

Clinical Profile of Post-Partum Patients Admitted with Jaundice in Medicine Wards and ICCU

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ABSTRACT

Aim and Objectives : The present study was undertaken to assess the clinical profile of post-partum patients admitted with jaundice and discuss the various factors associated with jaundice in post-partum patients admitted to Medicine Wards and ICU.

Method : 70 postpartum women admitted with jaundice in Medicine Wards and ICU were enrolled after taking written consents of the cases and approval from the ethical committee. Their hematological, biochemical radiological, and viral profiles were studied. The basic cause of jaundice in the diagnosis was sorted out and analyzed. We also divided the cases into two groups survivors and non-survivors and tried to find out the factors predicting mortality. The unpaired Student t-test and chi-square test were used to find out whether the differences were statistically significant.

Results : Acute viral hepatitis was the most common cause of jaundice (54.4%) followed by HELLP syndrome (24.3%) and sepsis (10%). 70% of patients survived and 30% of patients could not survive during treatment. The maternal factors (pregnancy outcome, PIH), investigations (hypoalbuminemia, raised prothrombin time, low platelet count, raised creatinine), complications, and outcomes were found to be significantly associated with the etiology of jaundice while comparing survivors and non-survivors.

Conclusion : Jaundice in postpartum patients due to HEV, sepsis, HELLP syndrome, tropical fevers with the complications like AKI, hepatic encephalopathy, severe coagulopathy is associated with a poor outcome.

Keywords : Post-partum, Jaundice, Hepatitis, HELLP syndrome, PIH.

Abbreviations : ICCU- Intensive Critical Care Unit, ECG Electrocardiogram, AST Aspartate Transaminase, ALT Alanine Transaminase, ALP Alkaline Phosphatase, IU/L International Units per Liter, USG Ultrasonography, PIH-pregnancy-induced hypertension, BP Blood pressure, HEV Hepatitis E Virus, AKI Acute Kidney Injury, PT-Prothrombin Time.

Introduction :

The pregnancy and the birth of a baby are significant life-changing events for a woman and her family. Extensive physiologic, endocrine, and immunologic adaptations occur in the mother in response to the demands of pregnancy. Although these demands increase incrementally over many months, resumption of the pre-pregnancy physiologic state after childbirth occurs at a far more rapid pace. This period is referred to as the postpartum period and is a critical phase in the lives of mothers and newborn babies. Postpartum or puerperium begins soon after

the placenta is expelled and lasts for approximately 6 weeks when the uterus becomes regressed almost to non-pregnant size¹.

In this period, common complications are postpartum hemorrhage, endometritis, urinary tract infection, breast engorgement or infection, episiotomy breakdown or infection, cesarean section breakdown and infection, venous thromboembolism², urinary retention, constipation, postpartum depression, postpartum cardiomyopathy, postpartum thyroiditis. Due to all these complications, women in the postpartum period are at higher risk for morbidity and mortality. Despite the standardized protocols in the management, many postpartum complications remain under diagnosed and sub-optimally treated resulting in maternal morbidity and mortality.

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3 to 5% of pregnancies are complicated by jaundice and are one of the major causes of maternal and neonatal morbidity and mortality worldwide with an incidence of 0.1% in developed countries, and higher (3 to 20%) in developing countries³. The incidence of jaundice in India varies from 0.4 to 0.9/1,000 deliveries⁴. Jaundice during the postpartum period is also one of the clinical features of various conditions like liver disorders (infective, non-infective), blood disorders, and liver disorders peculiar to the pregnancy, which are associated with significant morbidity as well as mortality amongst mothers. So these patients are frequently shifted from obstetric wards to medicine wards and ICCU.

Moreover, this postpartum phase offers a window of an opportunity for early detection of the underlying etiology of jaundice so that early prevention and treatment measures can be taken for the betterment of the mother and ultimately of the child. There are many studies of jaundice in pregnancy but very few studies of jaundice in postpartum women. Only a few individual case reports are available on this issue. The purpose of this study is to assess the clinical profile of post-partum patients admitted with jaundice and discuss various factors associated with jaundice in postpartum patients admitted to medicine wards and ICCU.

Materials and Methods :

This hospital-based cross-sectional observational study was conducted in 70 postpartum patients with jaundice admitted to medicine wards and ICCU at the tertiary care center of Central India during a period of two years from November 2017 to October 2019. Informed consent of the enrolled cases and approval from the ethical committee of the institute were taken. Patients with age <18 years, pre-existing conditions causing jaundice, and those who refused to give consent were excluded from the study.

