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ABO/Rh incompatibility in neonatal jaundice: a tertiary hospital based cross sectional study

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ABSTRACT

Background: Neonatal hyperbilirubinemia, defined as a total serum bilirubin level above 5 mg/dl (86 µmol/l). Haemolytic disease of the newborn due to blood group incompatibilities between mother and foetus is one of the commonest cause of hyperbilirubinemia in the newborn.
Methods: A Hospital based cross sectional study was conducted among newborns admitted with jaundice.
Results: In our study 51 cases of neonatal jaundice were due to ABO incompatibility and among them 24 were having O-A incompatibility and 27 were having O-B incompatibility. The mean serum bilirubin in patients with ABO incompatibility were higher (24.8) than those without ABO incompatibility.
Conclusions: In the present study, one third of newborns with neonatal jaundice were having ABO incompatibility. The mean serum bilirubin in patients with ABO incompatibility were higher than those without ABO incompatibility. This highlights the importance of recognizing ABO Rh incompatibility in neonatal jaundice.

Keywords: Neonatal jaundice, ABO incompatibility

INTRODUCTION

Jaundice is the visible manifestation in the skin and sclera of elevated serum concentrations of bilirubin and the commonest abnormal physical finding during the first week of life and is seen in approximately 60% of term and 80% of preterm neonates. Neonatal hyperbilirubinemia, defined as a total serum bilirubin level above 5 mg/dl (86 µmol/l) is a frequently encountered problem.[1]

Physiological jaundice is seen in nearly 60% of term and 80% or preterm neonates. In term neonates it appears between 36 to 72 hours of life, maximum intensity is seen on 4th day, serum bilirubin does not exceed 15 mg/dl and usually disappears by 10th day but it may persist upto 14th day in preterm neonates. The serum unconjugated bilirubin level of most neonates rises to >2 mg/dl in the first week of life. This level usually rises in term neonates to a peak of 6-8 mg/dl by 3-5 days and then falls. A rise to 12mg/dl is in the physiologic range. In premature neonates the peak may be 10-12 mg/dl on the 5th day of life, may possibly rise upto >15 mg/dl without any specific abnormality of bilirubin mechanism. [1]

All etiologies of jaundice beyond physiological, breastfeeding or breastmilk jaundice are considered pathological. The etiological factors may be affected by the population characteristics, gestational age, sex, maternal disease, feeding status and the geographical variations. However, in some cases even the most sophisticated investigations fail to reveal any etiological factors and these cases are then labelled as idiopathic.[2]

Features of pathologic jaundice includes the appearance of jaundice within 24 hours of life, presence of jaundice on arms and legs on day 2, yellow palms and soles anytime, serum bilirubin concentration increasing more than 0.2 mg/dl/hr or more than 5 mg/dl in 24 hours, if total serum bilirubin (TSB) is more than 95th centile as

per age specific bilirubin nomogram, signs of acute bilirubin encephalopathy or kernicterus and clinical jaundice persisting beyond 2 weeks in term and 3 weeks in preterm neonates.

Under certain circumstances severe hyperbilirubinemia can cause complications known as kernicterus, which was first described by Orth as yellow staining of the brain, in 1875 it was later referred to by Schmorl as kernicterus.[3] The effects range from fever, seizures and high-pitched crying leading to mental retardation, deafness, athetoid cerebral palsy with poor chance of survival in some cases.

Although more than 60 different RBC antigens are capable of eliciting a maternal antibody response, clinically significant disease is associated primarily with incompatibility of ABO blood and Rh D antigen.[2]

Haemolytic disease of the newborn due to blood group incompatibilities between mother and foetus is one of the commonest cause of hyperbilirubinemia in the newborn. The incompatibility may be between ABO, Rhesus or minor blood group systems (C, E, M and Kell). Any RBC antigen which is inherited by the foetus from the father and is not present in the mother, can cause haemolysis in the foetus due to maternal sensitisation.[1]

Foeto-maternal ABO incompatibility exists in about 25% of pregnancies but haemolytic disease develops in only one in ten such offspring. The subsequent babies may be more affected or less affected or even spared. The commonest foeto-maternal combinations are O group mother and A or B group foetus. The severity of haemolysis is more in OA incompatibility compared to OB incompatibility.[1]

