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Abstract

Neonatal Hyperbilirubinaemia is a common finding during the first postnatal week. Physiological jaundice occurs in first week of life in 60% of term and 80% of premature neonates. Non physiologic or pathologic jaundice occurs in 5-10% of newborns which require intervention. According to AAP guidelines laboratory investigation for jaundice include total serum bilirubin, blood Type and coombs test and if the baby has an elevation of direct reacting or conjugated bilirubin, there should be a urine analysis and urine culture. Here we are presenting 5 cases that developed indirect hyperbilirubinaemia and routine workup done according to AAP guidelines were normal. On extensive investigation all cases found to have urinary tract infection despite of having indirect bilirubin and they needed course of antibiotics according to sensitivities and follow up ultrasound. From our experience we suggest that UTI should be considered as a cause of neonatal jaundice especially when indirect bilirubin peaks after one week of life at mean age of 10.8 ± 2.38 days.

Keywords: Hyperbilirubenemia. UTI (urinary tract infection).

Introduction

Hyperbilirubenemia is the commonest morbidity in neonatal period. The incidence of jaundice in the first week of birth is 60% among term and 80% among premature neonates. About 5-10% of newborns required intervention.[1-3] Jaundice attributable to physiological immaturity, usually appears between 24 to72hrs of age in term and by 5th to7th day in preterm neonates and disappears by 10-14 days of life.[2] Most jaundice is benign, but because of potential toxicity of bilirubin to developing brain, newborn infants must be monitored to identify those who might develop severe hyperbilirubinaemia and in rare cases acute bilirubin encephalopathy or kernicterus.[1] AAP has published guidelines outlining the management of healthy newborn with hyperbilirubinaemia, which includes maternal and infant blood grouping, Rh typing, direct coombs test and total serum bilirubin level and if the baby has direct hyperbilirubinaemia then investigate for urinary tract infection. Urinary tract infections (UTIs) are a common problem in febrile infants younger than 8 weeks of age, with prevalence between 5% and 11%. Jaundice can be one of the earliest symptoms of urinary tract infection therefore investigating for UTI in the infants with unexplained hyperbilirubinaemia is suggested as part of the workup for jaundice.[2] Complete clinical assessment is needed in all cases of prolonged jaundice, however the indications and extent of investigation remain unclear.[3] With the literature review it is somehow clear that unexplained, prolonged and direct hyperbilirubinaemia requires urine analysis but the question remains, should one investigate urine in case of indirect hyperbilirubinaemia. Clinical manifestations of UTI are non specific in neonates. The incidence of UTI is between 0.1% and 1% of all newborn, with higher incidence in premature infants.[3] The manifestation of sepsis and UTI are nonspecific in neonates and the consequences of misdiagnosis and delayed treatment could lead to significant morbidity. Here we are presenting summary of five newborns who developed indirect hyperbilirubinaemia after one week of life. Hyperbilirubinaemia workup was found to be normal. However on extensive investigation they were found to have positive urine culture with gram negative organism.

Case Summaries

We are reporting 5 cases that presented with neonatal jaundice in the second week of life at mean age of 10.8 ± 2.38 days and were treated with photo therapy. On examination no signs of infection were found and on investigation no common cause like ABO incompatibility, Rh incompatibility, and G6PD deficiency was detected. On further investigating the babies, Case 1, 2, 4 and 5 had proven urinary tract infection with positive urine C/S with different sensitivities. Case 3 although had no growth in urine culture (Baby had received antibiotic at another hospital) but her urine detailed report was significant for TLC count of 16/HPF. On follow up ultrasound KUB all were reported as normal. All specimens were collected aseptically through bladder catherization. Details of cases are illustrated in the table.

Discussion

Nearly 60% of full term and 80%of premature infants develop jaundice[1-4] which in most cases is benign and considered physiologic. Jaundice in breast fed, healthy babies usually appears between 24-72 hours of age, peaks by 5-15 days of life and disappear by the third week of life.[4] Sepsis is a well known cause of neonatal jaundice in seriously ill newborns and it may be the only sign of sepsis.[2,3]

Garcia et al[4] reported that patients with an elevated conjugated bilirubin fraction were more likely to have UTI and AAP also recommend urine analysis and culture in patient with conjugated and prolonged jaundice. But in our reported cases neither has prolonged jaundice (>2 weeks), nor have direct hyperbilirubinaemia; rather all of the them have predominantly indirect hyperbilirubinaemia.

