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A STUDY OF REBOUND HYPERBILIRUBINEMIA IN POST PHOTOTHERAPY NEONATES

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ABSTRACT

Background: Phototherapy is widely accepted as a relatively safe and effective method for treatment of neonatal Hyperbilirubinaemia. Billirubin level often increases following cessation of phototherapy. This rebound hyperbillirubinemia may be dangerous to the neonate. However, routine measurement of billirubin rebound following phototherapy will definitely increase the workload, add to the expenses, bring anxiety to the parents and prolong the hospital stay. This study was conducted in our institution to throw some light on rebound hyperbilirubinaemia. **Aims and Objectives:** This study was designed with an aim and objective to, a) find out the incidence of rebound hyperbillirubinemia in neonates following cessation of phototherapy, b) determine the specific etiological factors responsible for the condition, c) determine the necessity of therapy and d) find the specific therapy needed to treat billirubin rebound. **Materials and Methods:** Newborns with hyperbilirubinaemia and needing Phototherapy were considered for study purpose. Given phototherapy after detailed history, physical examination and relevant investigation. Post-Phototherapy serum bilirubin estimated to see if rebound hyperbilirubinaemia is there and followed up as per the result. **Results:** In this series of total 126 neonates, 46 (36.5%) had post phototherapy rise of serum bilirubin to some extent which was found to decrease with time when followed up subsequently. Only 14 neonates, which constitutes 11.1% of all jaundiced neonate had developed post phototherapy rise of serum bilirubin to a significant level requiring retreatment. All babies recovered uneventfully. **Conclusion:** Post-Phototherapy rebound hyperbilirubinaemia is not uncommon. It is benign in course and resolves uneventfully. Regular post phototherapy bilirubin estimation may not be that much essential; but chance of occurrence of rebound hyperbilirubinemia and its subsequent consequences must not be ignored especially in presence of the risk factors.

KEYWORDS: Neonatal Hyperbilirubinaemia, Phototherapy, "SBR" Serum Bilirubin Rebound.

BACKGROUND

New born baby is unique because of its limited ability to clear bilirubin load from plasma and also because this is about the only period in life when hyperbilirubinemia possesses a threat to baby's life and intact brain survival *(O. Dell, G.B. et al. 1982)*.[6] Its timely detection and optimal management are crucial to prevent brain damages and subsequent neuromotor retardation due to bilirubin encephalopathy. It needs closer observation and prompt investigation to find out the etiopathogensis and the accentuating factors like asphyxia, prematurity, dehaydratin, septiacaemia etc. The degree of danger depends upon the various factors that affect the production, metabolism and distribution of bilirubin after birth.

Phototherapy is widely accepted as a relatively safe and effective method for treatment of neonatal Hyperbilirubinaemia. In view of poor quality of phototherapy units in our country it is recommended that phototherapy may be started early when serum bilirubin approaches upper limit of physiological range. The use of phototherapy has significantly decreased the need for exchange transfusion in term and preterm infants with hemolytic & non-hemolytic jaundice. However, phototherapy dose not treat the root cause that leads to neonatal jaundice but, only the effect i.e. raised serum billirubin. Hence, billirubin level often increases following cessation of phototherapy. This rebound hyperbillirubinemia may be dangerous to the neonate. However, routine measurement of billirubin rebound following phototherapy will definitely increase the workload, add to the expenses, bring anxiety to the parents and prolong the hospital stay. There is paucity of studies related to rebound hyperbilirubinaemia in our country in general and in our institution in particular. Hence this study was proposed to be conducted.

AIMS AND OBJECTIVES

This hospital based prospective study was conducted in the department of Pediatrics, S.C.B. Medical College and Hospital, and S.V.P. P.G.I.P., Cuttack, during the period extending from September 2010 to September 2012.This has been designed with an aim and objective to, a) find out the incidence of rebound hyperbillirubinemia in neonates following cessation of phototherapy, b) determine the specific etiological factors responsible for the condition, c) determine the necessity of therapy and d) find the specific therapy needed to treat billirubin rebound.

