁷, studies was 95%, as reproductive age group is having the maximum fertility rate and deliveries.

The present study shows that majority (70-85%) of jaundice cases belong to rural areas, low socioeconomic status ,illiterates, concurs with study of Greeshma Reddy et al¹. This shows the influence of malnutrition, deprived sanitation, water contamination and poor health awareness may be influencing factors.

Present study displays 65.2% of patients were primi gravida, according to study Reddi Rani et al¹², J.S. Chauhan et al¹⁴, the incidence 50% ,but in Jeyaram K et al⁷, Devinder Kaur et al¹³ shows only 30%. Our study represents high percentage with early age of marriage; poor literacy, preeclampsia and HELLP syndrome were more in primigravidae⁶.

Jaundice complication during pregnancy was observed more (73.9%) in 3rd trimester, less in postpartum period. Study by C.M. Alwaniet al¹⁵, Reddi Rani et al¹², reveals probably due to excess nutritional stress in late pregnancy. Weinstein et al, has reported the mean gestational age of presentation of HELLP syndrome was 33.6 wks¹⁶.

HELLP Syndrome was found to be commonest cause(65.21%) was the leading cause of jaundice in our study correlates with Greeshma Reddy et al¹ study. Viral hepatitis being the second common cause however studies of Chedhaet al¹⁷, Alwaniet al¹⁵, Sachdevi.s.sk et al¹⁸ displays viral hepatitis was the leading cause of jaundice.

Anaemia was associated factor in 12 patients, among them two had severe anaemia (Hb<7gm%) and rest were between 7-10gm%. Interpretation to Devinder Kaur et al¹³, Jeyaram K et al⁷ establishes associated features like anaemia, low socioeconomic status worsen the condition in jaundice.

Preterm deliveries were 45.65%, spontaneous abortions 4.35% in our study nearly coincides with studies Sheth Abhay et al¹⁹ reported 55% preterm, 3% abortions, although Subodh Singh et al²⁰ reported high 64% preterm delivery, 8% abortion . Labour inductions were 54.3 % due to HELLP syndrome to reduce the maternal and fetal morbidity and mortality. Early delivery in pre-eclampsia and HELLP syndrome sources prematurity but helps better outcome of both⁶

Majority delivered normally in jaundiced pregnant patients to a lesser extent 17.3% by caesarean section for obstetric indications. Peter’s et al²¹, Burrough’s et al²² recommended that further progression of the disease was arrested by early delivery through caesarean section to improve maternal and fetal survival. Nonetheless the risk of anaesthesia, coagulation abnormalities is the factors against it. Serum bilirubin levels had statistical significance on mode of delivery as *p* value is 0.0386.

Maternal outcome was determined as 60.8% of the patients were recovered without major maternal complications, 39.2% of the patients had complications, multiple complications like DIC, abruption, atonic PPH contributes to major, to a less extent multi organ failure hepatic, renal, hepatorenal failure, hepatic coma and oesophageal varices. “Table-2” reflects as serum bilirubin levels raising from 2 to 6- to 10mg% the complications were more, increased the morbidity and mortality with 10-14 mg% and above. Serum bilirubin levels effects on maternal outcome establish via statistical significance *p* value of 0.0166.

The incidence of PPH was 21.74%, study by C.V Hegde and Alwaniet al²³ reported 31%, serum bilirubin does not express any statistical significance in postpartum haemorrhage 0.3219.

Incidence of maternal mortality contributes to 0.021%, in jaundiced women 13.04% near to Jeyaram K et al⁷, Bhaskar Rao⁸ study it was 10%. Maternal deaths were six, three due to DIC, one each PPH, hepatorenal failure and hepatic coma. Maternal mortality was enhanced as the serum bilirubin levels raised especially above 10mg%, according to Chadda et al¹⁷ more than 15mg% represented in "Table-3". The effect of serum bilirubin levels over maternal mortality displays statistical significance with *p* value of 0.034.

Two maternal deaths were due to HELLP Syndrome, one each viral hepatitis, acute hepatitis B infection in present study. Baha et al²⁴ maternal mortality with viral hepatitis was 14.3% whereas in non-pregnant 5.6%²⁵ Mirghani et al²⁶, observed more than 80% of deaths occurred in postpartum period. It is concluded that HELLP syndrome, viral hepatitis during pregnancy are risk factors.

Almost all women show elevated transaminase levels 100 IU to 400 IU and above. Early stages of liver diseases the transaminase levels released profoundly, in later stages because of prior exhaustion the levels fall down in near miss cases². Issel Backer²⁷ report supports our present study as relation between serum transaminases and maternal mortality was not statistically significant as *p* value is 0.546.

Majority had normal values of prothrombin time, only 10.87% cases raised. The prothrombin time is most sensitive indicator of severity of liver dysfunction and the prognosis depends on its level as per study of Weinstein et al¹⁶. A mildly elevated prothrombin time usually indicates concurrent DIC, whereas grossly elevated prothrombin time signifies hepatic necrosis¹⁶. Khuroo M.S. & Kamili reported poor prognosis in patients with prothrombin time >30 secs²⁸. In our study out of six maternal deaths three had prothrombin time >30 seconds, this shows prolongation of prothrombin time has an effect on the outcome of pregnancy in jaundice.

Perinatal mortality was 26.08%. Most of the neonatal deaths were because of prematurity and low birth weight, to lesser extent birth asphyxia, meconium stained liquor and IUGR. The present study is connecting to the studies of, Subodh Singh et al²⁰, Devinder Kaur et al¹³. If serum bilirubin advances more than 6 mg% uninvited fetal outcome observed, maternal serum bilirubin had significant effect over fetal outcome as *p* value was 0.0021

In our study no maternal mortality was seen in cases of intrahepatic cholestasis of pregnancy, typhoid, and malaria and Gilbert's disease. Maternal outcome is not so much affected except in cerebral malaria².

There was no congenital anomaly, jaundiced baby at birth in present study. A jaundiced mother giving birth to a jaundiced baby is rare because conjugated bilirubin does not cross placenta as it is impermeable.

VI. Conclusion

Incidence of jaundice in pregnancy was 0.16% and 1.61 per 1000 pregnant women. Majority women were in reproductive age primigravida during IIIrd trimester; belong to rural area, illiterates and low socioeconomic status. Lack of hygiene, malnutrition, meagre sanitation, water contamination, illiteracy, lack of health awareness possibly the influencing factors

Preeclampsia, HELLP Syndrome was the commonest next being Hepatitis B infection, associated anaemia. Maternal complications like PPH, DIC, abruption were higher with increased levels of serum bilirubin more than 6 mg%, maternal morbidity, mortality were higher with 10-14 mg% and more

Incidence of preterm delivery is 41.3%. Perinatal mortality was 26.08% prematurity being the common cause, next IUGR, meconium stained liquor and birth asphyxia, fetal outcome i.e. morbidity and mortality was effected by hyperbilirubemia

Levels of serum transaminase indicate marked hepatocellular damage, it did not affect the prognosis in jaundice. Serum prothrombin time is a good indicator of prognosis. PT of > 30 sec indicates worst prognosis.

Recommendations: Hyperbilirubemia demonstrates significant influence over outcome of mother and fetus. Improvisation of standards and quality life, regular antenatal care, early detection of pre-eclampsia, HELLP syndrome, anaemia, jaundice and others, prompt management and early recognition of complications with timely intervention will reduce maternal and fetal morbidity mortality.

Vertical transmission of HBV can be greatly minimized by giving HBV immunoglobulin vaccine to the newborn immediately after delivery

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