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RESEARCH ARTICLE

A PROSPECTIVE STUDY OF MATERNAL AND FETAL OUTCOME OF VIRAL HEPATITIS IN PREGNANCY.

Madhuri Patil[1], Priyanka Jain[2] and Alka Patankar[3].

1. Assistant Professor, Department of Obstetrics and Gynaecology, Indira Gandhi Govt. Medical College, Nagpur.
2. Senior Resident, Department of Obstetrics and Gynaecology, Indira Gandhi Govt. Medical College, Nagpur.
3. Associate Professor, Department of Obstetrics and Gynaecology, Indira Gandhi Govt. Medical College, Nagpur.

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Abstract

Background and Aims: This study was conducted to evaluate the causes ,clinical course & feto-maternal outcome and prognostic factors affecting the outcome in cases of viral hepatitis in pregnancy.

Methods: Sixty-one pregnant women reporting to the hospital with hepatitis during the study period of 2 years from January 2015 to December 2016 were enrolled as cases and their haematological, biochemical and viral profiles were studied. A comparison was done between the survivors and non- survivors and factors predicting mortality were studied . The unpaired student t test and fischre exact test were used to find out whether the differences were statistically significant.

Results: Most of the patients were primigravida (51 %) and were in the third trimester of pregnancy(82%).Viral Hepatitis in pregnancy caused a very high maternal mortality (18%). Hepatitis E virus was the commonest causative organism (55%) responsible for viral hepatitis during pregnancy. It also caused the highest maternal mortality due to fulminant hepatic failure. Maternal mortality was significantly higher in those women presenting with features of encephalopathy, high bilirubin levels, high liver enzymes and prolonged prothrombin time.

Conclusions: Hepatitis E is the chief causative organism causing fulminant hepatic failure in pregnant women.

Introduction:-

Viral hepatitis in pregnancy has been a subject of continuing interest & controversy. Opinions differ over the course of viral hepatitis in pregnancy.[1,2,3] There are studies showing results ranging from no difference in maternal & fetal outcome to virtually lethal outcome in the form of fulminant hepatitis & hepatic failure.[4,5,6]

Pregnancy with jaundice is considered as a high risk pregnancy. Each type of viral hepatitis has different implications over the course of pregnancy. Hepatitis A doesn't influence the course of pregnancy[7]while hepatitis B has a high risk of vertical transmission and thus predisposes to a chronic carrier state, liver cirrhosis and development of hepatocellular carcinoma in young adults.[8]

Corresponding Author:- Priyanka Jain
Address:- Senior Resident, Department of Obstetrics and Gynaecology,Indira Gandhi Govt. Medical College, Nagpur.

There is substantial risk of mother to fetal transmission of Hepatitis C & this can lead to hepatocellular carcinoma in mother as well as child.[9]Hepatitis E , usually a self limiting and benign infection in non-pregnant women, presents a challenging situation to the obstetrician as it is associated with more severe infection in pregnancy & might lead to fulminant hepatic failure.[10]Recently, there are emerging concerns regarding vertical transmission of Hepatitis E virus & consequent poor perinatal health outcome.[2,4]

Jaundice in pregnancy is a deadly combination resulting in a very high perinatal as well as maternal morbidity and mortality & requires an early diagnosis and careful monitoring .Hence , this study was conducted to evaluate the causes , clinical course &feto-maternal outcome and prognostic factors affecting the outcome in cases of viral hepatitis in pregnancy.

Materials And Methods:-

The present study design was a prospective observational study conducted at Indira Gandhi Government medical college &Hospital, Nagpur OBGY dept over a period of 2 years from January 2015 to December 2016. All pregnant women presenting at any gestational age with hepatitis were systematically assessed. The total number of cases studied was 61.The course of their pregnancy was closely followed and the end point of observation was the natural / artificial termination of pregnancy or death of the woman. The detailed Biochemical, Hematological and Virological workup was done for the women. The biochemical workup included Liver function and Kidney function tests. Haematology included the blood picture, prothrombin time and INR. The virological studies included Anti-Hepatitis A IgM (for recent Hep A), Hepatitis B Surface Ag (for Hep B), Anti Hepatitis C IgM and IgG (for Hep C), Anti Hepatitis E IgM (for HepE).Maternal features such as gestational age at the time of first detection of infection, clinical progression of the disease, laboratory parameters, and obstetric outcomes were noted in detail. Similarly, comparison was done between the 'survivor' and 'non survivor' cases regarding the type of viral hepatitis, biochemical and haematological picture. This was done to find out the factors responsible for maternal mortality.
The difference between 2 mean/median of quantitative variables was assessed by using unpaired t test& the association between 2 qualitative variables was assessed by fischre exact test. A difference of < 0.05 was considered statistically significant.