MATERIALS AND METHODS

The study was carried out in neonatal wards of S.C.B. Medical College & Hospital, Cuttack and S.V.P. P.G.I.P., Cuttack, during a period extending from september 2010 to september 2012. Total 138 neonates were included in the study during this period, out of which 1 neonate died & 11 neonates left against medical advice (LAMA) before complete data was obtained and thus were excluded from study. Finally, our study population included rest 126 neonates. Newborns, who were treated with phototherapy in the neonatal units during this period were included in the study after fulfilling the inclusion criteria a) Neonates having clinically significant icterus, b) Neonates undergoing phototherapy for jaundice. Neonates a) who were irregularly treated, b) having conjugated hyperbilirubinemia, c) who were very sick, d) weighing less than 1000gm and e) having serum billirubin concentration >25mg/dl, were excluded from the study.

Methods: After detailed antenatal, natal and postnatal history and physical examination completed within 24hrs of admission, all 126 newborns included in the study were categorized into two groups a) Group-I, Neonates ≥ 35 completed weeks and b) Group-II, Neonate born before 35 completed weeks. All the babies were subjected for detailed investigations like detailed Haemogram, Serum Bilirubin (Total, Direct and Indirect), Blood group, Rh typing of baby and mother (if not knowen), Reticulocyte count, Urinalysis, Sepsis screening of neonate and special tests including Direct Coombs Test (DCT), G-6 –PD activity, Osmotic fragility test, STORCH screening, Blood C/S, Urine C/S, Thyroid function test, USG abdomen Urine for reducing sugar.

Clinically suspected and Jaundiced babies were subjected to phototherapy, a) Neonates ≥ 35 completed weeks of gestation basing on AAP guideline chart and b) Neonate born before 35 completed weeks of gestation or with body weight < 2500gm, Phototherapy was initiated when serum billirubin was i) > 5mg/dl in 1st 24hrs of post gestational age or ii) >10mg/dl or 0.8% of body weight when 24-48 hrs of post gestational age (whichever is lower) and iii) >15mg/dl or 0.8% of birth weight (whichever was lower) when > 48 hrs of post gestational age. Double/single surface phototherapy was administered using special blue compact fluorescent tubes. Irradiance of the phototherapy unit at level of abdominal skin of the neonate was monitored once a day using a standard flux meter (Gineveri) sensitive to wavelengths of 425-475nm. The tubes were replaced during the study period as and when they were visibly discolored or were producing less light or when the irradiance fell to less than 15 µ W/cm^2/nm.

In babies under Group-II, phototherapy was stopped when serum bilirubin fell 2mg/dl below the level at which phototherapy was initiated whereas **i**n babies under Group-I, phototherapy was stopped when serum total bilirubin was <14 mg/dl in 2 consecutive measurements at least 6-12 hrs apart in haemolytic jaundice and in non-haemolytic jaundice phototherapy was stopped when single value of total serum bilirubin was <14mg/dl.

Serum bilirubin (direct and total) was measured 24 ± 6hrs after stopping the phototherapy. For all neonates under "Observation" serum bilirubin was estimated at 6–12 hrs after initiation of observations. For neonates with rebound hyperbilirubinaemia, who needed retreatment, were provided as per above guidelines.

RESULTS

In this study total 126 jaundiced neonates admitted for phototherapy were observed to find the incidence of the post phototherapy rise of serum bilirubin. They were analyzed to determine the important etiological risk factors that lead to this condition and the therapeutic measures to treat rebound hyperbilirubinemia.

