Original article:

Etiological profile of neonatal hyperbilirubinaemia in the rural area of Rajasthan

[1]Dr.Ahmad Ali , [2]Dr.Anurag Tomar

[[1]3rd year Resident , [2]Professor]

Dept. Of Pediatrics , National Institute Of Medical Sciences, Shobhanagar, Jaipur (Rajasthan) . India

Corresponding author : Dr.Ahmad Ali

Abstract:

Introduction: Jaundice is most common problem faced by neonates in the first few week of life. The aim of the study is to find out the etiology of hyperbilirubinemia in neonates admitted in neonatal intensive care unit and post natal ward in a tertiary care hospital.

Methods: This Observational study was conducted in Neonatal Intensive Care Unit (NICU) and Post Natal Ward in NIMS Medical College & Hospital, Shobha Nagar, Jaipur.(Rajasthan),after approval from the hospital ethical committee , over a period of 12 months (May 2013 to April 2014). Study was carried on 250 neonates presenting clinically with neonatal hyperbilirubinemia.

Results: The onset of jaundice was seen maximum between live hour 24-72 hours (n=145, 58% cases), followed by live hour 72 hours-14 days (n=80, 32%). At more than 2 weeks there was only 1 case (0.4%). The etiological factors in the causation of jaundice in the decreasing order of frequency were Physiological (28%), ABO incompatibility (24.4%), Rh incompatibility (13.6%), Idiopathic (10.4%), Cephalhematoma (10.4%), Septicemia (6%), IUI (4%), BMJ (2%), G6PD deficiency (0.8%), and Galactosemia (0.4%).As per the gestational age, physiological jaundice was more common in the healthy full term babies. ABO and Rh incompatibility were more common in the preterm babies. Cephalhematoma was more common in full term babies. Moreover cephalhematoma was associated with H/o of induced labour with oxytocin in 3 cases.

Conclusion: All newborn babies presenting with neonatal jaundice should be promptly investigated to search for underlying treatable conditions.

Keywords: Neonatal jaundice, Kernicterus, Physiological jaundice, ABO incompatibility

Introduction:

Neonatal hyperbilirubinemia is a common problem in neonates with an incidence of about 60% in term babies and 80% in preterm babies. It is the commonest cause of admission to the hospitals in the newborn period.[1] Jaundice refers to the yellowish discolouration of the skin and sclera of newborn babies that result from accumulation of bilirubin in the skin and mucus membranes. Clinically it becomes apparent when the serum bilirubin exceeds 7 mg/dl in neonates & >2mg/dl in adults. [2] In most of the cases, it is benign and no intervention is required. Approximately 5-10 % of them have clinically significant hyperbilirubinemia mandating the use of phototherapy [3, 4].

The percentage is quite high in preterm babies, due to their physiological abnormalities and other hazards of prematurity like asphyxia, septicaemia, respiratory and circulatory insufficiency. Non physiological or pathological jaundice is also known to occur in 8-9%

of newborns with approximately 4% after 72 hours of age. Its timely detection and optimal management are crucial to prevent brain damage and subsequent neuro-motor retardation such as hearing loss, athetosis and rarely intellectual deficits [5]Dermal staining with bilirubin (Cephalo-caudal progression), first reported by Kramer[6] in 1969 has been widely used to visually assess the severity of neonatal jaundice in clinical practice. However, Moyer et al[7] in 2000 have reported marked discrepancies between visual assessment by health worker and actual bilirubin levels.Recently, the pathological conditions associated with hyperbilirubinemia were brought to light again as kernicterus re-emerged as a risk factor for infants in countries where this complication had essentially disappeared [8]. "Kernicterus" refers to the neurologic consequences of the deposition of unconjugated bilirubin in brain tissue. Subsequent damage and scarring of the basal ganglia and brainstem nuclei may occur[9]. Common risk factors for hyperbilirubinemia include fetal-maternal blood group incompatibility, prematurity, and a previously affected sibling[10]. All healthy newborns are at potential risk if their jaundice is unmonitored or managed inappropriately.This study is being conducted to ascertain the various etiologies of neonatal jaundice in the rural area of Rajasthan. The aim of the study is to find out the etiology of hyperbilirubinemia in neonates admitted in neonatal intensive care unit and post natal ward in a tertiary care hospital

Material and Methods:

This Observational study was conducted in Neonatal Intensive Care Unit (NICU) and Post Natal Ward in NIMS Medical College & Hospital, Shobha Nagar, Jaipur.(Rajasthan),after approval from the hospital ethical committee , over a period of 12 months (May 2013 to April 2014). 250 live, singleton neonates admitted with neonatal jaundice in the Neonatal Intensive Care unit (NICU) and Post Natal Ward were included in the study.Children more than 28 days of age and parents who refused to sign the consent were excluded from the study.

