

HEPATITIS IN PREGNANCY

by

LEELA CHOGTU,* M.B., M.D., D.G.O.

KUNDAN LAL CHOWDHURY,** M.B., M.D.

and

VIJAY CHOWDHURY,*** M.B.B.S.

The association of jaundice with pregnancy has been reported with the incidence varying from 1 in 2000-3000 (Sheehan, 1961) to 1 in 1500 (Haemmerli, 1966) deliveries. Viral hepatitis is the commonest cause of such jaundice (Sherlock, 1970). The incidence of hepatitis during an epidemic is reported to be as high in the pregnant woman as in the general population (Martini, 1953) and any case of jaundice during an outbreak is possibly one of the cases of the epidemic (Sheehan, 1961). Divergent opinions exist about the foetal and maternal outcome of pregnancy complicated by jaundice. Increased maternal mortality and foetal wastage was reported from Israel (Zondek and Bromberg, 1947) and India (Wahi and Arora, 1953; Malkani and Grewal, 1957), while other authors (Roth, 1953; Thorling, 1955; Cahili, 1962) did not observe any alteration in the course of hepatitis in pregnancy nor in the case fatality rates between pregnant and non-pregnant women.

The present article deals with the observations on an unprecedented increase in jaundice associated with pregnancy in the

*Assistant Professor of Obstetrics & Gynaecology, Medical College, Srinagar.

**Assistant Professor of Medicine, Medical College, Srinagar.

***Registrar, Obstetrics and Gynaecology, Medical College, Srinagar.

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last 5 months as seen in the S. M. H. S. Hospital attached to Medical College, Srinagar, Kashmir.

Material and Methods

The maternity beds of the hospital are divided into three equal units. All the cases of jaundice associated with pregnancy admitted in one unit during the 5 months period from July to December, 1973 were studied and investigated. In the history, attention was given to the details of past transfusions and injections, drug intake during or before pregnancy, family history of jaundice or history of jaundice in previous pregnancies and any history suggestive of gall bladder disease. The investigations included a blood and urine analysis, haemogram, ESR, serum bilirubin, serum albumin and globulin and serum enzymes, namely alkaline phosphatase, glutamic oxalic transaminase and glutamic pyruvic transaminase. Liver biopsy was done in 6 patients.

Results

The results are summarised in Table I and Table II.

a—Incidence, age, parity, duration of pregnancy and cause of jaundice

The total number of patients admitted on the maternity side during this period was 680 and 16 out of them had associat-

TABLE I

Important Clinical Findings in Patients of Hepatitis

No.	D.O.O. date & month	Age in years	Parity	Duration pregnancy at the onset of symptoms	Symptoms on admission	Important clinical findings
1.	5-7	20	Primi	9 months	Labour pains	Jaundice, anaemia, hepatomegaly 2 Cms.
2.	30-7	23	Primi	3 "	Pruritus vomiting	Jaundice, hepatomegaly spleen 1 Cm.
3.	2-8	28	Multi	7½ "	A.P.H.	Jaundice deep, normal liver.
4.	5-9	20	Primi	9 "	Labour pains	Jaundice, hepatosplenomegaly.
5.	15-9	25	Primi	5½ "	Jaundice anorexia	Jaundice, liver 3 Cms.
6.	7-11	28	Multi	9 "	Abdominal pain	Anaemia, edema, jaundice, hepatomegaly 3 Cms.
7.	10-11	27	Multi	5½ "	Anorexia, fever, vomiting	Jaundice deep, liver 3 Cms. Spleen 1 Cm.
8.	27-11	16	Primi	1 "	Jaundice, fever, vomiting	Jaundice, hepatomegaly 4 Cms. Spleen 1 Cm.
9.	30-11	21	Multi	3 "	Pruritus, jaundice	Jaundice, hepatomegaly 4 cms.
10.	23-8	25	Multi	5 "	Coma	Jaundice, deep, liver shrunken, encephalopathy.
11.	23-10	21	Primi	3½ "	Coma	Coma, deep jaundice, shrunken liver, pneumonia.
12.	8-11	30	Multi	6½ "	Convulsions fever, coma	Coma, deep jaundice shrunken liver.
13.	1-12	37	Multi	Postpartum	Coma and convulsions	Jaundice, shrunken liver and spleen 1 Cm.
14.	10-12	40	Multi	9 "	Drowsy, vomiting	Asterexis, Precoma, Jaundice and Liver 1 Cm.
15.	22-12	20	Primi	Postpartum	P.P.H. shock	Liver 2 Cms. Jaundice deep, perineal tear.