Results:-

Most of the patients were in the age group of 26 – 30 years (45%) with mean age at presentation of illness was 27.46 $\pm$ 4.28 years.Majority of patients were in the third trimester of pregnancy (82%) with mean gestational age at presentation of symptoms was 34.44 $\pm$ 6.28 weeks.
Primigravida constituted the major group of patients having viral hepatitis (51%).Majority of them were from low socioeconomic strata (78%) and approximately 74 % of pregnant women were literate with education upto middle class and 26% were illiterate.

Table 1:-Demographic Profile Of Cases.

PARAMETERS		NO. OF PATIENTS	PERCENTAGE (%)
AGE GROUP (years)	26-30	27	45
PARITY	Primigravida	31	51
GESTATIONAL AGE	29-40 wks	50	82
SOCIOECONOMIC STATUS	Low socio-economic strata	48	78
EDUCATION	Upto middle class	45	74

Most common cause of viral hepatitis in our study was found to be Hepatitis E virus (55%), followed by Hepatitis B (36%).Co-infection with HAV & HEV was seen in 2 patients and in other 2 patients suffering from hepatitis, no virus could be detected.

Table 2:- Viral Markers.

Etiology (Viral infection)	No. of patients	Percentage
HAV	2	3
HBV	22	36
HCV	1	1.6
HEV	34	55

NO VIRUS DETECTED	2	3	
CO-INFECTION OF 2 OR MORE VIRUSES	2	3	

Maternal Outcome:-

The analysis of maternal mortality rates revealed that in our study , there were total 11 (18%) maternal deaths, out of which 10 patients were found to be positive for virological marker of HEV and in 1 patient, no virus could be detected. Complications frequently encountered were hepatic encephalopathy (18%),Coagulopathy (16%), renal failure (13%) , ascites (6%), post partum hemorrhage (13%) and preterm labor (19%).32% patients required blood products transfusion & 24 % patients required intensive care.

Table 3:- Maternal complications.

Maternal complications	HAV	HBV(%)	HCV	HEV (%)
Hepatic encephalopathy	-	3	-	8
Coagulopathy	-	2	-	9
Fulminant hepatic failure	-	-	-	10
Maternal death	-	0	-	10

Mode Of Delivery:-

67% patients delivered vaginally & 31 % by LSCS. The indication for LSCS was obstetrical. Most common indication being fetal distress, previous LSCS or contracted pelvis.

Fetal Outcome:-

45 women with hepatitis delivered live babies out of which 2 early neonatal deaths occurred.There were 13 (21%) intrauterine deaths, 2 (3%) still births, 2 (3%) early neonatal deaths, 12 (19%) preterm births, 21 (34%) low birth weight babies, 15 (25%) babies required NICU admission.

Table 4:- Fetal outcome.

FETAL OUTCOME	NO. OF PATIENTS	PERCENTAGE (%)
INTRAUTERINE FETAL DEATH	13	21
STILL BIRTH	2	3
PRETERM BIRTHS	12	19
NEONATAL DEATHS	2	3
LOW BIRTH WEIGHT	21	34
NICU ADMISSISON	15	25

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

Parameters	Survivors N=50	Non- survivors N=11	P-value
Age	27.78 ± 4.40	26 ± 3.64	.215
Hbgm%	10.2 ±1.29	10.5 ± 2.50	.586
TB mg%	4.38 ± 3.36	9.91 ± 3.27	.000
DB mg%	2.6 ± 2.40	4.91 ± 2.25	.005
SGOT	243 ± 261	809 ± 972	.001
SGPT	220 ± 201	587 ± 451	.000
ALKP	182 ± 61.2	234 ± 83.28	.019
TLC	9752 ±1968	18027 ± 13890	.000
PT	14.34 ± .91	16.55 ± 3.20	.000
INR	1.04 ± .19	1.73 ± 1.48	.002
Urea	30.5 ± 9.36	50.3 ± 44	.004
Creatinine	.86 ± .40	1.45 ± 1.12	.004

Table 5:-Comparision between survivors and non survivors.

Categorical data		Survivor N=50	Non survivor N = 11	
Trimester of pregnancy	II	9	2	
	III	41	9	
Features of encephalopathy on admission	Absent	47	3	P<.000 with 1 degree of freedom
	Present	3	8	

We further divided the cases into two groups 'survivors' and 'non – survivors' and compared the biochemical &virological findings between them. This was done to find out the various factors affecting maternal mortality. Amongst the various biochemical parameters, the average Serum Bilirubin was found to be significantly higher among the non survivors (9.91 $\pm$ 3.27) as compared to the survivors (4.38 $\pm$ 3.36); p =0.000. The values of SGOT and SGPT were also a found to be significantly higher in the 'non-survivor' group as against the 'survivor' group with p=0.001 and p=0.000 respectively. Similarly average INR value was also found be significantly higher in the non-survivor group ; p=0.002.