Out of total 126 neonates, 46 (36.5%) neonates had post phototherapy rise of serum bilirubin to some extent, which was found to decrease with time when followed up subsequently. Only 14 neonates, which constitutes 11.1% of all jaundiced neonate had developed post phototherapy rise of serum bilirubin to a significant level requiring retreatment. (Table-1-a) In maximum number of cases with "SBR" the initial jaundice appeared on day 2 of postnatal age (i.e.28.6%). Among the neonates with significant bilirubin rebound 71.4% developed jaundice within first 3 days of postnatal life. A statistically significant association was found between early onset of jaundice (within 3 days) and significant rebound hyperbilirubinemia (p=0.008). (Table-1-b).

Male neonates had significant bilirubin rebound 1.2 times more than female ones. But no statistically significant association was found between sex of neonate & "SBR" status. (Table-2) Maximum number of neonates (71.4%) with significant bilirubin rebound ("SBR") were delivered by normal vaginal delivery. Rest 28.6% of neonates were delivered by complicated vaginal delivery (CVD) & lower segment caesarian section (LSCS) delivery in equal proportions. No statically significant association could be found between

any modes of delivery with "SBR". (Table-3-a and Table-3-b).

About 17.9% of neonates who were below 2000gms, developed significant bilirubin rebound following cessation of phototherapy, which constitutes 71.4% of total number of neonates with "SBR". But only 5.7% of babies above 2000gms birth weight had significant bilirubin rebound. A statistically significant association was found between the birth weight of the child (<2000gms vs ≥2000gms birth weight), and the occurrence of rebound hyperbilirubinemia in post phototherapy neonates (p=0.001). (Table4-a &Table4-b).

Among the maternal risk factors, 'PROM' & 'Prolonged labour' each was present independently in 14.7%of neonates with significant bilirubin rebound. About 50% of neonates in that group did not have history of any maternal risk factors. No maternal risk factor found to have any significant association with "SBR" status of neonate. (Table-5-a and Table-5-b)).

Mean total serum bilirubin level in babies with significant rebound at onset of phototherapy was (16.32±3.997)mg/dl. Maximum 42.9% of neonates in "SBR" group had serum bilirubin between 15 to19.9 mg/dl ranges. No significant association could be found between serum bilirubin levels at onset of phototherapy with "SBR" status. (Table-6-a and Table-6-b)

Mean duration of primary phototherapy in neonates with significant rebound is (66.86±23.4) hrs. There is a significant association between duration of primary phototherapy with "SBR" status of neonates following phototherapy cessation with p = 0.029.It indicates that more the time required to normalize the initial raised serum bilirubin level increases the chance of bilirubin rebound. (Table-7-a and Table-7-b).

When neonates with "SBR" are grouped according to etiological diagnosis hemolytic causes of neonatal jaundice found to be most common (57.14%) diagnosis. Other neonates found to have etiological diagnosis of prematurity (28.6%), cephalohematoma (7.1%) and breast feeding jaundice (7.1%) among "SBR" group of neonates. Hemolytic jaundice found to have a significant association with significant bilirubin rebound. (Table-8-a and Table 8-b)

In this study population of jaundiced neonate, 13.8% of babies; who had received primary phototherapy within first 3 days of postnatal life, developed significant post phototherapy rebound hyperbilirubinemia in comparison to, only 8.2% for babies who had received primary phototherapy after first 3 days of postnatal life. However no statistically significant association could be established between age of neonate at onset primary phototherapy & "SBR" status (p = 0.3997). (Table-9-a and Table-9-b)

All neonates with "SBR" after primary phototherapy cessation were retreated again with phototherapy & all of them recovered completely. None of the neonates required exchange transfusion for treatment of rebound hyperbilirubinemia. Most of neonates (57.1%) with significant rebound recovered within 24 hrs of retreatment with phototherapy. Only 2 (14.3%) required ≥ 48hrs of phototherapy. Rest (28.6%) recovered in 24-48hrs of phototherapy. Majority (64.3%) of babies with "SBR" stayed in hospital for 5-8 days for treatment. 21.4% required more than 8days of hospital stay.

In this series of total 126 neonates 88.2% recovered completely.10.3%neonates left hospital before complete recovery. Only 1.6% neonates succumbed.

