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Liver Pathology of Viral Hepatits in Pregnancy Related Deaths

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ABSTRACT

In this study we evaluated clinical, biochemical parameters, gross, histopathological and complication in maternal deaths due to viral hepatitis

Methods It is a retrospective study of 152 maternal deaths over a period of 6.5 years. Complete autopsy was performed. Main emphasis was on noting the gross and morbid anatomy of liver at autopsy.

Results We had one case of hepatitis B and seven cases of hepatitis E which were conformed on serology. The common gross feature of hepatitis E was shrunken, necrosed liver. Liver function test were markedly deranged. The common presenting symptom was jaundice, abdominal pen and altered sensorium.

Histologically features of fulminant hepatitis were seen in hepatitis E.

Conclusion Incidence of HEV infection is high in pregnant women with significant number progressing to fulminant hepatitis which were seen in our study.

KEYWORDS Hepatitis B, Hepatitis E, fulminant hepatitis.

INTRODUCTION:

Acute viral hepatitis is a systemic infection affecting the liver predominantly. Almost all cases of acute viral hepatitis are caused by one of five viral agents: hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), the HBV-associated delta agent or hepatitis D virus (HDV), and hepatitis E virus (HEV).[21] These range from asymptomatic and inapparent to fulminant and fatal acute infections common to all types, on the one hand, and from subclinical persistentinfections to rapidly progressive chronic liver disease with cirrhosis and even hepatocellular carcinoma, common to the blood borne types (HBV, HCV, and HDV), on the other.[21] Grossly there is hepatomegaly along with congestion and spotty necrosis.

Microscopically typical acute viral hepatitis with spotty necrosis is a panlobular disease, although the changes may predominate in the centrilobular region in hepatitis B and C, and in the periportal zone in hepatitis A. Due to extreme low immune status of Indian/pregnant women, pregnancy appears to be a potential risk factor for viral replication. Mortality rates among pregnant women, especially those infected in the 3rdtrimester[20], have ranged between 5% and 25%.

In pregnant women, however, the illness can be particularly sever, with average mortality rates reaching as high as 27%. HEV is a leading cause of fulminant hepatic failure in pregnancy.

AIMS AND OBJECTIVES

1. To study various lesions of Liver (gross and histomorphological) in Pregnancy related deaths due to viral hepatitis.
2. To analyze and correlate the clinical observations, bio-chemical parameters with the post mortem findings.
3. To find out the complications arising due to viral hepatitis.

MATERIAL AND METHODS

Type of study – Retrospective

Duration of study – January 2006 to June 2012 (6.5 years)

1. The study was done on all pregnancy related deaths in this hospital where autopsies were requested.
2. All the cases of maternal deaths autopsied by the Pathology department were included in the study.
3. The cases which were not autopsied and those which were subjected to medico-legal autopsy (caused by burns, trauma, suicide, homicide etc.) were excluded from the study.
4. Post-partum deaths up to 42 days after delivery were also included.
5. Out of total number of 3825autopsies these deaths comprised 152 (3.97%).
6. Of this viral hepatitis accounted for eight cases which was studied in detail.
7. Whereas the protocol followed during autopsy in a maternal mortality is similar to other pathological autopsies, with special emphasis on liver. All cases underwent an external and in situ examination followed by dissection and preservation of the organs in 10% formalin.
8. Gross features of the liver specimen, along with the weight, measurements were noted. Multiple sections were studied from the liver in an attempt to identify specific changes occurs during pregnancy.
9. The clinical history, clinical presentation, biochemical parameters and other investigations were obtained from the medical records of the hospital at autopsy. Main emphasis was on noting the important pathological features and gross & morbid anatomy of the liver at autopsy.

Tissue fixation, sectioning and staining :-

Autopsy specimens were fixed in 10% formalin. Multiple sections were studied.

The sections were stained routinely with H & E stains for the overall evaluation of the tissue. Addition to H & E following special stains were performed whenever necessary.

- PAS stain
- Reticulin stain
- Orcein stain

Observation and results

Table 1 (a). Acute viral hepatitis

Sr. No.	Age (yrs)	Gravida	Gestation Period (wks)	Parity	PP Days	Symptoms	Signs	Investigation
1.	22	1	30	0	A--	Jaundice, fever.	Pallor, icterus.	Bili=4.3, AST=345, ALT=232, ALP=657, PT=17, BUN=12, Creat=0.5, Hb=7.8, PLT=198000, HbsAg positive
2.	23	1	32	0	--	Jaundice, fever.	Icterus.	Bili=4.1, AST=6894, ALT=2461, ALP=590, PT=22, BUN=56, Creat=3.3, Hb=10.1, PLT=35000, HEV IgM positive
3.	20	1	--	1	6	Jaundice, fever, altered sensorium	Pallor, icterus.	Bili=7.9, AST=961, ALT=1020, ALP=501, PT=24, BUN=8, Creat=1.1, Hb=7.9, PLT=240000, HEV IgM positive
4.	25	1	--	1	2	Jaundice, fever, breathless	Icterus, crepts	Bili=12.1, AST=337, ALT=674, ALP=387, PT=23, BUN=98, Creat=2.1, Hb=10.2, PLT=40000, HEV IgM positive
5.	20	2	32	1	--	Bleeding PV, abdominal pain, jaundice	Icterus, tender abdomen	Bili=9.8, AST=1768, ALT=1520, ALP=483, PT=31, BUN=7, Creat=1.4, Hb=10, PLT=316000, HEV IgM positive

Table 1 (a) (cont…). Acute viral hepatitis
Mostly patient presented with jaundice and altered sensorium.

