Case study

Breastmilk Jaundice – Could it be more common than we realize?

Abstract

Aim: Breastmilk jaundice is a benign often undiagnosed condition occurring in healthy, term exclusively breastfed neonates. It is characterized by unconjugated hyperbilirubinaemia usually appearing from the second week of life and persisting for more than two weeks. It's specific aetiology remains unknown. Controversies exist regarding the best treatment option. The American Academy of Paediatricians recommends continuation of breastfeeding with temporary addition of formula. This series aims to increase awareness of this condition.

Presentation of cases: Three cases of unconjugated hyperbilirubinaemia persisting for greater than two weeks, in term, healthy, exclusively breastfed infants in Enugu State, South-East Nigeria are reported. Investigations did not reveal pathological jaundice, and all cases received phototherapy. In the three cases however, the most significant reduction in serum bilirubin occurred after temporary cessation of breastfeeding, with commencement of formula feeds, and subsequent recommencement of breastfeeding.

Discussion: The three cases reported fulfil established criteria for recognizing breastmilk jaundice. This condition is largely underdiagnosed with no recent reports in literature. The aetiology remains a subject of research. However, several genetic and environmental factors have been suggested. Though the total bilirubin did not reach thresholds for phototherapy in any of the cases, this treatment modality was still used. In addition, in variance to recommendations of the American Academy of Paediatricians, all cases were treated by breastfeeding cessation instead of mixed feeding.

Conclusion: Breastmilk jaundice is largely not remembered as a cause of prolonged jaundice. Its awareness and treatment would greatly reduce both parental anxiety and unnecessary treatment given to babies.

Key words: Breast-milk, Jaundice, Unconjugated, Hyperbilirubinaemia

Comment [1]: This seems to disagree with what is in the body of the paper, its rather a case series to be specific

Comment [2]: Don't start an abstract with an aim, you need to give a liitle background or introduction, which was what you did, however the title of aim is not correct.

Comment [3]: This is also not completely true, it can start from the 3-4th day of life

Comment [4]: This is not completely true, it is believed that it is caused by a metabolite of progesterone and increased content of beta glucoronidaze activity in breastmilk

Comment [5]: This is where your aim should be

Comment [6]: Why?

1. Introduction

Breastmilk jaundice is a condition characterized by unconjugated hyperbilirubinaemia. It occurs in term and otherwise healthy, exclusively breastfed infants and often goes undiagnosed.[1,2] This benign condition is largely a diagnosis of exclusion.[1] Despite its benign nature, it still poses a source of anxiety and guilt, especially among first-time mothers.[3] Because it is often not diagnosed, its incidence may be on the increase.[3] Incidence rates as high as 36% have been reported in the literature.[4] Although widely studied, it's aetiology remains unknown.[2,3] Affected babies are characteristically healthy, with jaundice persisting for more than two weeks and total serum bilirubin within the range of 13 -15mg/dl.[2] Controversies exist regarding the best treatment option for this condition.[3,5,6] Approaches include continuing breastfeeding while monitoring bilirubin levels; temporarily withholding breastfeeding and substituting formula; and alternating breastfeeding and formula.[3] The American Academy of Paediatricians however

recommends that breastfeeding should not be discontinued.[7] This is because resumption of breastfeeding after its cessation often does not occur, exposing the child to later feeding difficulties.[8]

We report three cases, over a nine-month period, of unconjugated hyperbilirubinaemia persisting for greater than two weeks amongst term, otherwise healthy exclusively breastfed infants in Enugu State, South East Nigeria.