The frequency of Rh-negative blood group is 5% in Indian population as against 15% in Europeans. As there is no inborn antibodies in the Rhesus blood group system, when an Rh negative mother is carrying an Rh positive foetus, the antigen of the foetal RBC may invoke antibody response by the maternal immunologic system. Each subsequent pregnancies with an Rh-positive foetus leads to increasing antibody response. The anti-D antibodies being IgG in type, crossover to the foetus and destroys D-positive foetal red blood cells.[1]

The severity of HDN ranges from only laboratory evidence of mild haemolysis to severe anaemia with compensatory hyperplasia of erythropoietic tissues, hepatosplenomegaly, cardiac decompensation, massive anasarca and circulatory collapse. Excessive abnormal fluid in two or more foetal compartments termed hydrops fetalis frequently leads to in death in utero or shortly after birth. [1]

The definitive diagnosis of HDN requires ABO and Rh typing of both mother and baby, direct Coomb's test, haematocrit, reticulocyte count, peripheral blood smear for RBC morphology, total serum bilirubin, and estimation of maternal IgG anti-A or anti-B antibodies in an antibody- dependent cell-mediated cytotoxicity (ADCC) assay and detection of antigen density of A or B antigens on the red blood cells.[1]

Phototherapy remains the mainstay of treatment of neonatal hyperbilirubinemia. Exchange transfusion is used to remove bilirubin when intensive phototherapy fails to prevent a rise in bilirubin to potentially toxic levels or in infants with neurologic signs suggestive of bilirubin toxicity. In cases of isoimmune haemolytic disease, exchange transfusion also removes antibody and sensitised RBCs which are replaced with donor RBCs lacking the sensitising antigen. Intravenous immunoglobulin (IVIG) has been used in infants with haemolytic disease caused by ABO/Rh incompatibility.[3]

With the above background, the present study is taken up to study the prevalence of ABO/Rh incompatibility in neonates admitted with jaundice in Paediatrics Ward, RIMS, Imphal, Manipur.

METHODS

Stud design

Hospital based cross sectional study design was used.

Study setting

Study conducted at department of paediatrics.

Study duration

The study was conducted for two years from January 2021 to December 2022.

Study population

All neonates admitted in paediatric ward, RIMS hospital, Imphal with jaundice, irrespective of gestational age, birth weight, mode of delivery were taken up for the study.

Inclusion criteria

All newborns admitted with jaundice were included in study.

Exclusion criteria

Neonates with major congenital anomalies were excluded from the present study.

Sample size

The calculated sample size was 183 neonates with jaundice.

Independent variables

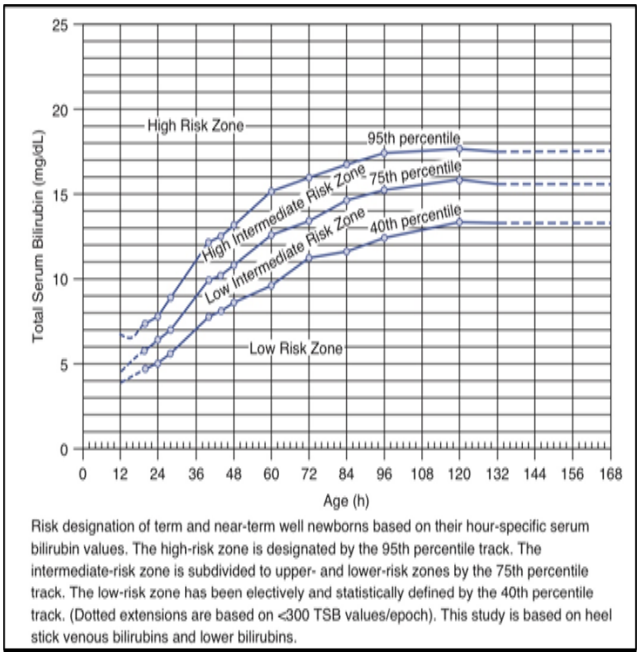
Age in days, gender, birth weight (gram), gestational age, axillary temperature in Fahrenheit, timing of first feed, mode of delivery, total serum bilirubin, ABO grouping and Rh typing of mother, ABO grouping and Rh typing of neonate and history of ABO/Rh incompatibility in the family used as independent variables.