D.O.O. means date of first observation of the patient

NOTE:—A continuous line has been drawn after case No. 9 to show the difference in the course of pregnancy, the maternal and fetal outcome and the symptomatology in the patients of infectious hepatitis without complications and those with complications like coma or precoma (case No. 10 to 15). These later cases were suffering from the severe form of hepatitis namely acute yellow atrophy.

TABLE II

The Results of Important Biochemical Tests and the Maternal Fetal Outcome in Hepatitis

Case No.	Biochemical and other tests	Diagnosis and complications	Maternal outcome	Fetal outcome
1.	Enzymes +, Hb 5 G.	Infectious hepatitis	Recovered	Normal live baby.
2.	Liver biopsy positive Serum bilirubin 7 mg.	Infectious hepatitis	Prolonged course of jaundice, Improved	Normal live baby.
3.	Enzymes +++ , Hb 8 G Serum bilirubin 4 mg.	-do-	Improved, prolonged course	Premature baby, died 3rd day.
4.	Enzymes +++ , Liver biopsy positive	Infectious hepatitis	Recovered	Normal live baby after caesarian section.
5.	Liver biopsy normal, Enzymes ++	Infectious hepatitis	Improving	Undelivered so far.
6.	Liver Biopsy positive Serum bilirubin 6 mg.	Infectious hepatitis with P.P.H.	Recovered	Normal live baby.
7.	Liver biopsy positive Enzymes +++ , Serum bilirubin 5 mg.	Infectious hepatitis	Improving	Undelivered so far.
8.	Enzymes ++	Infectious hepatitis	Recovered	Undelivered so far.
9.	Liver biopsy positive	-do-	Improving	Undelivered so far.
10.	Enzymes ++ , Hb 6 G. Serum bilirubin 8 mg.	Acute yellow atrophy	Recovered after abortion	Aborted fifth month.
11.	Enzymes +++ , Hb 8 G. Serum bilirubin 7 mg.	Acute yellow atrophy	Died in hepatic coma	Died in utero.
12.	Enzyme + , Hb 7 G. Serum bilirubin 4 mg.	Acute yellow atrophy	Died of hepatic failure	Died in utero.
13.	Enzyme +++ , Serum bilirubin 10 mg.	Acute yellow atrophy	Died of hepatic failure	Normal live baby.
14.	Enzymes ++ , Hb 4 G. Serum bilirubin 2 mg.	Acute yellow atrophy	Died in coma and shock	Still born.
15.	Serum bilirubin 9.4 mg. Hb. 7.8 G.	Acute yellow atrophy with P.P.H.	Died of hepatic failure	Normal live baby.

+ means raised, ++ means moderately raised ++-markedly raised.
P.P.H. means Postpartum haemorrhage.

ed jaundice, an incidence of 2.35 per cent.

Eight patients were primigravidas and another 8 were multiparous. Their ages ranged from 16 to 40 years with an average of 25 years. Most of the patients belonged to a poor socio-economic class. Only three of them had a proper antena-

tal check up before admission. History of past transfusions was not available from any patient. Two patients had blood counts done for some other illness in the three to four months before admission. None of the patients had any history of having taken tetracyclines, phenothiazine

derivatives, contraceptive pills or other known hepatotoxic drugs. There was no evidence of gall bladder disease in any patient and none of the multiparous patient had any history of jaundice in earlier pregnancies.

Only one patient had noticed intermittent jaundice in the last 10 years and was suffering from chronic active hepatitis. The remaining 15 patients were having infectious hepatitis.

At the onset of symptoms three patients were in the first trimester of pregnancy, four in the second trimester and six in the third trimester. The other two patients had delivered at home and one of them was admitted with postpartum haemorrhage while the other had developed convulsions and coma soon after delivery. In both jaundice had not been noticed earlier.

b—Signs and Symptoms

Only four patients were aware of jaundice at the time of admission. Vomiting was present in the five while anorexia, abdominal pain, fever and history of passing high coloured urine was present in 4 patients each. Two patients complained of pruritus. Four patients were admitted in hepatic coma and one with signs and symptoms of precoma.