Jaundice was ascertained by clinical methods and confirmed by biochemical methods. Pre-test proforma was filled to record detailed history, clinical findings and investigations in each baby with hyperbilirubinemia.Each baby delivered at hospital has been carefully observed from birth onwards in day light, for appearance of jaundice and in the babies with dark complexion, digital pressure over fore head has been used to detect the icterus. In addition, babies coming from peripheries have been examined thoroughly clinically and detailed investigations have been done to detect the cause of jaundice.Other investigations have been done depending upon the clinical presentation and the report of initial investigations. Collected data has been analysed statistically.

Observation and results:

Figure no : 01

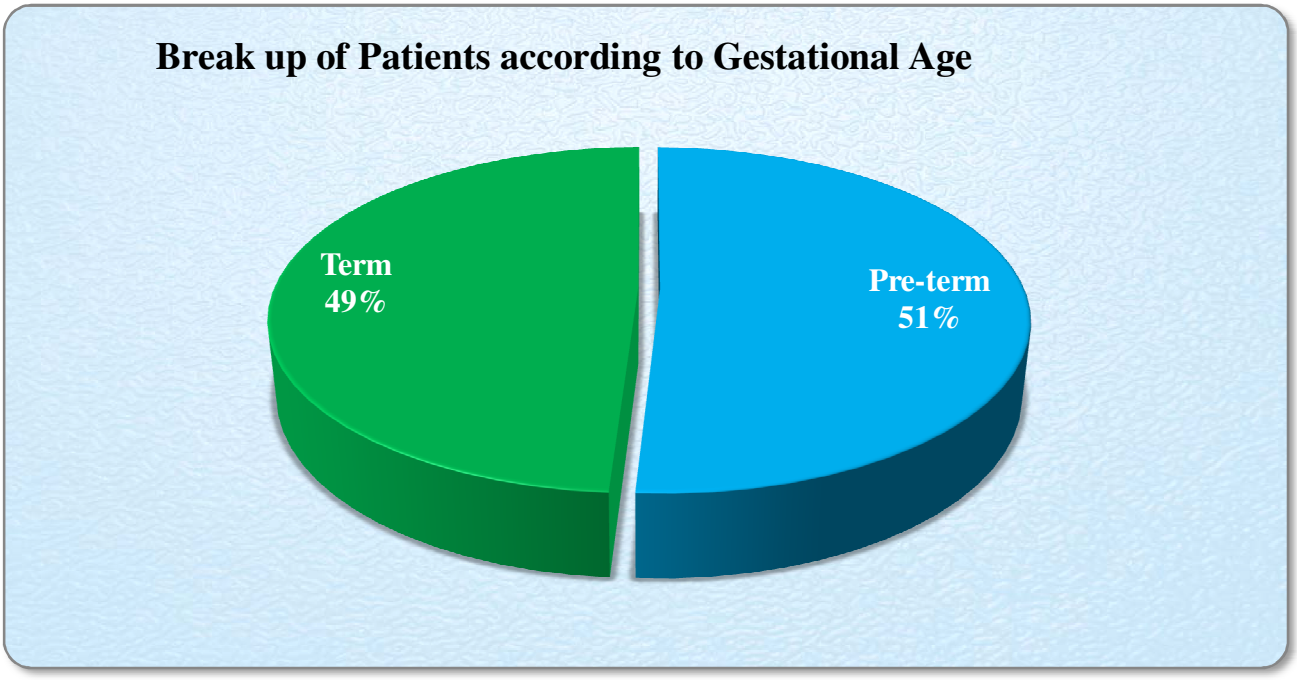

Table No 1: Day of Onset of Jaundice according to Etiology

Cause	Live Hours and Days				Total
	< 24 Hrs.	24-72 Hrs.	72 Hrs.-14 Days	>2 weeks	
Exaggerated Physiological Jaundice 28%	0	62	8	0	70
ABO Incompatibility (24.4%)	8	39	14	0	61
Rh incompatibility (13.6%)	15	18	1	0	34
Idiopathic (10.4%)	1	15	10	0	26
Cephalhematoma (10.4%)	0	8	18	0	26
Septicemia (6%)	0	2	13	0	15
Intrauterine Infection (4%)	0	0	9	1	10
Breast Milk Jaundice (BMJ) (2%)	0	1	4	0	5
Galactosemia (0.4%)	0	0	1	0	1
G_6PD (0.8%)	0	0	2	0	2
Hypothyroidism (0%)	0	0	0	0	0
Total	24	145	80	1	250