Dependent variables

Dependent variables were presence of ABO/Rh incompatibility.

Working definition

Neonatal hyperbilirubinemia: Total serum bilirubin concentration more than the hour specific nomogram as depicted in the chart below.[48]



Risk designation of term and near-term well newborns based on their hour-specific serum bilirubin values. The high-risk zone is designated by the 95th percentile track. The intermediate-risk zone is subdivided to upper- and lower-risk zones by the 75th percentile track. The low-risk zone has been electively and statistically defined by the 40th percentile track. (Dotted extensions are based on <300 TSB values/epoch). This study is based on heel stick venous bilirubins and lower bilirubins.

Figure 1: Risk designation of term and near terms.

ABO incompatibility: serological evidence of blood group incompatibility between mother and neonate with mother being 'O' positive and neonate being either A positive or B positive.

Rh incompatibility: Refers to an incompatibility in Rh types between a donor and recipient, or between an Rh-positive foetus, and an Rh negative mother.

Sample collection

Under proper aseptic and antiseptic precautions, 1-2 ml venous blood sample was collected from both the mother and neonate in two sterile vials each with sterile needles and will be sent immediately for determination of total serum bilirubin and ABO/Rh typing.

Data management and statistical analysis:

Data was checked for consistency and completeness and was entered and analyzed using SPSS version 21.0 (IBM, INC, ARMONK, NY, USA). Descriptive statistics like mean and SD was used to summarize age, height, weight, duration of hospital stay and laboratory findings.

Ethical approval

The written informed consent was taken before the recruitment for study. The approval of protocol of the thesis was sought from the research ethics board for ethical approval, RIMS, Imphal.

RESULTS

Among the enrolled participants, 54% were male, whereas females constituted 46% of the study population. Among the study population, more than half of the participants (105) were residing in rural area. Around 16% neonates in the population were small for their gestational age, while more than 4/5th of them were having normal or average weight for gestational age. In our study more than 50 percent neonates were born by normal vaginal delivery while 47% were born by LSCS, of the study participants (more than 3/4th) were found to be initiated breast feeding within 4 hours of birth.

The mean serum bilirubin was found to be higher in males than females, more in participants with delayed initiation of feeding and higher in neonates born by normal delivery. Out of the 183 participants with neonatal jaundice, 115 were having O group mothers. Other blood groups were found to have no significant difference in the frequency of neonatal jaundice

In our study 51 cases of neonatal jaundice were due to ABO incompatibility and among them 24 were having O-A incompatibility and 27 were having O-B compatibility. Among the study population, 20.2% were found to be anemic whereas majority (79.8%) were not having anaemia.

Among the 183 participants 98 were not having a significant family history of ABO incompatibility whereas 37 participants were not. The mean serum bilirubin in patients with ABO incompatibility were higher (24.8) than those without the ABO incompatibility.

Table 1: Distribution of age in days among study population, (n=183).

Age group (days)	N	Percentage (%)
0-7	47	25.7
8-14	40	21.8
15-21	52	28.4
>21	44	24.1

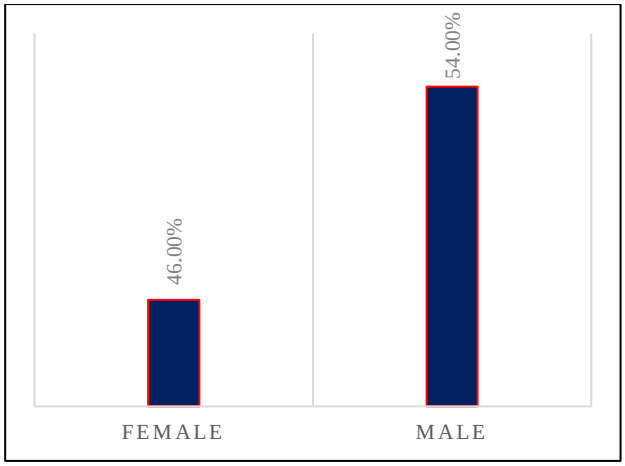


Figure 2: Distribution of gender among study population, (n=183).