Among the survivors, there were 9 women in IInd trimester and 41 in IIIrd trimester of pregnancy. Among the non-survivors, there were 2 in IInd trimester and 9 in IIIrd trimester. The trimester of pregnancy was not a significant factor for prediction of mortality.

Presence of encephalopathy at the time of admission correlated very closely with maternal mortality. Eight women who subsequently died (non-survivor group) had presented in varying grades of hepatic encephalopathy.

Discussion:-

Acute viral hepatitis is the most common cause of jaundice in pregnancy.[7]Variations have been reported in presentation of hepatitis during pregnancy ranging from asymptomatic to fatal outcome. Most of the cases of Hepatitis in India have been attributed to Hepatitis E, for which it is an endemic zone .[2]

In our study, most of the cases were young with the mean age at the time of presentation being 27.46 $\pm$ 4.28 years.The results were consistent with the studies done by Sahai et al[2] ,Krishnamoorthy et al [11] and Madan et al[12].

Majority of patients were from low socio-economic status (78%) and approximately 74 % of pregnant women were literate with education upto middle class and 26% were illiterate. Similar higher incidence of patients belonging to low socio-economic status was also seen in studies done by Krishnamoorthy et al [11],Prasad et al[10] and Madan et al[12].Similar literacy status was also seen by Shukla et al[13](70% literacy rate) and Ashoka et al[14](73.8% literacy).
Primigravida constituted the largest group of pregnant patients with hepatitis (51%).The results are similar to the studies done by Veronica et al[15](48% primigravida), Miranda et al[16] (51.2% primigravida) and shukla et al[13]. The results are not consistent with the Elsheikhet al[17] where maximum patients were 2ndgravida. In our study 84% patients were in the third trimester of pregnancy at the time of presentation. Similarly studies done by shukla et al[13], Patraet al[18] and Singh S et al [19] showed that maximum patients were in the 3rd trimester i.e. 75 %, 72% and 72% respectively, whereas the study done by Sahai et al[2] found maximum patients in 2nd trimester of pregnancy.

Hepatitis E virus was responsible for the maximum cases of viral hepatitis in our study (55%).Similar higher incidences of HEV as a causative factor of viral hepatitis was found in the studies done by Jaiswal et al[20] (58%), Aziz et al[21](62%) &Prasad et al[10] (68%).The results are in contrast to the study done by Shukla et al[13] where hepatitis B was the major cause of infection & hepatitis E was seen only in 18% of the patients.

In our study maternal mortality rate was 18%. Maternal mortality rate was comparable to the other studies done by Sahai et al[2](19.1%).This is in contrast to the certain other studies done in other parts of world ,e.g. a study from Egypt [5]found a very high rate of hepatitis E infection (84.3%) with zero percent maternal mortality. In our study HEV infection was a major cause of maternal mortality (16.3%).Similarly HEV was the main causative agent for maternal mortality in studies done by shukla et al[13] , Madan et al[12] .

As regards to fetal outcome, there were 13 (21%) intrauterine deaths, 2 (3%) still births, 2 (3%) early neonatal deaths, 12 (19%) preterm births, 21 (34%) low birth weight babies, 15 (25%) babies required NICU admission. Similarly in study done by Prasad et al[10], preterm and low birth weight formed the bulk of NICU admission(40%).
In our study, the average Serum Bilirubin was found to be significantly higher among the non survivors (9.91 ± 3.27) as compared to the survivors (4.38 ± 3.36); p =0.000. The values of SGOT and SGPT were also a found to be significantly higher in the 'non-survivor' group as against the 'survivor' group with p=0.001 and p=0.000 respectively. Similarly average INR value was also found be significantly higher in the non-survivor group ; p=0.002.These finding correlated well with the study done by Sahai et al[2] and with the SOFA scoring system[23] for prediction of mortality.

Presence of encephalopathy at the time of admission was highly predictive of maternal mortality and this is in accordance with the study of Banaitet al[24] who found higher mortality among those women reporting in a higher grade of encephalopathy**.**

Conclusions:-

Viral hepatitis during pregnancy is an important cause of maternal mortality and foetal wastage. Most of the studies have not found any correlation between Hepatitis E infection and trimester of pregnancy. Hepatitis E is the chief causative organism of hepatitis during pregnancy with an increased attack rate and severe course of disease in pregnant women compared to non pregnant women.

Since Hepatitis E is transmitted by faeco-oral route, the importance of cleanliness and availability of clean drinking water should be emphasized so as to improve the sanitary condition.This will go a long way in minimizing the HAV & HEV infection.

The need for early hospitalization should be explained at the primary level, especially if the patient is a pregnant woman with jaundice.

Limitations:-

Shortcomings in our study was a small sample size was and also there could be a selection bias as the study was carried out in a tertiary care centre, hence only the women in a very critical condition would be reporting here.

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