Table 1(a): Frequency distribution of Rebound hyperbilirubinemia according to postnatal age at onset of jaundice (n=126).

Age at onset of jaundice (in days)	Babies with Serum bilirubin rebound			Total (%)
	Absent	Present but insignificant	Significant	
1	0	1	3	4
	0%	2.2%	21.4%	3.2%
2	15	15	4	34
	22.7%	32.6%	28.6%	27.0%
3	18	20	3	41
	27.3%	43.5%	21.4%	32.5%
4	25	5	2	32
	37.9%	10.9%	14.3%	25.4%
5	6	4	1	11
	9.1%	8.7%	7.1%	8.7%
6	2	1	1	4
	3.0%	2.2%	7.1%	3.2%
≥7	0	0	0	0
	0%	0%	0%	0%
Total	66	46	14	126
	100.0%	100.0%	100.0%	100.0%

Table 1(b): Observation of rebound hyperbilirubinemia in relation to age at onset of jaundice (after grouping the neonates).

Onset of jaundice	Serum bilirubin rebound			Total
	Absent	Present but insignificant	Significant	
≤3 days	33	36	10	79
	50%	78.3%	71.4	62.7
4th & 5th days	31	9	3	43
	47.0	19.6%	21.4	34.1
≥6th days	2	1	1	4
	3.0 %	2.2 %	7.1%	3.2
Total	66	46	14	126
	100%	100%	100%	100%

Table 2: Distribution of rebound hyperbilirubinemia according to sex of neonate.

Sex of baby	Serum Bilirubin Rebound			Total
	Absent	Present but insignificant	Significant rebound	
Female	30	21	5	56
	45.5%	45.7%	35.7%	44.4%
Male	36	25	9	70
	54.5%	54.3%	64.3%	55.6%
Total	66	46	14	126
	100.0%	100.0%	100.0%	100.0%

X^2=0.487, df=2, p=0.784

Table 3(a): Observation of rebound hyper bilirubinemia in relation to mode of delivery.

Mode of delivery	Serum Bilirubin Rebound			Total
	Absent	Present but insignificant	Significant rebound	
NVD	52	37	10	99
	78.8%	80.4%	71.4%	78.6%
complicated VD	4	6	2	12
	6.1%	13.0%	14.3%	9.5%
LSCS	10	3	2	15
	15.2%	6.5%	14.3%	11.9%
Total	66	46	14	126
	100.0%	100.0%	100.0%	100.0%

Table-3(b).

Mode of delivery	Absent / bilirubin rebound present but not significant	Significant rebound hyperbilirubinemia	Total
Lower Segment Cesarean Section (LSCS) & Normal Vaginal Delivery	102	12	114
	91.1%	85.7%	90.5%
Complicated Vaginal Delivery	10	2	12
	8.9%	14.3%	9.5%
Total	112	14	126
	100.0%	100.0%	100.0%

X^2=0.414, df=1, p=0.520

Table 4(a): Distribution of rebound hyperbilirubinemia in relation to weight of baby.

Weight of baby (gms)	Serum Bilirubin Rebound			Total
	Absent	Present but insignificant	Significant rebound	
<1500	9	8	4	21
	13.6%	17.4%	28.6%	16.7%
1500-1999	18	19	6	43
	27.3%	41.3%	42.9%	34.1%
2000-2499	18	4	0	22
	27.3%	8.7%	0%	17.5%
2500-2999	16	11	3	30
	24.2%	23.9%	21.4%	23.8%
3000-3499	3	4	0	7
	4.5%	8.7%	.0%	5.6%
≥3500	2	0	1	3
	3.0%	.0%	7.1%	2.4%
Total	66	46	14	126
	100.0%	100.0%	100.0%	100.0%

Table 4(b): Observation of rebound hyper bilirubinemia in relation Weight of baby (After grouping).