All the patients were evaluated as per predesigned proforma which included age, area of residence, clinical presentation, complete clinical examination and investigations like CBC, LFT, KFT, hepatitis serologies, coagulation studies, urine examination, and required imaging. The basic cause of jaundice in the diagnosis was sorted out and analyzed.

Appropriate statistical software, including but not restricted to MS Excel, SPSS was used for statistical analysis. Qualitative data was presented with the help of a frequency and percentage table. Association among the study groups was assessed with the help of the Fisher test, and Chi-Square test. 'P' value less than 0.05 was taken as significant.

Observations and Results :

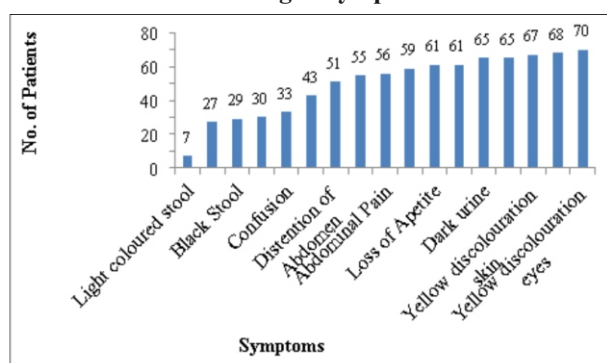
As per *Table 1*, the majority (41%) of the patients were from the age group of 21-25 years with a mean age of 25 years. More patients (54.3%) were from urban areas. Most (68.6%) of post-partum women were primigravidae with the commonest (47.14 %) gestational age in the range from 28 to 36 weeks. The commonest mode of delivery was cesarean section (57.1%).

Table 1 : Distribution of patients according to maternal factors

Maternal factors	Frequency (%)	
Age (Years)	=20	8 (11.4%)
	21-25	29 (41.4%)
	26-30	27 (38.6%)
	31-35	(8.6%)
Residence	Rural	32 (45.7%)
	Urban	38 (54.3%)
Parity	Primi	48 (68.6%)
	Multipara	22 (31.4%)
Gestational Period	28-36 weeks	33 (47.14%)
	=37 weeks	32 (45.71%)
	<28 weeks	5 (7.14%)
Mode of Delivery	Vaginal	30 (42.9%)
	Cesarean	40 (57.1%)
Pregnancy Outcome	Live-birth	51 (72.9%)
	IUD	11 (15.7%)
	Stillbirth	8 (11.4%)
Pregnancy Induced Hypertension	No	52 (74.3%)
	Preeclampsia	17 (24.3%)
	Gestational Hypertension	1 (1.4%)

Among all patients, the majority had yellow discoloration of the skin (95.7%), fever (92.9%), dark urine (92.9%), vomiting (78.6%), loss of appetite (87.1%), nausea (87.1%) as an associated symptom depicted in **Figure 2**.

Figure 2 : Distribution of the patients according to symptoms



Most of the patients (35.7%) had bilirubin in the range of 10 to 19.99 mg/dl, serum AST in < 200 IU/L (28.6%), (40%) had serum ALT levels < 200 IU/L, and 50% had serum ALP (300-600 IU/L). Hypo-albuminemia and increased PT were seen in 67.1% and 65.7% of patients respectively (**Table 2**). 44.3% of patients had deranged kidney function.

Table 2 : Distribution of the patients according to liver function test parameters

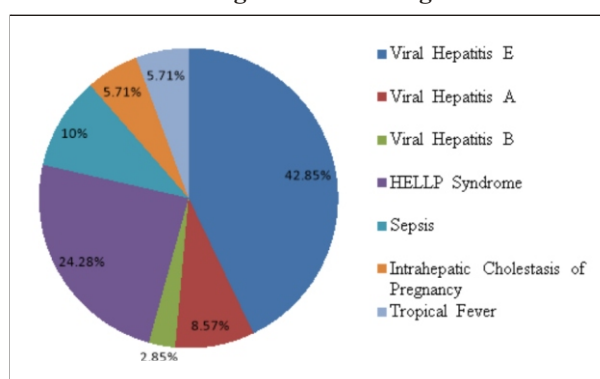
Maternal factors (Mean ± SD)	No. of patients (%)	
T. Bilirubin (Mg/dl) (8.49 ± 4.76)	< 3	2 (2.9%)
	3-4.99	18 (25.7%)
	5-9.99	24 (34.3%)
	10-19.99	25 (35.7%)
	≥ 20	1 (1.4%)
AST (IU/L) (945.97 ± 1244.92)	< 200	20 (28.6%)
	200-500	20 (28.6%)
	500-1000	11 (15.7%)
	> 1000	19 (27.1%)
ALT (IU/L) (708.91 ± 1035.58)	< 200	28 (40%)
	200-500	21 (30%)
	500-1000	7 (10%)
	> 1000	14 (20%)
ALP (IU/L) (464.21 ± 359.73)	< 300	23 (32.9%)
	300-600	35 (50%)
	> 600	12 (17.1%)