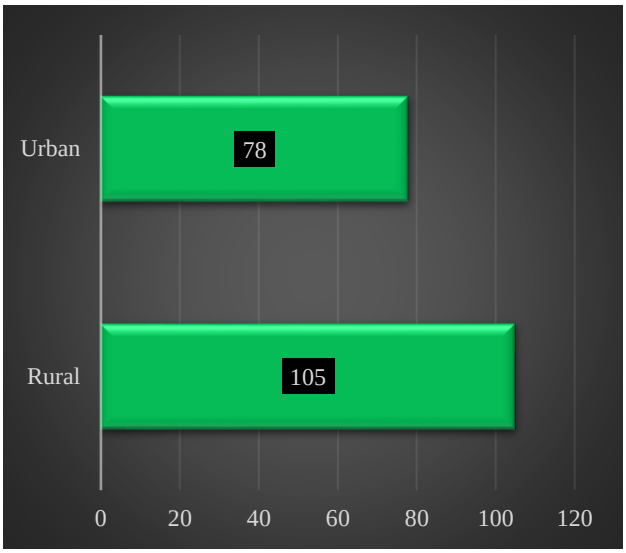


Figure 3: Urban and rural distribution of study participants, (n=183).

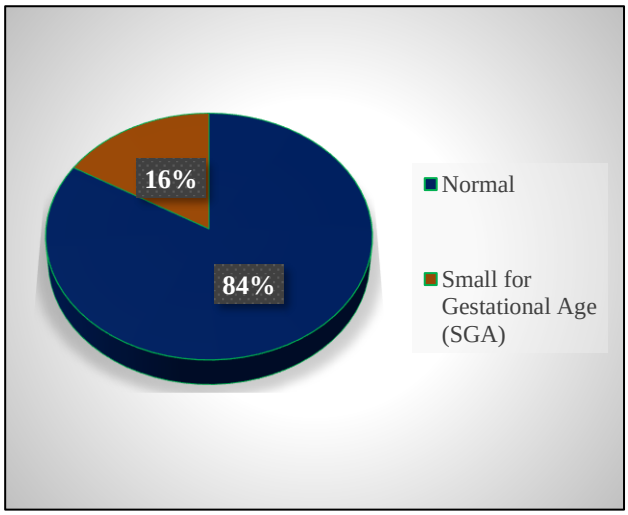


Figure 4: Distribution of neonates based on birth weight, (n=183).

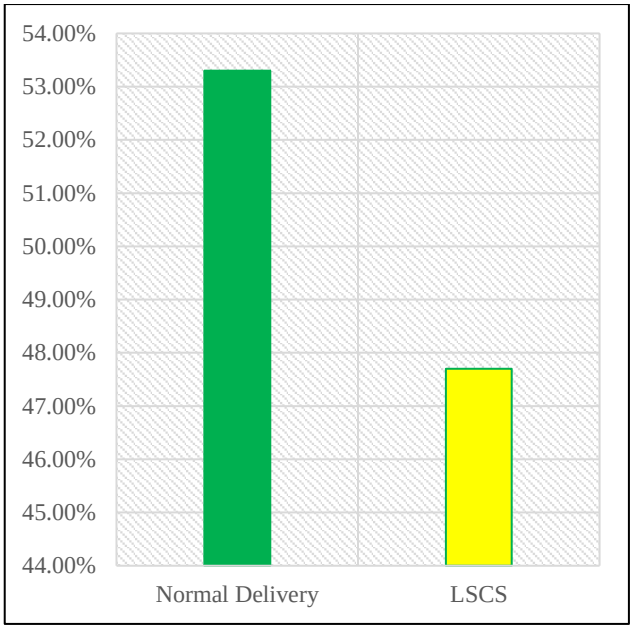


Figure 5: Mode of delivery among study participants, (n=183).

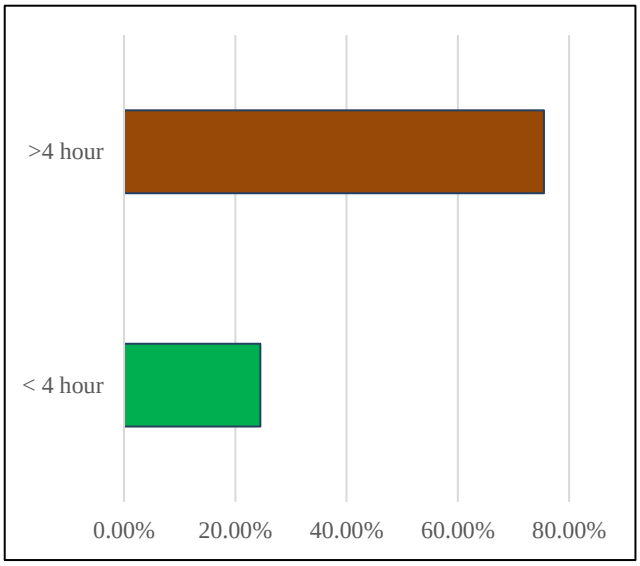


Figure 6: Timing of breast-feeding initiation, (n=183).