Sr.No.	Age (yrs)	Gravida	Gestation Period (wks)	Parity	PP Days	Symptoms	Signs	Investigation
6.	25	4	24	2	--	Jaundice, altered sensorium	Pallor, icterus	Bili=5.4, AST=567, ALT=657, ALP=680, PT=25, BUN=13, Creat=0.7, Hb=7.5, PLT=144000, HEV IgM positive
7.	26	2	--	1	3	Abdominal pain, jaundice	Pallor, icterus, drowsy	Bili=18.1, AST=181, ALT=216, ALP=1061, PT=28, BUN=15, Creat=0.9, Hb=9.5, PLT=135000, HEV IgM positive
8.	23	2	32	1	--	Bleeding PV, abdominal pain, jaundice	Icterus, tender abdomen, pallor	Bili=12.6, AST=310, ALT=252, ALP=678, PT=34, BUN=23, Creat=1.1, Hb=8.1, PLT=89000, HEV IgM positive

- Patients presented in the third trimester.
- LFT were deranged.
- Single case of hepatitis B virus infection was noted which presented as fever and jaundice in third trimester. It showed moderate derangement of LFT and was positive for HBsAg.
- There were 7 cases of hepatitis E virus infection. Out of which 3 cases were in 3rd trimester and post-partum each. All were showing moderate to severe derangement in LFTs. All cases were positive for HEV IgM.

Table 1 (b). Acute viral hepatitis

Sr. No.	Liver Weight (gm)	Gross	Microscopy	Complication
1.	1200	Patchily Congested	Ballooning degeneration of hepatocytes, focal hepatic necrosis, periportal lymphocytic infiltrate.	Hepatic failure
2.	1800	Hepatomegaly, Patchily congested	Massive necrosis	Renal failure, Hepatic failure
3.	1300	Necrosed, shrunken	Ballooning degeneration, focal hemorrhagic necrosis, canalicular bile plug, portal tract show lymphocytic infiltrate.	Hepatic encephalopathy
4.	2200	Hepatomegaly, Patchily congested	Ballooning degeneration, focal hemorrhagic necrosis, canalicular bile plug, portal tract show lymphocytic infiltrate, focal fatty change	Multiorgan disfunction
5.	1400	Necrosed	Ballooning degeneration, focal hemorrhagic necrosis, canalicular bile plug, portal tract show lymphocytic infiltrate.	Hepatic failure

Table 1 (b) (cont…). Acute viral hepatitis

Sr.No.	Liver Weight (gm)	Gross	Microscopy	Complication
6.	1400	Focal necrosis	Sub-massive necrosis, ballooning degeneration, intracanlicular bile plug, intrahepatic cholestasis, portal lymphocytic inflamation	Hepatic encephalopathy
7.	1200	Necrosed, shrunken	Massive necrosis	Hepatic failure
8.	1250	Necrosed, shrunken	Extensive necrosis, intrahepatic bile cholestasis, microvesicular fatty change	Hepatic failure

- Most common gross finding in hepatitis E was shrunken and necrosed liver.
- Most of patients died of hepatic failure.
- Microscopically hepatitis E showed fulminant hepatitis with intrahepatic bile cholestasis, bile plugs and microvesicular fatty change.

Discussion

Acute viral hepatitis
(Total Cases = 8, Table No. 1a and 1b)

T.S.Panchabhai and colleagues[2] reported 15 (5.54%) cases of viral hepatitis.

Single case of hepatitis B virus infection was noted which presented as fever and jaundice in third trimester. It showed moderate derangement of LFT and was positive for HBsAg.

All the cases in our study progressed to fulminant hepatic failure with two cases going in to hepatic encephalopathy.

Similar study conducted by Dipak Joshi[7] showed similar findings.

Grossly liver in HBV infection was normal in size with patchy areas of congestion.

Microscopically there was ballooning degeneration of hepatocytes, focal hepatic necrosis, periportal lymphocytic infiltrate.

There were 7 cases of hepatitis E virus infection. Out of which 3 cases were in 3rd trimester and post-partum each. All were showing moderate to severe derangement in LFTs. All cases were positive for HEV IgM. Presenting features were jaundice and fever.

Premashis Kar[20] reported mortality rates ranging between 5% - 25%among pregnant women who were positive for HEV IgM, especially those infected in the 3rd trimester.

Association of HEV and viral hepatitis with pregnancy hasbeen reported earlier in many studies, Jaiswal[36] and colleaguesin central India and Aziz and associates in Pakistan have reported that HEV is responsible for 58% and 62% of cases of acute viral hepatitis in pregnant women, respectively.

In our study the most common gross finding in hepatitis E was shrunken and necrosed liver. Most of patients died of hepatic failure.

Microscopically most common findings were observed as ballooning degeneration, varying degree of hepatocellular necrosis, canalicular bile plug, and portal tract showed lymphocytic infiltrate.

Agrawal V. and colleagues, Jean Marie Paron et al described microscopy of HEV infection as acute cholestatic hepatitis with some resemblance to acute hepatitis A infection, dense portal inflammatory infiltrate with canalicular bile stasis and occasional cholestatic hepatocellular rosettes, with ballooned hepatocytes, acidophilic bodies, and focal or confluent hepatocellular necrosis.

SUMMARY AND CONCLUSION

Retrospective study of pregnancy related deaths from Jan 2006 to June 2012 were studied.

Out of total 3847 autopsies maternal deaths comprised of 152 (3.95%) cases.

Viral hepatitis was seen in 8 cases, one being HBsAg positive and 7 being due to HEV. The HEV seropositive patients died of fulminant hepatic failure which was evident on microscopy as well as seen in the liver function tests, confirming that HEV can be leading cause of maternal mortality in viral hepatitis.

The complications for maternal deaths were hepatic failure,hepatic encephalopathy.Single case each of maternal death due to renal failure and multiorgan failure was seen.

All the patients presented in the third trimester.

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