Weight of baby (gms)	Serum bilirubin rebound			Total	Test for statistical significance
	Absent	Present but insignificant	Significant		
<2000	19	27	10	56	X^2=19.651, df= 4, p=0.001
	28.8%	58.7%	71.4%	44.4%	
2000-2499	22	4	0	26	
	33.3%	8.7%	0%	20.6%	
≥2500	25	15	4	44	
	37.9%	32.6%	28.6%	34.9%	
Total	66	46	14	126	
	100.0%	100.0%	100.0%	100.0%	

Statistically significant association was found between the birth weight of the child and the occurrence of rebound hyperbilirubinemia in post phototherapy neonates (p=0.001).

Table 5(a): Observation of rebound hyperbilirubinemia in relation to maternal risk factors.

Maternal factors	Serum Bilirubin Rebound			Total
	Absent	Present but insignificant	Significant rebound	
Normal	37	11	7	55
	56.1%	23.9%	50%	43.7%
PROM	19	23	2	44
	28.8%	50.0%	14.3%	34.9%
Prolonged Labour	5	5	2	12
	7.6%	10.9%	14.3%	9.5%
IDDM	1	1	1	3
	1.5%	2.2%	7.1%	2.4%
Eclampsia	1	4	1	6
	1.5%	8.7%	7.1%	4.8%
Fever	2	1	1	4
	3.0%	2.2%	7.1%	3.2%
Others	1	1	0	2
	1.5%	2.2%	0%	1.6%
Total	66	46	14	126
	100.0%	100.0%	100.0%	100.0%

Table 5(b): Observation of rebound hyperbilirubinemia in relation to maternal risk factors.

Maternal factors	Serum Bilirubin Rebound			Total (N=126)
	Absent (N=66)	Present but insignificant (N=46)	Significant rebound (N=14)	
Normal pregnancy/ labour	37	11	07	55
	56.1%	23.9%	50%	43.7%
Medical illness during pregnancy (PROM, prolonged labour, IDDM, eclampsia, fever, others)	29	35	07	71
	43.94%	76.09%	50.0%	56.35%

X^2=11.648, df=2, p=0.003

Table 6(a): Observation of rebound hyperbilirubinemia in relation to serum bilirubin at onset of phototherapy.

Serum bilirubin (total) at onset of phototherapy (in mg/dl)	Serum Bilirubin Rebound			Total
	Absent	Present but insignificant	Significant rebound	
<10	3 4.5%	2 4.3%	0	5 4.0%
10-14.9	25 37.9%	17 37.0%	5 35.7%	47 37.3%
15-19.9	32 48.5%	21 45.7%	6 42.9%	59 46.8%
≥20	6 9.1%	6 13.0%	3 21.4%	15 11.9%
Total	66 100.0%	46 100.0%	14 100.0%	126 100.0%

Table 6(b): Comparison of serum bilirubin level at start of phototherapy for rebound hyperbilirubinemia status.

Serum bilirubin at onset of phototherapy (in mg/dl)	Serum Bilirubin Rebound			ANOVA (F-value)	P value
	Absent	Present but insignificant	Significant rebound		
N	66	46	14		
Direct	1.204±1.669	1.01±1.398	0.98±0.287	0.300	0.742
Total	15.732±3.336	15.91±3.901	16.32±3.977	0.159	0.853

Table 7 (a): Observation on rebound hyperbilirubinemia in relation to duration of primary phototherapy.

Phototherapy duration hours upto	Serum Bilirubin Rebound			Total
	Absent	Present but insignificant	Significant rebound	
24	25 37.9%	3 6.5%	1 7.1%	29 23.0%
48	29 43.9%	25 54.3%	5 35.7%	59 46.8%
72	8 12.1%	14 30.4%	4 28.6%	26 20.6%
96 and beyond	4 6.1%	4 8.7%	4 28.6%	12 9.5%
Total	66 100.0%	46 100.0%	14 100.0%	126 100.0%

Table 7(b): Observation on rebound hyperbilirubinemia in relation to duration of primary phototherapy (grouped information).