Table 2: Comparison of mean serum bilirubin among study population, (n=183).

Parameters	Characteristics	Mean	Standard deviation
Gender	Male	17.8	4.2
	Female	16.6	3.7
Birth weight	AGA	14.5	2.5
	SGA	17.6	3.5
Timing of breast feeding	>4hours	16.2	2.6
	<4 hours	15.0	3.0
Mode of delivery	Normal	18.5	3.4
	LSCS	17.6	2.3

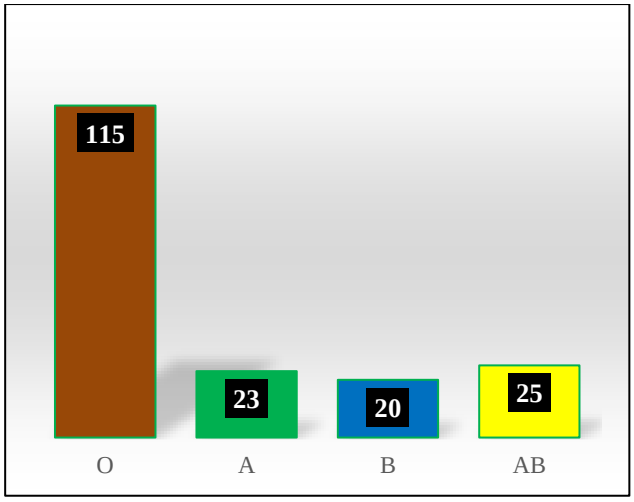


Figure 7: ABO grouping of mother, (n=183).

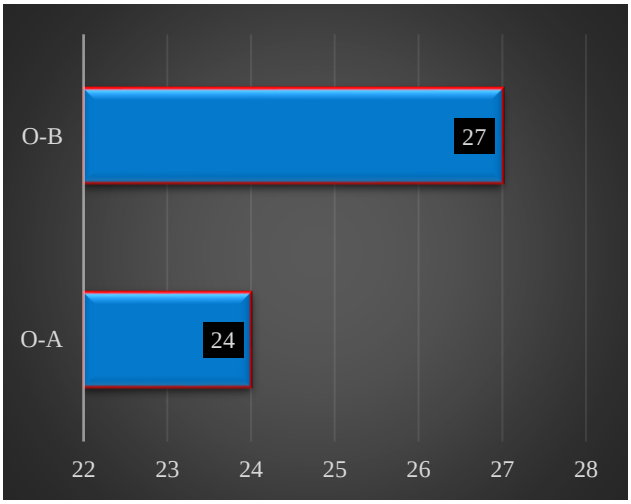


Figure 8: Frequency of ABO incompatibility, (n=183).

Table 3: Presence of anaemia among the study population, (n=183).

Anaemia	N	Percentage (%)
Present	37	20.2
Absent	146	79.8

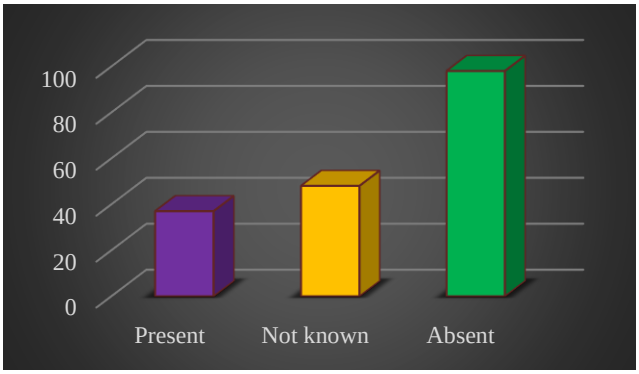


Figure 9: History of ABO incompatibility in family, (n=183).