Hypo-albuminemia (< 3.5g/dl) (3.21 ± 0.662)	Yes	47 (67.1%)
Pro-thrombin time (sec) (22.88 ± 11.29)	Normal	24 (34.3%)
	Increased	46 (65.7%)

Out of 70 patients, 29 (41.4%) patients who had positive serology for hepatitis E virus (HEV), 6 (8.6%) had hepatitis A, and 2 (2.9%) had hepatitis B. Hepatomegaly, Ascites, Splenomegaly, GB wall thickening, peri-cholecystic edema, were the commonest USG abdomen findings in these patients (18.6%) with the majority had bilateral pleural effusion (15.7%) in X-ray chest.

Four main causes of jaundice were identified as viral hepatitis, HELLP syndrome, sepsis, and cholestasis of pregnancy, among which maximum (54.4%) patients had viral hepatitis (42.85% had HEV hepatitis, 8.57% had HAV hepatitis and 2.85% had HBV hepatitis) as shown in **Figure 3**.

Figure 3 : Distribution of the patients according to the final diagnosis



70% of the patients in the study had multiple complications; most of them (28.26%) had more than one complication like hepatic encephalopathy (HE), AKI, and Coagulopathy. AKI was seen commonly in the setting of HELLP syndrome, sepsis, and tropical fevers. There is an increased rate of maternal mortality in pregnant women with hepatitis E. The association of the final diagnosis (cause of jaundice) and complications was found to be statistically highly significant (p=0.000), (**Table 3**).

Table 3 : Association of the cause of jaundice and complications

Complications	Final diagnosis							Total
	HEV	HAV	HBV	HELLP Syndrome	Sepsis	ICP	Tropical Fever	
None	6	3	1	7	0	4	0	21
Coagulopathy	9	1	0	0	0	0	0	10
HE + AKI + Coagulopathy	5	2	0	7	5	0	1	20
Coagulopathy + HE	7	0	1	0	0	0	0	8
AKI	1	0	0	2	1	0	2	6
Coagulopathy + AKI	0	0	0	1	0	0	1	2
HE	2	0	0	0	0	0	0	2
PRES	0	0	0	0	1	0	0	1
Total	30	6	2	17	7	4	4	70

49 (70%) of patients survived and 21 (30%) of patients could not survive during treatment. Most of the deaths occurred in the first 15 days of the postpartum period (47.61% died in 4 to 7 days, 23.80% died within 8-15 days of the postnatal period).

100% mortality was seen in the patients who had tropical fevers, 50% mortality in viral hepatitis B cases, 20% mortality in viral hepatitis E cases, 33.30% mortality was seen in viral hepatitis A cases, 29.40% of HELLP syndrome cases could not survive, and 42.90% mortality was seen in sepsis cases. The association of the final diagnosis (cause of jaundice) and the outcome of the postpartum patients was found to be statistically significant ($p=0.029$), (**Table 4**).

Table 4 : Association of final diagnosis and outcome of postpartum patients

Final diagnosis	Outcome		Total
	Survived	Mortality	
Viral Hepatitis E	24 (80%)	6 (20%)	30 (100%)
Viral Hepatitis A	4 (66.70%)	2 (33.30%)	6 (100%)
Viral Hepatitis B	1 (50%)	1 (50%)	2 (100%)
HELLP Syndrome	12 (70.60%)	5 (29.40%)	17 (100%)
Sepsis	4 (57.10%)	3 (42.90%)	7 (100%)
Intrahepatic Cholestasis of Pregnancy	4 (100%)	0 (0%)	4 (100%)
Tropical Fever	0 (0.00%)	4 (100%)	4 (100%)
Total	49 (70%)	21 (30%)	70 (100%)

We further divided the cases into two further groups ‘survivors’ and ‘non-survivors’, comparing the clinical and laboratory findings between them to find out the various factors responsible for maternal mortality (**Table 5**).