Phototherapy duration	Serum Bilirubin Rebound		Total
	Absent / Present but insignificant	Significant rebound	
Upto 72 hours	104 92.9%	10 71.4%	114 90.5%
Beyond 72 hours	8 7.1%	4 28.6%	12 9.5%
Total	112 100.0%	14 100.0%	126 100.0%
Fisher's exact p= 0.029			

Table 8(a): Observation on rebound hyperbilirubinemia in relation to etiological diagnosis.

Diagnosis	Serum bilirubin rebound			Total
	Absent	Present but insignificant	Significant	
*****Prematurity	30	27	4	61
	45.4%	58.6%	28.6%	48.4%
ABO incompatibility	1	2	3	6
	1.5%	4.3%	21.4%	4.8%
Rh incompatibility	0	1	2	3
	0%	2.2%	14.3%	2.4%
Other hemolytic causes (G-6-P-D deficiency)	7	3	3	13
	10.6%	6.5%	21.4%	10.3%
BFJ	8	2	1	11
	12%	4.3%	7.1%	8.7%
EPJ	13	1	0	14
	17%	2.2%	0%	11.1%
Cephalohematoma	1	5	1	7
	1.5%	10.8%	7.1%	5.5%
Sepsis	3	3	0	6
	4.5%	6.5%	0%	4.8%
Idiopathic	3	2	0	5
	4.5%	4.3%	0%	4%
Total	66	46	14	126
	100%	100%	100%	100%

*****When prematurity was also associated with other important etiology, then final diagnosis was considered to be of that etiology whereas, when no other diagnosis could be made other than prematurity then only, prematurity was taken as the final diagnosis.

Table 8(b): The comparisons between the etiological diagnosis distributions vide the SBR status.

Sl. No.	Diagnosis	Serum bilirubin rebound status (*N*=126)		Z test value	*P* value
		SBR (*n*=14)	Absent / Present but insignificant (*n*=112)		
1	Prematurity (<37 weeks)	4 28.57%	61 54.46%	1.950	0.0511
2	Hemolytic etiology (ABO/ R*h* incompatibility G6PD deficiency, etc)	8 57.14%	22 19.64%	2.634*	0.0084
3	BFJ and EPJ	1 7.14%	25 22.3%	1.866	0.062
4	Cephalohematoma	1 7.14%	7 6.25%	0.113	0.9096
5	Others (Sepsis, Idiopathic)	0 0.0%	11 9.82%	3.476*	0.0005

****Statistically significant by Z Test (2 Tailed) at 95% CI.***

Table 9 (a): Distribution of rebound hyperbilirubinemia according to age of onset of primary phototherapy.

Age at onset of primary phototherapy (in days)	Babies with Serum bilirubin rebound			Total
	Absent	Present but insignificant	Significant	
1	0	0	1	1
	0%	0%	7.1%	0.7%
2	14	12	4	30
	21.2%	26.1%	28.6%	23.8%
3	16	14	4	34
	24.2%	30.4%	28.6%	27%
4	23	14	3	40
	34.8%	30.4%	21.4%	31.7%
5	9	3	1	13
	13.6%	6.5%	7.1%	10.3%
6	1	2	1	4
	1.5%	4.3%	7.1%	3.2%
≥7	3	1	0	4
	4.6%	2.2%	0%	3.2%
Total	66	46	14	126
	100.0%	100.0%	100.0%	100.0%

Table 9(b): Observation of rebound hyperbilirubinemia in relation to age at onset of Primary phototherapy (after grouping the neonates).