Table 2: Distribution of Patients with Different Etiologies According to Gestational Age

Cause	Preterm Babies	Term Babies
Exaggerated Physiological Jaundice (28%)	33	37
ABO Incompatibility (24.4%)	35	26
Rh incompatibility (13.6%)	24	10
Idiopathic (10.40%)	12	14
Cephalhematoma (10.40%)	10	16
Septicemia (6%)	10	5
Intrauterine Infection (4%)	2	8
BMJ (2%)	1	4
Galactosemia (0.4%)	0	1
G_6PD (0.8%)	1	1
Hypothyroidism (0%)	0	0
Total	128 (51%)	122 (49%)

Table 3 : Multiple Factors Causing Jaundice

Cause	Prematurity	Asphyxia	Septicemia	H/o maternal drug use
Exaggerated Physiological Jaundice (70)	33	5	0	3
ABO Incompatibility (61)	35	11	12	2
Rh incompatibility (34)	25	2	2	0
Idiopathic (26)	12	0	0	0
Cephalhematoma (26)	9	2	0	3
Septicemia (15)	10	0	0	0
Intrauterine Infection (10)	2	0	0	0
BMJ (5)	1	0	0	0
Galactosemia (1)	0	0	1	0
G_6PD (2)	1	0	0	0
Hypothyroidism (0)	0	0	0	0
Total	128	20	15	8

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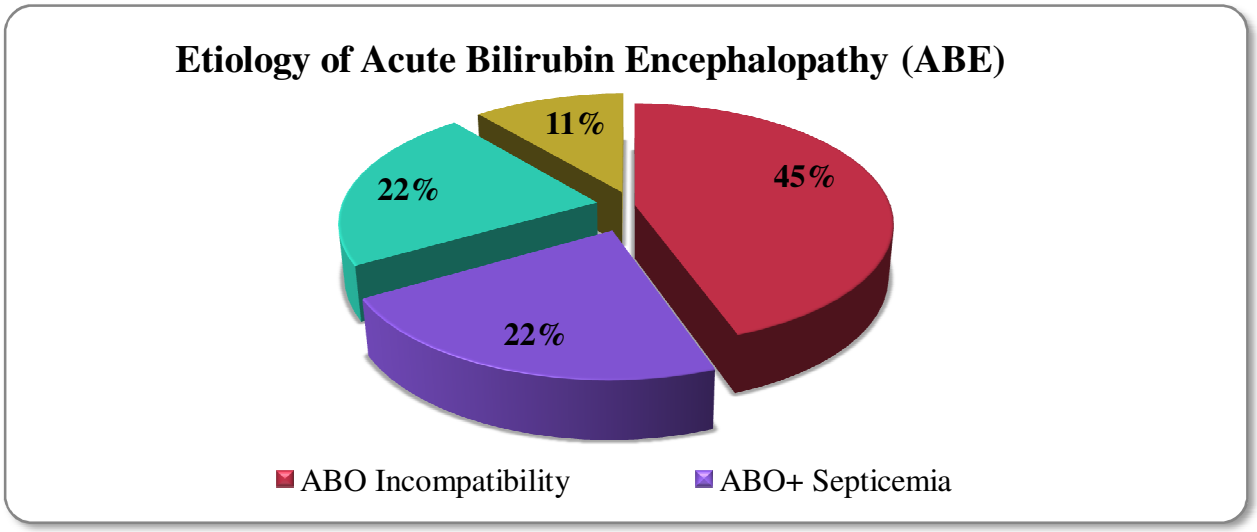
Table 4 : Etiology of Hemolytic Jaundice

ABO Incompatibility	
MBG (O+), BBG (A+/B+)	
OA Combination	22
OB combination	39
Total	**61**
Rh Incompatibility	34
G_6PD	2
Total	**36**
GRAND TOTAL	**97**