As per table 5, among the survivors, most of the cases (81.63%) were from the age group 21 to 30 years, and most cases (42.85%) from the age group 21 to 25 years didn't survive. The primigravidae had more mortality (34.69%) than multigravidae (23.80%). Most of the postpartum women (32.5%)

couldn't be survived who had the delivery of baby through caesarian section. Pregnancy outcome was also poor (IUD, stillbirth) in non-survivors (61.90%) as compared to survivors (12.24%). 11 (52.38%) patients from non-survivors died with the first week of the postpartum period (i.e., 3 to 7 days).

Table 5 : Comparison of parameters between survivors and non-survivors

Parameter	Survivors (n= 49)	Non- survivors (n= 21)	p-value
Age (Yrs)	25.6 ± 5.06	24.61 ± 6.42	0.520
Residence - Urban	29	20	9
Rural	12	0.209	
Parity - Primigravidae	32	16	17
Multigravidae	5	0.369	
Mode Of delivery - Vaginal	22	27	8
LSCS	13	0.598	
Pregnancy Outcome			<0.001*
Livebirth	43	3	
IUD	3	8	
Stillbirth	8	5	
PIH	9	9	0.05*
Hemoglobin (gm%)	9.27 ± 0.71	8.34 ± 2.73	0.197
Platelets / mm ³ < 100000	12	13	0.037*
T. Bilirubin (mg/dl)	8.58 ± 4.23	8.27 ± 6.18	0.207
AST (IU/L)	869.55 ± 1083.69	1124.28 ± 1587.48	0.911
ALT (IU/L)	618.97 ± 773.47	918.76 ± 1489.5	0.299
ALP (IU/L)	432.40 ± 323.34	538.42 ± 444.5	0.252
Prothrombin time (Sec)	21.83 ± 10.60	25.33 ± 13.65	
Albumin (gm/dl)	27. 0.71	3.07 c 0.83	0.243
Hepatitis - HEV	23	4	0.256
HAV	1	6	
HBV	2	1	
Sr. Creatinine (mg/dl)	1.31 ± 0.94	2.48 ± 1.75	<0.001*
Diagnosis -			0.037*
Viral Hepatitis	29	9	
HELLP Syndrome	12	5	
Sepsis	4	3	
IHCP	4	0	
Tropical Fever	0	4	
Complications	28	21	<0.001*

***Statistically significant**

Amongst the various biochemical parameters, the average total serum bilirubin was found near about the same in non-survivors (mean 8.58 mg/dl) and survivors (mean 8.36 mg/dl). Prothrombin time, serum creatinine, Serum AST, ALT, ALP, Prothrombin time, and INR found to be higher in 'non-survivors' cases than 'survivor' group while serum albumin found to be low in non-survivors.

Anemia was found in 67.34% of cases of survivors and 90.47% cases of non-survivors with the mean Hemoglobin 9.27 gm% and 8.34 gm% respectively. 24.48% of survivors and 61.90% of non-survivors had low platelets (< 11 ac/mm³) with mean platelet count 161656/mm³ and 158200/mm³ respectively.

Viral hepatitis was the most common cause of jaundice in postpartum women, among which

59.18% survived and 42.85% could not survive. The second most cause of jaundice in these women was HELLP syndrome (24.28% survived and 23.80% couldn't).

57.14% of survivors had multiple complications in the course of illness, coagulopathy was the commonest (20.40%), while all the non-survivors had complications of which 66.66% had multiple complications like hepatic encephalopathy, acute kidney injury, and coagulopathy.

Among all the factors like maternal factors, biochemical parameters in the survivor group and non survivor group of the postpartum patients admitted with jaundice towards medicine side, pregnancy outcome, PIH, low platelets, raised serum creatinine, the cause of jaundice and the complications were highly statistically significant in this study.