On examination all the patients had jaundice of varying intensity. Hepatic enlargement ranging from 2 to 6 centimetres below the right costal margin was found in 8 patients and splenomegaly of 1 to 2 centimetres was seen in 2 patients. 14 patients had anaemia of mild to severe degree, the haemoglobin being less than 6 grams per cent in 4 of them. The blood pressure was normal in all the patients except 3, two of whom came with postpartum haemorrhage and shock and the third developed unexplained shock after

delivery in the hospital. 4 of the 6 patients who developed hepatic coma had shrunken liver on palpation and percussion.

c—Course of Hepatitis and Maternal and Foetal Outcome

Ten patients showed clinical and biochemical signs of recovery. Recovery took place in one to three months time in most of them but one patient had an unusually prolonged course starting with jaundice in the 20th week and showing signs of abatement only after delivery. Among these patients four are still having jaundice but are improving, two of them have delivered and the other two are still carrying on with pregnancy.

Five patients were admitted with coma and another one with precoma. The first was 5 months pregnant. She aborted and made a complete recovery in one month's time. The second patient had four months pregnancy and coma in hepatic coma dying after seven days in the hospital with foetus in utero. The third patient 7 months pregnant, was admitted with convulsions and coma for 2 days at home and died on the 5th day of admission with foetus in utero. The fourth patient, having delivered a living male baby at home went into coma on the same day and died in the hospital on second day. The fifth patient full term pregnant was admitted with symptoms of increasing drowsiness and tremulousness. She had mild icterus with asterix and impalpable liver. After delivery of a stillborn female baby on the third hospital day, she developed unexplained shock and hepatic coma. Resuscitation measures failed and she died on the same day. The sixth patient had delivered a normal live baby at home and was brought on the same day in a state of shock due to postpartum haemorrhage. She went into hepa-

tic coma and died on the 3rd day in hospital.

So far as the foetal outcome is concerned, six patients delivered normal living babies, four are still undelivered, two patients died with foetus in utero, two delivered premature dead infants, one had abortion at 5 months and another delivered a premature live baby after a caesarean section done for "central placenta praevia, the baby died on the 3rd day.

d-Investigations

Most of the patients showed elevation of serum bilirubin ranging from 2 to 8 mg. per cent. Alkaline phosphatase was either normal or moderately raised (range 10-30 K. A. units). Serum proteins were generally within normal range. Serum glutamic oxalic transaminase and serum glutamic pyruvic transaminase levels, done in 10 patients were high. Blood urea was raised terminally in two patients with coma. Anaemia was present in 14 patients, being iron deficiency type in 6 and dimorphic in the other 8 patients. Liver biopsy was normal in one patient, no tissue was obtained in another, and the other four had histopathological changes of infectious hepatitis. Autopsy could not be conducted on the five patients who died because of hepatic coma.

Discussion

Though previous statistics of jaundice in association with pregnancy are not available from this hospital, it is obvious from the figures that the incidence has spiralled high during this period. The incidence may possibly have been higher than 2.35 per cent recorded here considering the fact that many of the patients were discharged quickly because of shortage in the number of beds and could have

been suffering from infectious hepatitis which went undetected. The incidence of hepatitis in pregnancy has been reported 0.0168 per cent by Vincent (1957) and 1 in two to twenty thousand cases by Dill (1950). It appears that infectious hepatitis has become endemic in Kashmir and further statistical data are necessary to confirm the general opinion from the increased observance of cases of infectious hepatitis in medical outpatients and wards that an outbreak has already occurred and is still raging in the valley. In the last year we have also experienced outbreaks of cholera, gastroenteritis and poliomyelitis, which are transmitted by intestinal-oral route like infectious hepatitis. The likely factors of these outbreaks are the increasing urbanization of the city and a relative drought in the last 2 years with diversion of the waters of the "Dal" lake, a tourist haunt, for drinking purposes.

All the patients described here except case No. 16 were suffering from infectious hepatitis. This is clear from the clinical picture, biochemical tests and liver biopsies. The distribution in various trimesters was almost uniform and mostly young mothers were involved. It is known that children and young adults are more susceptible to the disease accounting for 65 per cent cases in endemic areas (Bradley, 1963). This study bears out the observations of Sheehan (1961) that during an epidemic of infectious hepatitis any case of jaundice in pregnancy is possibly one of the cases of the epidemic.