Figure no 2



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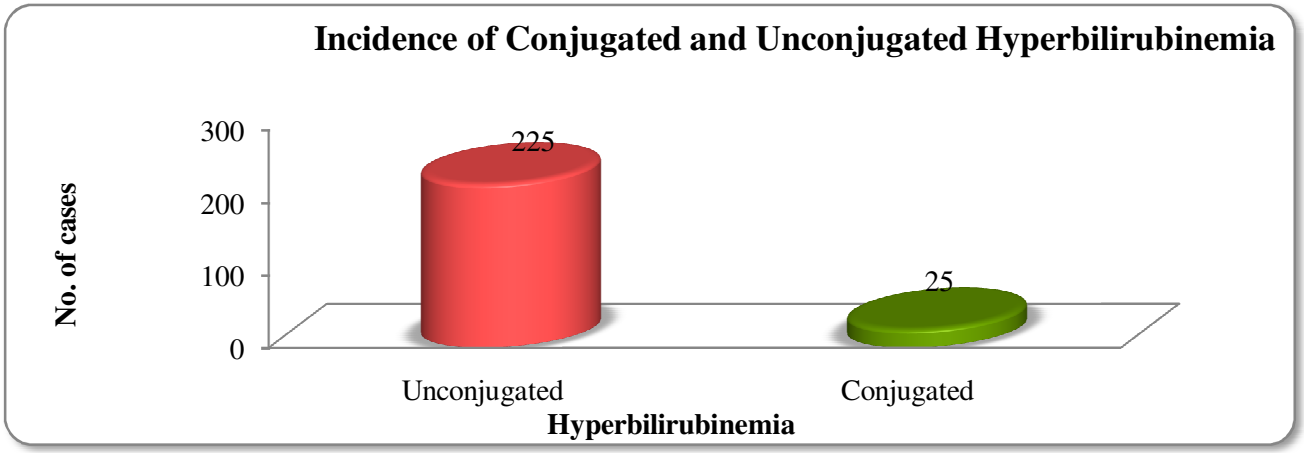

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Table 5: Etiology of Conjugated Hyperbilirubinemia

Etiology	Number of Patients
Intrauterine infection	10
Culture proven sepsis	7
Galactosemia	1
Perinatal asphyxia	1
Idiopathic	6 (out of 26)
Total	**25**

DISCUSSION:

The study comprises of 250 newborns less than 28 days of life in which 130 were Males (52%) and 120 were Females (48%). This is Comparable to study done by Effiong et al[11], Nigeria, 1972, Narang et al[12], 1996 India and Korejo et al[13], 2007 Karachi. A probable explanation may be due to social bias, males being more cared for, and promptly brought to medical attention. In our study, as per gestational age 128 (51%) were preterm and 122 (49%) were term delivered babies. Bhutani et al[14] in their study found out that prematurity was a significant risk factor for hyperbilirubinemia and is known to be a basis for increased biologic vulnerability to risk of bilirubin induced neurotoxicity. Bajpai et al[15], Indian Journal of pediatrics, had shown an incidence of 14% as physiologic jaundice with prematurity.Onyearugha et al[16], prematurity was the second leading cause of NNJ both in inborn and outborn babies. Singhal et al[17], had given an incidence of 16.7% (Prematurity) as a cause of neonatal jaundice probably more because of physiological handicaps in premature, LBW babies. Hussain et al[18], Karachi, too had shown that prematurity and LBW was an important risk factor for development of severe hyperbiliru-binemia. Preterm newborns are prone to developing jaundice due to immaturity of their bilirubin conjugating system, higher rate of hemolysis, increased enterohepatic circulation and decreased caloric intake [16].

In the present study, jaundice was detected maximum on Live hour (24-72) which consist of 145 cases (58%) followed by 72 hours to 14 days which contributes to 80 cases (32%). The onset of jaundice during live hour 24 was 24 cases (9.6%) which is always an indicative of pathological jaundice. After 2 weeks of post natal age, the number of cases decreased significantly to 1 case (0.4%). The results in our study are similar to work done by Anand et al, where the highest incidence of jaundice was on 3rd (45%) post-natal day followed by 4th day (35.5%). Bhatia et al noticed jaundice maximum on the 2nd day (67%) followed by 3rd day (14%)[19]. This may be because of increased bilirubin production due to increased RBC volume per kilogram and decreased RBC survival, increase ineffective erythropoiesis and increased turnover of nonhemoglobin heme proteins.

In our study, it was observed that exaggerated physiological jaundice was highest which accounts for 70 cases (28%). Table no 5 & 6 shows the comparison of our study with the other Indian studies and foreign studies with respect to various etiological agents. In the study by Bahl et al [20] had shown that physiological jaundice contributed to highest 63.8% incidence. It was comparatively higher as compared to our study. Singhal et al[17], (16.7%) and Merchant et

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al[21], (25.3%) too had reported highest incidence of physiological jaundice in their studies. In the study by Bedowra et al[22], Bangladesh (n=60), physiological jaundice contributes to 53.3% as the most common cause in their study. It was comparatively higher too as compared to our study. Suwimol et al[23], Thailand, and Joshi et al Nepal[24], had shown an incidence of 8.4% and 10% respectively as the cause of physiological jaundice in their studies. These higher incidence of physiologic jaundice may be due to increased enterohepatic circulation, decreased intestinal bacteria and decreased gut motility with poor evacuation of bilirubin-laden meconium, defective up take of bilirubin from plasma caused by decreased ligandin and binding of ligandin by other anions and defective conjugation due to decreased UGT activity and decreased hepatic excretion of bilirubin.

