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**ORIGINAL ARTICLE**

# Frequency of Hypocalcemia with Exchange Transfusion in Neonatal Jaundice

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## ABSTRACT

**Aim:** To determine the frequency of hypocalcemia with exchange transfusion in neonatal jaundice.
**Study design:** Descriptive cross-sectional study
**Place and duration of study:** Departments of Pediatrics and Pathology, Naseer Teaching Hospital Peshawar from 1st January 2018 to 31st December 2018.
**Methodology:** One hundred and sixty twopatients of jaundiced neonates having total serum bilirubin >20mg/dl, both gender and patients having age up to 14 days were included. Patients fulfilling the selection criteria had undergone exchange transfusion. Hypocalcaemia was evaluated and considered positive if calcium serum level is <8 mg/dl or <2 mmol/L.
**Results:** 50% of neonates were between 1-5 days, 45% of neonates were between 5-10 days, and 3% of neonates were in age 10-14 days. One hundred and ten (68%) of neonates were males and 52 (32%) of neonates were females. 30% neonates had hypocalcemia while 70% were without hypocalcemia.
**Conclusion:** The incidence of hypocalcemia was found to be 30% with exchange transfusion in neonatal jaundice.
**Keywords:** Hypocalcemia, Exchange transfusion, Neonatal jaundice

## INTRODUCTION

Neonatal jaundice is a common disorder worldwide, affecting 30-70% of newborn infants[1]. Severe neonatal jaundice progressed to kernicterus is a principal cause of disability and death among infants in poorly-resourced countries[2]. Mostly, jaundice is benign, the transitional phenomenon of no clinical significance and subsides itself, but in minority cases, it is pathological and needs treatment[1].

The 99.9% of unconjugated bilirubin found in bound form with protein and circulates until taken up by hepatic cells, and conjugated to form conjugated bilirubin. The breakdown of red blood cells produced unconjugated bilirubin in vascular system. The unconjugated bilirubin cannot cross blood brain, when bounded with protein as it is partially lipid soluble. The unconjugated bilirubin (unbound to protein) can cross blood brain barrier to cause damage to the brain and neurotoxicity[3,4]. This condition is manifested by sensory neural hearing loss, cerebral palsy, upward gaze paralysis, dental dysplasia and mental retardation[5].

As reported by routine investigation, measuring total serum bilirubin (TSB), physiological jaundice occurs after birth in most premature and term neonates during the first two weeks[3]. There is still controversy in defining critical levels in preterm and term infants. A Level of 20-25mg/dL considered as standard threshold but still recommended threshold differ between sources with modification for general condition and maturity. The treatment options are phototherapy, exchange transfusion, and pharmacological therapy[2]. In developing countries, exchange transfusion is still widely used in the management of severe neonatal jaundice[6]. The mortality rate associated with this procedure has been reported to range from 0.4% to 3.2%[7].

Complications associated with exchange transfusion include electrolyte abnormalities hypoglycemia, metabolic acidosis, hypocalcemia, volume overload, necrotizing enterocolitis, arrhythmias, infection, thrombocytopenia, graft vs. host diseases, and death[6]. Screening of neonates at the 24th and 48th hours after birth is necessary because early onset hypocalcemia is often asymptomatic and late onset hypocalcemia is symptomatic after 72 hours of birth till the 1st week of life. Excessive phosphate intake, hypomagnesaemia hypothyroidism, and vitamin-D deficiency are the most common causes of late onset hypocalcemia[7]. Transfusion of citrate-enriched blood products in early neonatal life is another typical cause of hypocalcemia from citrate toxicity due to neonatal renal and hepatic function immaturity. Hypocalcemia will be evaluated and hypocalcemia and considered positive if the serum calcium level is <8 mg/dl or <2 mmol/L)[8].

This study aimed to look for the frequency of adverse events of exchange transfusion in neonatal jaundice, which provided us local statistics as no such study is carried out in our local population. This study can be used to formulate policy recommendations regarding reviewing our protocol for exchange transfusions for neonates who are profoundly jaundiced and are a candidate for exchange transfusion.

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## MATERIALS AND METHODS

This descriptive cross-sectional study was conducted at the Paediatrics and pathology Departments, Naseer teaching Hospital, Peshawar from 1st January 2018 to 31st December 2018 after approval from Institutional Ethical Board. A total of 162 patients of jaundiced neonates having total serum bilirubin >20mg/dl, both gender and patients aged up to 14 days were included. Neonates with history of exchange transfusion for polycythaemia, birth asphyxia grade III, and sepsis & DIC were excluded from the study. A detailed history, physical examination was done. Appropriate investigations like serum bilirubin were done to look for neonatal jaundice. Patients fulfilling the selection criteria had undergone exchange transfusion, and they were subsequently observed. Hypocalcemia was considered positive if serum calcium level is <8 mg/dl or <2 mmol/L).

The data were analyzed using SPSS version 20. Data were stratified by age and gender concerning the presence of hypocalcemia and analyzed. Chi-square test at <0.05 significance level was used to know statistically significant.

## RESULTS

Eighty one (50%) neonates were in age 1-5 days, 73 (45%) neonates were in age 5-10 days and 8 (3%) neonates were in age 10-14 days. There were 110 (68%) neonates were male while 52 (32%) neonates were females. Forty nine (30%) neonates had hypocalcemia while 113(70%) neonates were without hypocalcemia (Table 1). Stratification of hypocalcemia with age and gender is given in table 2.