The disease produced bizarre and rather scanty symptoms in the patients. Only four patients were aware of jaundice while most of the others gave history of anorexia, vomiting, abdominal pain, pruritus or transient fever, which they attributed to the pregnancy state. Even the

patients who came in coma had non-specific symptoms like abdominal pain or fever preceding coma and in none of them had jaundice been suspected or seen. Thus, hepatitis may be overlooked in pregnancy unless jaundice attracts attention. On clinical examination there may be no significant hepatomegaly. In fact an impalpable liver, showing evidence of shrinking in the presence of icterus is a bad sign and these patients go into acute yellow atrophy due to massive hepatic necrosis. Daily percussion for liver dullness is a useful guide in this direction. Onset of hepatic encephalopathy may be abrupt in the form of convulsions and coma or rather subacute with delirium, tremulousness and drowsiness. Cerebral symptoms do not necessarily run parallel with the depth of icterus, as one of our patients who though admitted in precoma was only mildly jaundiced and subsequently died due to hepatic failure. Such symptoms should, therefore, be watched carefully.

The maternal mortality in our patients with hepatitis is quite high. Of the 15 patients 5 (33.33 per cent) died. The outlook is probably not as gloomy as reflected by these figures, because many of the uncomplicated patients either escape notice or prefer to deliver in their homes and only the serious and complicated patients land in the hospital. While Vincent (1957) reported 26 per cent maternal mortality, especially prone to occur in the early pregnancy and Malkani and Grewal (1957) observed 35 per cent mortality with grave prognosis for the mother in the second trimester, it appears to us that the last trimester and the postpartum period is especially dangerous for the pregnant women with hepatitis. Four of our 5 patients who died were in this period of pregnancy. Other Indian

Authors have also described high maternal mortality rates (Naidu and Wishwanathan 1957; Das 1968) and a recent report from Iran (Fathali *et al.*, 1973) emphasise the high risks to the mother with hepatitis, especially in the last trimester of pregnancy. Except for Long *et al.*, (1955) and Vincent (1957) who described high mortality rates for pregnant women suffering from infectious hepatitis other Western and U.S. authors (Cahill, 1962; Adams and Combes, 1965; Haemmerli, 1966) have not found any difference in the maternal mortality between pregnant and non-pregnant women with hepatitis. Our patients hailed from low income groups and most of them exhibited anaemia and signs of malnutrition. It appears that undernutrition, deficiency of various aminoacids and anaemia make the liver more amenable to severe damage by hepatitis. This is all the more true in the pregnancy state which puts increased demands for protein anabolism on the liver. The sensitivity of the liver in pregnancy to agents like tetracyclines is well known (Schultz *et al.*, 1963; Kunelis *et al.*, 1965) and may serve as an analogy to infectious hepatitis in pregnancy.

We did not observe much difference in the course of hepatitis between the patients who delivered or aborted and those who are carrying on with pregnancy. One patient recovered from coma after aborting, and another with a prolonged icterus for about 5 months showed signs of its subsidence only after delivery. On the whole, patients took longer to recover. It is possible that pregnancy puts a damping effect on the natural process of recovery in hepatitis. This is another pointer to a guarded prognosis and careful watch for the course of the disease in pregnancy. There is also a variance in the reports on the foetal outcome. While Cahill

(1962), Adams and Comber (1965) did not observe increased foetal mortality, Martini (1953) reported a tendency to abortion or premature delivery. Haemmerli (1966) commented that foetal survival depends on the stage of maturity at birth and not on the mother's disease. From our study the foetal mortality figures are again high and foetal survival appears to be dependent on the maternal condition and the stage of maturity at birth. The foetus may die in utero along with the mother or get aborted or be still born, or born prematurely and die later. Five babies met such an end in our 15 cases of hepatitis showing an incidence of 33.3 per cent mortality. Hepatitis seems to precipitate labour prematurely which accounts for the high foetal wastage. There is, however, no evidence of increased tendency to malformation or neonatal hepatitis in the babies born of mothers with hepatitis.

Summary

In a short period of five months from July to December, 1973, a total of 680 patients were admitted in the maternity wards out of which 16 cases of jaundice with pregnancy were seen, 15 of whom had infectious hepatitis. The disease is endemic in Kashmir and an outbreak has possibly occurred.

Hepatitis is an unfavourable complication of pregnancy with high maternal mortality and increased foetal wastage. The duration of pregnancy does not seem to have any relation with the mortality figures. Every pregnant mother with this complication should be watched carefully.

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