Onset of jaundice	Serum bilirubin rebound			Total
	Absent	Present but insignificant	Significant	
≤3 days	30	26	9	65
	45.5%	56.5%	71.4%	51.6%
4^{th}-6^{th} days	33	19	5	57
	50%	41.3%	35.7%	45.2%
≥7^{th} days	3	1	0	4
	4.5%	2.2%	0%	3.2%
Total	66	46	14	126
	100%	100%	100%	100%

DISCUSSION

This study involved total 126 term & preterm neonates with jaundice who received phototherapy during the study period. They were subsequently examined for rebound hyperbilirbinemia usually (24±6) hrs after cessation of phototherapy. The study population included both inborn and outborn neonates.

Out of total 126 neonates, 11.1% (14) developed" SBR" following termination of phototherapy. This finding is comparable with that of Kaplan, *et al, 2006*, who studied 226 neonates and found 13.2% of neonates having phototherapy rebound hyperbilirubinemia.[5]

The highest incidence of jaundice was observed between 2^{nd}-4th day of postnatal life, which accounts for 84.9% of all cases of neonatal hyperbilirubinemia. Mean post-natal age of onset of jaundice was (3.19 ± 1.12) days in total study population. Among the neonates with "SBR", mean age of onset of jaundice was (2.79±1.12) days. In 78.6% of babies with "SBR", onset of jaundice was within 1^{st} 3days of life. Among all neonates with onset of jaundice within 72 hrs of postnatal life, 13.8% showed "SBR" following cessation of phototherapy.

A slight male preponderance was observed in the present study. 9% of female & 12.9% of male neonates developed "*SBR"* following cessation of phototherapy. Male preponderance may be explained due to higher incidence of sepsis & G-6-PD deficiency predisposing more male babies to pathological hyperbilirubinemia compared to female babies. Diamond LK et al, [4], proposed a hypothesis for greater susceptibility to infection in male babies due to factors responsible for defective immunoglobin synthesis, which is located on 'X' chromosome. However, there was no statistically significant association of rebound hyperbilirubinemia status with sex of the baby (p=0.487).

After termination of phototherapy, "SBR" was found in 10.1%, 16.6% and 13.3% of neonates born through NVD, complicated vaginal delivery & LSCS respectively but no statistically significant association could be elicited (p=0.520). Similar observations were made by Bansal,et al, 2008.[3]

Birth weight < 2000gms found to be a significant risk factor for "SBR" (Table-4a and b). Similar results were found by *Bansal A. et al, 2008* [3] and *Kaplan M* et al, 2006.[5]

In this study, 50% of babies with significant bilirubin rebound did not have any association with any maternal risk factors.14.3% had history of prolonged labour & PROM each. IDDM, Eclampsia, maternal fever each accounts 7.1% amongst the neonates with "SBR". It is found that there is no statistically significant association of any maternal risk factor with "SBR" after phototherapy termination. Similar observation was made by *Bansal A et, al 2008* [3], who found maternal risk factors are comparable in babies with or without "SBR".

The mean serum bilirubin at onset of phototherapy in neonates with "SBR" of this study was (16.321±3.97) mg/dl. Among the neonates with significant bilirubin rebound 42.9% had serum bilirubin between 15-19.9 mg/dl at the onset of phototherapy. Therefore, longer duration of phototherapy (>72 hrs) required to treat the neonates could be an indicator for increased chance rebound hyperbilirubinemia after phototherapy termination.

Significant bilirubin rebound was observed in "Hemolytic etiologies of neonatal jaundice" (i.e. ABO incompatibility, Rh incompatibility, G-6-PD deficiency together) (57.2%) followed by Prematurity as final diagnosis (28.6%), Breast-feeding jaundice, cephalohematoma (7.1% each). *W*hen neonates with "SBR" having final diagnosis of hemolytic causes of jaundice were compared with other causes, a statistically significant difference was noted in the proportions of babies with "SBR" as compared to others for hemolytic etiologies (p=0.008).