Discussion :

Results and outcomes of this study provided us with the various causes of jaundice, frequency of occurrence of each, and association of cause with mortality so that patients can be managed to keep in mind the severity of various causes. In a country like India, still, the infective etiology predominates in the cause of jaundice. In this study, among the causes of jaundice, acute viral hepatitis the most common was seen in 54.27% of the total cases, among them 78.94% of cases had viral hepatitis E and 15.78% of cases had hepatitis A with 20% and 33% mortality respectively. As in current study results, various studies observed that viral hepatitis especially hepatitis E was the leading cause of jaundice in pregnant women³⁻⁶. The second most common cause of jaundice was HELLP syndrome found in 17 patients (24.28%), according to Tennessee classification⁹ with a mortality of 30% with multiple complications out of which 15 patients (88.23%) had complete syndrome (Platelets < 1,00,000 / mm³, AST/ALT > 70 IU/L and LDH > 600 IU/L) and 2 (11.76%) had partial HELLP syndrome. WHO estimates that the global prevalence of maternal sepsis is 4.4%, we found 10% of cases had sepsis with 43% mortality which was quite higher. 5.8% of cases had a tropical fever with significant

mortality, one had complicated falciparum malaria, one had scrub typhus and 2 had dengue fever.

The maternal factors like pregnancy outcome, pregnancy-induced hypertension (PIH), blood pressure were found to be significantly associated with the etiology of jaundice in the study population which is comparable with other studies of pregnant women with jaundice^{4,5,12-14}. There were a lot of variations in the symptoms in the different studies with fever, nausea, vomiting, high colored urine as common symptoms as similar to the current study^{5,11,12,14,15}.

Similarly, there was a lot of variation in liver enzyme levels in comparison with prior studies as the causes of jaundice were different in different studies^{15,18,19}. In the present study, a high level of S. bilirubin, SGPT, and SGOT levels of more than 500 IU/ml were associated with viral hepatitis. We also reported that marked elevation of bilirubin and transaminases (10 fold) occurred in viral hepatitis whereas patients with pregnancy-associated liver disease like HELLP, Intrahepatic cholestasis of pregnancy, and hyperemesis had only 2-3 fold elevation and higher alkaline phosphatase levels were seen in cholestatic jaundice. 67.1% of patients had hypo-albuminemia, 65.7% of patients had increased prothrombin time which are suggestive of the synthetic dysfunction of the liver, both of these were found to be highly significantly associated with the cause of jaundice. In the present study, more patients having deranged coagulation compare with the study done by *Arora et al*¹⁸. The findings of the USG abdomen were variable in comparison with previous studies like *Sudhamshu KC et al*, *Ozturk A et al* with the similarities in the common finding of hepato-splenomegaly and ascites^{19,20}.

The majority (70%) of patients had multiple complications like hepatic encephalopathy, coagulopathy, and acute kidney injury. Most of the cases of viral hepatitis had coagulopathy and cases of HELLP syndrome, sepsis, and tropical fevers had AKI as a major complication. The association of the final diagnosis and complications was found to be statistically highly significant (p=0.000). Our study results were comparable with other studies of

jaundice in pregnant women like *Krishnamoorthy J et al*, *Nagaria T et al*, *Choudhary N et al*, suggestive of coagulopathy, hepatic encephalopathy, and acute kidney injury to be common complications that increased the morbidity and mortality in postpartum women^{5,11,14}.

30% of patients could not survive, most of them died within the first week of the postpartum period i.e., early postpartum period. The mortality in postpartum patients with jaundice was found to be comparable with a maternal mortality of 24.4% in *Nagaria et al* study & 31.70% in *Negi et al* study^{11,12}. So we recommend that family members, health care workers, and treating doctors should be aware to pick up dangerous symptoms / signs of the causes of jaundice in this window period so that measures to control them can be implemented at the earliest. Early detection and treatment can reduce morbidity and mortality.

Conclusions :

In post-partum patients, viral hepatitis, HELLP syndrome, sepsis, intrahepatic cholestasis of pregnancy, and tropical fevers / vector-borne diseases are the common causes of jaundice. We found HELLP syndrome and Viral Hepatitis E, as the most common etiologies of jaundice in the rural and urban areas respectively. In post-partum patients with jaundice, complications like AKI, hepatic encephalopathy, and severe coagulopathy are associated with a poor outcome.

The first 6 weeks after delivery should be regarded as a high-risk period for women, regardless of the outcome of the pregnancy. Jaundice in postpartum women should not be ignored by patients, family members, and health personnel as it caused 30% mortality in the current study. We recommend that the antepartum, as well as postpartum patients with jaundice, should be tested for viral hepatitis (A, E, B, and C) under the National Viral Hepatitis Control Programme.

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