2. Presentation of Cases

2.1 Case One

ED, a 26-day-old female, presented with yellowness of the eyes noticed by the mother on the 6th day of life. There was no fever, abnormal body movement, reduced activity or excessive/abnormal cry. She was delivered vaginally at term with a birth weight of 3.4kg to a 36-year-old teacher. Antenatal care was commenced at a gestational age of 14 weeks. Booking investigations (VDRL, HBsAg, RVS) were all negative. She was regular with her antenatal visits and compliant with her medications. There was no fever or vaginal discharge in the last trimester of pregnancy. Both mother and father were blood group O-ve. She is the third in a family with two other children. None of her siblings had jaundice during the neonatal period. ED was exclusively breastfed from the second day of life until the presentation. When the jaundice was first noticed, she was exposed to early morning sunlight for two days before presenting to the first hospital. The total serum bilirubin was 272µmol/l with an unconjugated fraction of 272µmol/l. She subsequently received three days of phototherapy before being discharged on the 12th day of life with a total and conjugated serum bilirubin of 231.2µmol/l and 188.7µmol/l respectively. On the 16th day of life, she presented to the second hospital due to anxiety over the persisting yellowness of the eyes. She was still being exclusively breastfed and had no other signs of illness. Total serum bilirubin was 238µmol/l with an unconjugated fraction of 209.1µmol/l. A complete blood count was done with no evidence of infection. Other investigations carried out included blood group, blood film for malaria parasite and cell morphology, glucose-6-phosphate dehydrogenase (G6PD) assay, coombe's test, liver function test and serum protein, Admitting diagnosis was Prolonged Hyperbilirubinaemia ? Cause. She was then placed on phototherapy for four days during which time the serum bilirubin gradually reduced. She was discharged on the 19th day of life with a total and conjugated serum bilirubin of 180.2µmol/l and 149.6µmol/l respectively. However, on the 22nd day of life, the mother noticed the skin was becoming yellow again. She, however did not present to the hospital on the advice of her relative. On the 26th day of life, she presented to our facility after being counselled about the complications of jaundice by a friend. At presentation, she was healthy looking and moderately icteric. There were no significant findings on systemic examination. Her weight was 4.8kg. Total serum bilirubin was 255µmol/l with an unconjugated fraction of 236µmol/l. Her blood group was O-ve, and the G6PD assay showed normal activity. Her complete blood count showed no evidence of infection. The blood film also showed no malaria parasites. She was commenced on phototherapy and discharged after two days with a total and conjugated serum bilirubin of 219µmol/l and 180.6µmol/l, respectively. A diagnosis of Breastmilk Jaundice was then made. The mother was advised to stop breastfeeding and use only formula milk for two days, then recommence breastfeeding and come for a repeat serum bilirubin in four days. On follow-up, ED was only mildly icteric and had a total and unconjugated serum bilirubin of

Comment [7]: If non of her siblings had jaundice during the neonatal period, will it still be breastmilk jaundice?

Comment [8]: Why did breastfeeding commenced on the 2nd day and not the 1st?

Comment [9]: Add the value in mg/dl for audience clarity

140.5µmol/l and 122.6µmol/l respectively. She came for follow-up a week later and was feeding well with good activity and no clinically demonstrable jaundice.

2.2.Case Two

NU, a one month old female infant presented with yellowness of the eyes since the 3rd day of life. For this, she was exposed to early morning sunlight for fourteen days with no significant improvement before it was discontinued. No laboratory investigations were carried out. She was delivered through an emergency caesarean section following poor progress of labour. Her birth weight was 3.8kg. Antenatal care commenced from the 11th week of life, and booking investigations were normal. Pregnancy was uneventful and she was carried to term. There were no significant peri-partum events. Mother and father's blood groups were A+ve and O-ve respectively. She was put to breast within an hour of birth and was exclusively breastfed with adequate lactation. On examination she was moderately jaundiced and her weight was 4.6kg. All other examination findings were unremarkeable. At presentation, the total serum bilirubin was 171.2µmol/l, with an unconjugated fraction of 154.3µmol/l. Other tests done included complete blood count, blood film for malaria parasite and cell morphology, blood group, liver function test, coombs (direct and indirect), serum protein and G6PG assay. These were all normal. Admitting diagnosis was Prolonged Hyperbilirubinaemia ? Cause.

Comment [10]: Be more explicit? 11week of postnatal or IUL?

After receiving phototherapy for four days, the total serum bilirubin reduced to 156.4µmol/l with an unconjugated fraction of 134.8µmol/l. A diagnosis of Breastmilk Jaundice was then made and she was then discharged. Mother was asked to stop breastfeeding, give formula milk only for two days, and then have serum bilirubin repeated in four days. On follow up, she was breastfeeding well and the repeat serum bilirubin showed a total of 126.7µmol/l with an unconjugated fraction of 103.6µmol/l.

Comment [11]: No family hx? Any sibling with jaundice?

2.2 Case Three

IA presented on the 14th day of life with yellowness of the skin noticed on the fifth day of life. She had a birth weight of 2.6kg and weighed 3.15kg at presentation. She was otherwise healthy. She was delivered at term through an elective caesarean section on account of a previous maternal caesarean section. She cried well at birth and there were no significant peri-partum events. Pregnancy was booked at the 17th week of gestation. All booking parameters were normal, mother was both compliant with routine antenatal care medication and regular with antenatal visits. There were no illnesses or adverse events during pregnancy. Mothers blood group was B+ve, while the father's was unknown. She received water for the first four hours of life and was subsequently exclusively breastfed. At presentation, she was active, afebrile, but moderately icteric. Both general and systemic examination revealed no significant findings. Total serum bilirubin was 251µmol/l with an unconjugated fraction of 18µmol/l and her blood group was B+ve. All other investigations (G6PD assay, complete blood count, reticulocyte count, blood film for malaria parasite and cell morphology and liver function test) were within normal limits. The admitting diagnosis was Prolonged Hyperbilirubinaemia ? Cause.