As high as 71.4% of neonates with significant bilirubin rebound had received primary phototherapy within first 3 days of post natal life compared to only 35.7% of neonates in same group who had received the primary phototherapy after 3rd day of postnatal life. However no significant association could be established between beginnings of phototherapy within ≤ 3days of post natal life in respect to significant bilirubin rebound. (p = 0.3997). This is in contrast to observation made by *Bansal, et al, 2008* [3] who studied 232 neonates for post phototherapy bilirubin rebound and found that age of onset of phototherapy < 60 hrs of post natal life is a risk factor for "SBR", This finding is also not similar to *Kaplan, et al, 2006* [5] who found that onset of phototherapy within first 3 days of post natal life is a significant risk factor to significant bilirubin rebound 21.

Neonates who had post phototherapy rise of serum bilirubin were treated as per standard guidelines mentioned before. All 14 babies (i.e.100%) with "SBR" recovered by retreatment with phototherapy for variable period alone without requiring any other form of therapy suggesting that retreatment with phototherapy was found to be an effective therapy for neonates with significant post phototherapy rise of serum bilirubin.

Therefore, in this study, it is observed that in the absence of risk factors significant rise of serum bilirubin in post phototherapy period is rare & routine measurement for rebound hyperbilirubinemia is unnecessary. Similar observations were made by Al-Saedi sa *et al*, 2002.[1]

SUMMARY AND CONCLUSION

Natural history of increased serum bilirubin level after stopping phototherapy is still unclear. Though incidence of rebound hyperbilirubinemia to a significant level after cessation of primary phototherapy is uncommon, it still possesses a great risk to the newborn baby because of high vulnerability of developing neonatal brain to bilirubin toxicity in the initial days of postnatal life. It is further aggravated by 'the increase in bilirubin load' and limited ability of neonate to clear bilirubin from plasma. Bilirubin neurotoxicity may be accentuated by presence of factors like immature blood brain barrier, low serum albumin concentration, rapid rise of serum bilirubin, presence of hemolysis & other comorbidities.

It is generally accepted that post phototherapy serum bilirubin rise to significant level is rare and routine measurement of rebound serum bilirubin is unnecessary. The etiopathologic conditions that increases the risk of rebound hyperbilirubinemia are prematurity (gestational age < 35 weeks), low birth weight (< 2000 gms), age at onset of jaundice (< 72 hrs / 3 days of birth), Hemolytic jaundice, Presence of significant bruising, duration of primary phototherapy >72hrs etc.

Neonates with post phototherapy bilirubin rebound usually responds within 24-48 hrs of retreatment with phototherapy. Baby should have proper nutrition & adequate hydration to both prevent & treat rebound hyperbilirubinemia. The rise of serum bilirubin to a significant level after phototherapy cessation is not that uncommon. Though routine measurement of serum bilirubin after phototherapy cessation is not required, it should be done in cases of high-risk neonates. Therefore, chance of rebound hyperbilirubinemia must not be ignored especially in presence of the risk factors. However, it is highly essential to prevent the condition hyperbilirubinemia (therefore rebound hyperbilirubinemia) than to manage it; thereby preventing the complication & succeeding in giving a healthy newborn in the hands of future for everything it needs.

REFERENCES

1. Al-Saedi S A. Rebound hyperbilirubinemia in term infants after phototherapy. Saudi Med J, 2002; 231394–1397.
2. Avery Diseases of newborn, 19th edition, 2011; 605.
3. Bansal A, Jain S, Parmar V, Chawala D. Bilirubin rebound after intensive PT for neonatal Jaundice. In xxviii Annual conference of National Neontology Forum of India; Kolkatta, 2008.

4. Diamond I. Kernicterus-revised concepts of pathogenesis and management. Pediatrics, 1966; 38: 539.
5. Kaplan M, Kaplan E, Hammerman C, Algur N. Bromiker R, Schimmel MS, Eldelman Al. post phototherpy neonatal bilirubin rebound ; a potential cause of significant hyperbilirubineemia. Arch Dis child, 2006; 91: 31-34.
6. Odell GB, Paul. Bilirubin in neonatal hyperbilirubinaemai, 1982; 8: 23-25.