Table 4: Comparison of Bilirubin between ABO incompatibility and non-ABO incompatibility, (n=183).

Characteristics	ABO incompatibility	Non- ABO incompatibility
Mean	18.8	15.6
Standard deviation	4.7	3.2

DISCUSSION

During the study period, 183 newborns admitted to paediatrics ward, with jaundice neonatal jaundice were enrolled to determine the frequency of ABO and Rh incompatibility. The observations thus made were discussed in comparison with that of other similar studies. In our study, various parameters and their association with the clinical manifestation of ABO incompatibility were analysed. Maternal factors like parity, mode of delivery, medication with oxytocin and initiation of breast feeding within 4 hours and fetal factors like sex, weight, blood group were considered. The association between these parameters and development of jaundice and or anaemia in ABO incompatibility were studied and the results were compared with other studies.

In the present study, participants were uniformly distributed with 46% female and 54% male babies. There was no significant correlation between the serum bilirubin levels and the sex of the newborn and other socio-demographic factors. This observation were comparable with that of studies done by Kumar et al, Akgul and Shah et al.[4-6]

In the present study, 24% neonates were breastfed within 30 minutes of birth and time of initiation of breast feeding was not significantly associated with serum bilirubin level. These findings were similar to the study done by Awasthi et al in which no significant correlation between the time of initiation of breast feeding and jaundice was found.[7] Moreover in the present study, maternal factors like parity, gestational hypertension, mode of delivery, medication with oxytocin and initiation of breast feeding within 30 minutes and neonatal factors like sex, weight, blood group had no significant association with development of jaundice or anaemia due to ABO incompatibility. These findings were similar to the studies conducted by Kumar et al, Akgul et al and Kalakheti et al.[4,5,8] However, in a univariate analysis done by Kalakheti et al factors such as gravida, maternal age, gestational age, size of the baby, male sex were significantly associated with development of jaundice or anaemia due to ABO incompatibility.[8]

In our study it was found that around one third of the neonatal jaundice was due to ABO incompatibility. There was no significant difference in severity and outcome in both O-A and O-B incompatibility, although O-B

incompatibility was more. Similar observations were made by Kumar et al, Ella et al, Akgul and Bhat et al.[4,5,9,10]

The high readmission rate within days after initial discharge indicates a need for a more thorough assessment of newborn infants and consideration of strategies to identify at-risk newborns, such as predischarge measurement of serum bilirubin levels.

After evaluating the results of our study, it can be concluded that mean serum bilirubin in patients with ABO incompatibility were higher (24.8) than those without ABO incompatibility (19.6). Hence, we recommend early identification of at-risk newborn and proper evaluation by blood grouping, Coombs' test and measurement of serum bilirubin. Also, a proper follow up for rebound rise in serum bilirubin following discontinuation of phototherapy is recommended in this population.

Our study on ABO/Rh incompatibility in neonatal jaundice could be considered as the first cross sectional study with a proper sample size to be done in this area. Another strength of our study is the use of dedicated software for analysis which could reduce the error. Similar to other cross-sectional studies, it is difficult to establish a causal relationship in the present study due to lack of temporal relationship between the independent and dependent variables, which could be considered as a major limitation of our study. Hence after analysing the results of our study, we suggest further studies with a larger sample size on a multicentric level for better understanding and management of ABO Rh incompatibility in neonatal jaundice.

CONCLUSION

Our study was conducted to elucidate the prevalence of ABO Rh incompatibility in neonatal jaundice. The study population consisted of 183 newborns admitted to Paediatrics ward, with jaundice. In our cross-sectional study, maternal factors like parity, gestational hypertension, mode of delivery, medication with oxytocin and initiation of breast feeding within 30 minutes and neonatal factors like sex, weight, blood group had no significant association with development of jaundice and or anaemia due to ABO incompatibility. We found that one third of the total neonatal jaundice were having ABO incompatibility. The mean serum bilirubin in patients with ABO incompatibility were higher than those without ABO incompatibility. This highlights the importance of recognizing ABO Rh incompatibility in neonatal jaundice. After scrutinizing the results, we recommend further studies with a larger sample size on a multicentric level for better understanding and management of ABO Rh incompatibility in neonatal jaundice.

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