Serial serum bilirubin values over the next few days showed a slow but gradual reduction. On the 21st day of life, after receiving phototherapy for seven days, her total serum bilirubin was

165.2µmol/l with an unconjugated fraction of 160.6µmol/l. The diagnosis was then modified to Breastmilk Jaundice. She was discharged home and asked to stop breastfeeding, give formula milk only for two days, and then have serum bilirubin repeated in three days. On follow up, she was healthy looking with a weight of 3.7kg and a total serum bilirubin was 90.0µmol/l with an unconjugated fraction of 70.4µmol/l

Comment [12]: Family hx?

3. Discussion

Breast milk jaundice often goes unnoticed and is thus largely underdiagnosed and under-reported. In the first case, the diagnosis was made only after the patient was exposed to several investigations and interventions. In the other two cases, the diagnosis was made following recognition of the slow and poor response to phototherapy, and after none of the investigations carried out pointed to a specific diagnosis. Breastmilk jaundice is not usually reported in studies as a cause of jaundice.[9,10,11] As such, its actual actual prevalence is not widely reported. Recent case reports are lacking, with available reports spanning three to six decades ago. [9,12,13,14]

Amongst the cases reported, there was similarity in the onset of yellowness of the eyes and skin, with onsets on the 6th, 8th and 5th days of life. However, common to all was the persistence for more than two weeks. This is consistent with standard definitions stating this condition starts within the second and third weeks and persists beyond three weeks of life.[1,10] Unlike healthy formula fed infants who do not have hyperbilirubinaemia in the third week of life, approximately one third and two third of all breastfed infants have jaundice and hyperbilirubinaemia respectively in the third week of life.[1,15] Breastmilk jaundice is also reported to occur in healthy term babies.[3] The three cases we reported were all healthy term neonates with normal birth weight.

Only one of the cases had a serum bilirubin above 15mg/dl. It has been recommended that serum bilirubin levels within this level are less likely to be due to breastmilk jaundice alone, and that investigations should be carried out to determine other causes of pathological jaundice.[1,10] In cases one and two, all available investigations were carried out to establish the aetiology and rule out other causes of pathological jaundice. In case three however, a coombs test was not done. In this case, the reticulocyte count did not show evidence of increased haematopoiesis, which would point towards increased haemolysis as a possible cause for the hyperbilirubinaemia. The aetiology of breast milk jaundice is still a subject of research, as no clear aetiology has been described.[4] The role of several genetic and environmental factors has been suggested.[2,3,4,10,14,16] These include: reduced uptake (mutation in the solute carrier organic anion transporter protein SLCO1B1); reduction in bilirubin conjugation (defective uridine diphosphate-glucuronyl transferase (*UGT1A1*) activity, increased concentrations of nonesterified free fatty acids; increased pregnane-3-alpha 20 beta-diol in breast milk); increased enterohepatic circulation (delayed establishment of enteric flora, increased beta glucuronidase activity in breast milk and reduced intestinal motility from increased levels of epidermal growth factor (EGF) in breast milk); and reduced uptake, metabolism, and excretion of bilirubinfrom increased levels of inflammatory cytokines in human milk. [2,3,10,16,17]

In all three cases reported, breastfeeding was discontinued and formula feeds given for 48 hours. Breast feeding was then successfully recommenced subsequently. The American Academy of Paediatricians however recommends that unless Serum bilirubin exceeds 340µmol/l, breastfeeding should not be discontinued due to concerns about its subsequent successful

recommencement.[7] Below this value, formula feeds should be introduced while breastfeeding continues.[7]

4. Conclusion

We have reported three cases of breastmilk jaundice amongst otherwise healthy, term exclusively breastfed babies with similar presentation and treatment. Breastmilk jaundice is largely not remembered as a cause of prolonged jaundice in our environment, and is thus grossly under reported. Physicians should be aware of this condition and its treatment, especially after excluding other cases of pathological jaundice. This would greatly reduce both parental anxiety and unnecessary treatment given to babies.

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