Table no 6 :ETIOLOGIES OF NEONATAL JAUNDICE IN DIFFERENT STUDIES IN INDIA

Worker (India)	Etiology (%)											
	Exaggerated physiological	**ABO Incompat.**	**Rh Incompat.**	**G6PD**	**Idiopathic**	**Cephal**	**Septicemia**	**IUI**	**BMJ**	**Galactosemia**	**Hypothy-roidism**	**Others**
Present Study, NIMS Medical College, 2014 (n=250)	28%	24.4%	13.6%	0.8%	10.4%	10.4 %	6%	4%	2%	0.4%	-	-
Narang et al[26], 2001, PGI Chandigarh, India (n=512)	-	1.95%	0.39%	12.1 %	73.3%	2.93 %	4.49%	-	-	-	-	2.34 %
Narang, Geeta et al[25] 1996 PGI (n=551)	-	5.6%	9.2%	17.2 %	35.4%	1.4%	24.4%	-	-	-	-	7%
Bahl et al[24],	63.8%	4.7%	1.9%	2.9%	11.4%	1.9%	10.5%	-	2.9 %	-	-	-

1994, Shimla (n=105)												
Singhal et al[23] (1992), AIIMS (n=454)	16.7%	14.3%	8.1%	5.1%	34.4%	2.9%	5.7%	1.3 %	0	0.2%	0.7%	-

Table no 7 :ETIOLOGIES OF NEONATAL JAUNDICE IN DIFFERENT STUDIES IN OTHER COUNTRIES

Other Countries Or Worker	Etiology (%)											
	Physiological	ABO Incompat	Rh Incompat	G6PD	Idiopathic	Cephal	Septicemia	IUI	BMJ	Galactosemia	Hypothyroidism	Others
Present Study, NIMS Medical College 2014(n=250)	28%	24.4%	13.6%	0.8%	10.4%	10.4 %	6%	4 %	2%	0.4%	-	-
Shao-WEN et al[36] Taiwan 2012 (n=485)	-	18.3%	2.4%	20%	12.9%	5.5%	1.8%	-	32.5 %	0.2%	0.2%	5.4%
Bedowara et al[37],Bangladesh 2010 (n=60)	53.3%	13.3%	3.3%	1.7%	1.7%	-	26.7%	-	-	-	-	-
Farhad et al[38] Iran , 2010 (n=118)	-	38.1%	16.1%	3.4%	25.4%	3.4%	8.5%	-	-	-	-	3.4%

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In our study it was observed that ABO incompatibility was 24.4%. In the study conducted by Sgro M et al[25] concluded that ABO incompatibility 51.6% was the most common cause, which was much higher than in our studies. Farhad et al[26] and Joshi et al[27] in their studies found that ABO was 38.1% and 28.8% respectively, in which the incidences were similar to our study.

Hemolytic jaundice due to isoimmunization in the mother and baby was seen in 38% of cases which on splitting up was (24.4%) due to ABO and due to Rh isoimmunization (13.6%). Hemolytic jaundice due to G6PD deficiency was seen in (0.8%) of the cases. In our study, ABO incompatibility was found to be the most common cause, followed by Rh incompatibility & G6PD. Direct antiglobulin test (DAT) was positive only in 9 cases (9.2%) of cases. The results are consistent with Sgro M et al[28] in which ABO (51.6%) incompatibility was the most common cause followed by G6PD (21.5%) and other antibody incompatibility (12%). Farhad et al[26] too had consistent results with ABO (38.1%), Rh (16.1%) and G6PD (3.4%).

Conclusion:

Health care providers working with neonates play a key role in identifying and assessing neonates at risk for pathologic jaundice. Parents counseling is required for bringing their babies early to prevent acute bilirubrubin encephalopathy and subsequent kernicterus. Clinicians need a systematic approach to identify the infants who may develop severe hyperbilirubinemia and keep them in follow up. The early identification and adequate treatment of children with cholestasis is essential to prevent morbidity and mortality.Also, to prevent of rh incompatibility an appropriate antenatal care, consisting of administration of Anti D Ig to unsensitized rh negative mothers, can reduce neonatal hemolytic disease profoundly.In conclusion, in cases of severe hyperbilirubinemia, ABO incompatibility was the most common cause of ET and unknown etiology was the next one.

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