Incidence of UTI in asymptomatic, afebrile,

Table:

	Case #1	Case#2	Case #3	Case # 4	Case#5
Age of presentation (days)	12	10	7	12	13
Gender	M	M	M	M	F
Total stay in hospital	3	2	3	2	2
Birth weight	3.4	4.16	3.2	2.9	2.6
Weight on admission	3.2	3.8	3.15	3.1	2.9
Gravid		3	4	G3	Primigravida
Para		2	3+0	2+0	0
Mother on medication	None	None	None	None K/C of thalassemia minor	Aldomet (PIH) Augmentin (vaginal infection) Glucophage(PCOS)
Mode of delivery	Elective C-section	SVD	SVD	EL-LSCS(Scar)	SVD
Apgars	Immediately cried after birth	Good apgars	Immediately cried after birth	8/1,9/5	Good
Breast Feeding/bottle feeding	both	Exclusive Breast feeding	Exclusive breast feeding	Exclusive breast feeding	Exclusive breast feeding
Age of jaundice peak(days)	7	8	6	10	8
Total bilirubin	23.4	20.5	16.7	23.4	20.2
Direct	0.5	0.5	0.3	0.5	0.5
Indirect	22.9	20.0	16.4	22.9	19.7
Mother blood group	O+ve	O+ve	O+ve	A+ve	B+ve
Baby blood group	O+ve	B +ve	O+ve	A+ve	B+ve
Coombs	Negative	Negative	Negative	Negative	Negative
Retic	0.7%	0.7	0.89	0.3	1.92
G6PD	Normal		Normal	Normal	Normal
Creatinine	<0.2	0.6	Not done	0.2	Not done
HB/HCT	16.8/50.3	15.7/43.5	14.4/42.5	16.8/50.3	12.0/34.9
Platelet count	424	679	222	424	559
TSH level	4.56	1.45	Not done	4.56	Not done
CRP level	<0.3	0.6	0.5	<0.3	0.8
Blood C/S	No growth	No growth	No growth	No growth	No growth
Urine D/R					
TLC	02	Not done	16	02	08
Nitrates	Negative	Negative	Negative	Negative	Positive
Urine C/S	E-coli, pan-sensitive	E-coli sensitive to amikacin and resistant to cefotaxime	Negative(already received antibiotics)	E-coli Pansensitive IV cefotaxime and amikacin for 48hours then cefspan total 10 days)	Klebsiella Pneumo Sensitive to amikacin, cipro, imipenum, resistant to Ampi, genta, Ceftriaxone
Antibiotics Name/Duration of antibiotics	Cefotaxime for 48 hrs and Amikacin for 10days	Cefotaxime for 48hrs and Amikacin for 10days	Cefotaxime and amikacin for 3 days then cefspan (total 10days)		IV ceftaxime Amikacin for 48hours then Cipro for total of 10 days
Phototherapy	Double phototherapy	Double phototherapy	Single phototherapy	Double Phototherapy	Double phototherapy
Exchange Transfusion	No	No	No	No	No
Follow up	Yes	yes	Yes	Yes	Yes
Ultrasound KUB	Normal	Not done	Normal	Normal	Normal

jaundiced infants younger than 8 weeks age was reported as 7.5%[4] in one study from USA. In another study from Turkey Hulya Bilgen et al[5] emphasized on the importance that UTI can occur in asymptomatic jaundiced neonates even in the first week of life and urine culture should be in the workup of neonatal jaundice, they have reported UTI in 8% of 102 asymptomatic unexplained hyperbilirubinaemia. Jafarzaden M et al.[6] found UTI in 8.2% of asymptomatic unexplained afebrile jaundiced infants and mean age of presentation was 8.9 days. To the best of our knowledge these are the first reported cases of indirect hyperbilirubinaemia, secondary to urinary tract infection in neonates. Most of them presented in the second week of life and none of them had prolonged history of jaundice.

From the literature review above and with our reported cases, urine culture should also be included in the workup of indirect hyperbilirubinaemia not explained by other causes. We do not know the exact mechanism of haemolysis and subsequent hyperbilirubinaemia secondary to UTI. Clinically, none of these infants are septic and all of them have negative blood cultures. To the best of our knowledge these are the first reported cases from Pakistan of neonatal UTI which has presented as jaundice predominantly indirect hyperbilirubenaemia in the second week of life.

Conclusion

Urine analysis should be the part of investigation for neonatal hyperbilirubinaemia especially when indirect bilirubin peaks after one week of life because untreated UTI can cause severe morbidity.

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