Table 1: Demographic information of the neonates (n=162)

| Variable | No. | % |
|---|---|---|
| **Age (days)** | | |
| 1-4 | 81 | 50.0 |
| 5-9 | 73 | 45.0 |
| 10-14 | 8 | 5.0 |
| **Gender** | | |
| Male | 110 | 68.0 |
| Female | 52 | 32.0 |
| **Neonatal jaundice** | | |
| Yes | 162 | 100.0 |
| No | - | - |
| **Hypocalcemia** | | |
| Yes (serum calcium level <8mg/dl or <2 mmol/L) | 49 | 30.0 |
| No (serum calcium level>8 mg/dl or >2 mmol/L) | 113 | 70.0 |

Table 2: Comparison of hypocalcemia with age and gender

| Variable | Hypocalcemia | | P value |
|---|---|---|---|
| | Yes | No | |
| **Age (years)** | | | |
| 1-4 | 25 | 56 | 0.942 |
| 5-9 | 22 | 51 | |
| 10-14 | 2 | 6 | |
| **Gender** | | | |
| Male | 33 | 77 | 0.920 |
| Female | 16 | 36 | |

## DISCUSSION

Jaundice in infants is a common cause of morbidity in newborns worldwide and the most common cause of hospitalization and readmission in the early days of life[9]. Recent global surveys curtail that approximately 1.1 million infants would develop severe jaundice every year, and morbidity of cases exists in South Asia and sub-Saharan Africa[10]. Phototherapy is a suitable and safe measure to reduce jaundice in infants[11-13]. Khan et al[14] reported the association of hypocalcemia in newborns after phototherapy.

In the newborn, the calcium hmoeostasis is of considerable interest. Calcium is an essential iron required for many biologic processes, including synaptic transmission neuronal conduction[15], hormonal secretions[16], cardiac automaticity[17] and excitation-contraction coupling in muscle.[18] Calcium is also a principal intracellular messenger and essential for many cellular processes, intracellular messenger, is essential for cellular processes and enzymatic activity.[19] During the initial days of life, the level of plasma calcium progressively decreases in normal infants, so as to compare the second and third day infants to the older infants, their level of plasma calcium is lower.20 In full-term newborns, the calcium plasma level reach normal level by ten days of life.[21] Phototherapy has the hypocalcaemia effect, which was reported by inhibiting the pineal gland via transcranial illumination, which cause the decrease of melatonin secretion that in turn inhibits the effect of cortisol on bone calcium[22] Romagnodi et al[23] also hypothesized this mechanism. Eghbalian[24] further reported this phenomenon of direct relationship between development of hypocalcemia and duration of phototherapy treatment.

In the present study, 50% of neonates were in age 1-5 days, 45% of neonates were in age 5-10 days and 3% were in age 10-14 days. 68% of neonates were males and 32% neonates were females. All the 162 neonates had neonatal jaundice, in which 30% of neonates had hypocalcemia while 70% of neonates did not have hypocalcemia. Same results were established by Khan et al[14] in which 74% of exchange transfusions were associated with adverse reactions; metabolic acidosis (24%), hypocalcemia (29%) and thrombocytopenia (44%), of which 44%, 74% and 69% respective required treatment.

Our results correlate with another study conducted by Khan et al[14], in which 62.6% male and 37.4% female out of 123 full term neonates were included. The mean age of newborns was 8.35±6.74 days and the mean duration of phototherapy was 1.74±0.98 days. The calculated serum calcium level before and after phototherapy treatment was 8.73±0.68mg/dl and 7.47±0.82mg/dl, respectively. The cases of hypocalcemia with jaundice interm infants receiving phototherapy was 22.76% (28/123). Stratification analysis was performed and observed that hypocalcemia was not significant among the different gestational age (p=0.65), gender (p=0.117), age groups (p=0.86) and also not found significant with jaundice (p=0.77) and phototherapy duration (p=0.56).

Another study conducted by Kramifer et al[25] reported hypocalcaemia with the mean gestational age and age of the newborns at the time of birth was 39.08±1.37 weeks and 8.35±6.74 days respectively. There were 46 (37.4%) females and 77 (62.6%) males.

Karamifar et al[25] and Ehsanipoor et al[26] reported the incidence of hypocalcemia in neonates to be 8.7% and

15%, respectively. Jain et al[27] reported hypocalcemia in 30% of term neonates after continuous phototherapy for 48 hrs. In contrast, Yadav et al[28], observed a much higher frequency of hypocalcaemia in 66.6%infantsafter phototherapy. Also, Medhat[29] reported hypocalcemia in 75% of infants by end of phototherapy. A recent study by Bahbah et al[30] included 50 term newborns, who had jaundice and treated with phototherapy and another 25 neonates having physiological jaundice were taken as control, required no phototherapy. 26% of neonates were reported with hypocalcaemia after 48 hours of phototherapy.

## CONCLUSION

The incidence of hypocalcemia was found to be 30% with exchange transfusion in neonatal jaundice. In any exchange transfusion case, hypocalcemia cannot be ruled out unless proven otherwise.

**Conflict of interest:** Nil

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