



Article

Risk Factors of Hypocalcaemia in Neonates at Wasit Province, Iraq

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Abstract: Neonatal hypocalcaemia is a metabolic disturbance typically observed in clinical settings and is associated with significant morbidity across different populations. In Iraq, neonatal hypocalcaemia remains exhibiting higher prevalence rates; therefore, this study aims to evaluate risk factors associated with serum calcium in neonates. A total of 50 neonates admitted to Neonatal Care Unit in Al-Zahra Teaching Hospital as well as Al-Kut Hospital for Gynecology and Pediatric in Wasit (Iraq) were involved in this study with no exclusion criteria. Data were collected for approximately 6 months starting from February 2023 until August 2023. Demographic data of study population were classified according to sex [male (66%) and females (34%)], gestational age [term (84%) and preterm (16%)], delivery mode [NVD (8%) and CS 46 (92%)], and maternal blood group, [A (48%), B (6%), AB (4%), and O (42%)]. The findings showed a significant decrease in serum calcium among the preterm, CS, and A blood group compared to other related categories with lack of significance between female and male neonates. Also, serum calcium was reduced in infants of diabetic mother compared to non-diabetic ones, as well as in infants exposed to phototherapy compared to non-exposed ones. In conclusion, incidence of hypocalcaemia in neonate of Wasit remains high with possible existence of many consequences. Therefore, furthermore studies are necessary to investigate the more related risk factors to hypocalcaemia in neonates in particularly asymptomatic cases.

Keywords: Cesarean Section, Diabetes, Gestational Age, Neonatal Calcium Concentration, Phototherapy.

1. Introduction

Neonatal hypocalcaemia is an epidemiological metabolic imbalance of low calcium serum levels that may either appear as the early onset or late onset disease, depending on the onset of the metabolic disorder [1]. Early-onset hypocalcaemia is the development of hypocalcaemia within the first 72 hours of life and is commonly associated with the perinatal stressors, such as prematurity, intrauterine growth retardation, birth asphyxia, and maternal diseases, such as diabetes mellitus or toxemia [2], [3]. Late-onset hypocalcaemia, on the contrary, occurs after the first 72 hours and is commonly caused by excessive phosphate intake or hypomagnesaemia, the lack of vitamin D, or parathyroid hormone dysfunction [4], [3].

Ionic calcium is a vital element in physiology, like blood coagulation, neuromuscular excitability, cell membrane integrity, and cellular enzymatic functions [5]. Calcium homeostasis malfunctions may hence have severe clinical outcomes, including neuromuscular irritability and cardiac arrhythmias up to life-threatening seizures [2], [3]. Hypocalcaemia may have ambiguous clinical manifestations as the affected patients may experience symptoms such as jitteriness, irritation, lethargy, poor feeding, or apnoea, which can be similar to other common neonatal diseases [6]. This means that the index of suspicion and laboratory confirmation is essential to identifying the disorder, as any level of total serum below 2.2mmol/L or ionized serum below 1.2mmol/L is normally considered a sign of the disorder [4]. This metabolic derangement occurs disproportionately in high-risk groups and is reported to occur in approximately one-third of preterm infants and most very-low-birth-weight infants as a result of the sudden stoppage of placental calcium transport and prior to secretion of parathyroid hormone [6], [3].

Hypocalcaemia late in infancy (after the initial 72 hours of life) has a different etiological profile, which is usually caused by excessive phosphate intake, hypomagnesaemia, and vitamin D deficiency [1], [7]. The variant of the condition often requires a comprehensive diagnostic history to detect underlying disorders in maternal metabolism of calcium, parathyroid hormone activity, or magnesium, which may lead to long-term hospital care and complicated treatment issues [6]. Although most affected infants are clinically silent, there are groups of high risk, such as preterm infants whose gestational age is below 32 weeks, small babies, infants of diabetic women, and those with severe prenatal asphyxia, that need regular monitoring of serum total or ionized calcium levels [1]. Routine screening of infants with high risks (low birth weight of birth, preterm birth, mother who was diabetic, and those born with prenatal asphyxia) should be conducted during the first 48 hours of life [1], [2].

Hypocalcaemia occurs especially early in patients of preterm birth because of the premature cessation of transplacental calcium supply and decreased sensitivity to parathyroid hormone [8]. This physiological immaturity leads to a characteristic nadir in serum calcium levels, which normally is 7.5-8.5mg/dL in healthy term newborns after 24-48hours of life [9]. This calcium loss rate and magnitude are negatively proportional to gestation age because premature babies undergo a reduced period of placental calcium accretion and have reduced responsiveness of parathyroid glands [10], [1]. Moreover, intestinal absorption of calcium and renal processing processes are not fully matured until 2 to 4 weeks of age, which is also a developmental delay that greatly increases the risk of preterm neonates to early-onset hypocalcaemia [11]. Hypomagnesaemia may also cause the dysfunction of the secretion and production of the parathyroid hormone, which further complicates the pathophysiology of this condition due to an interaction of magnesium, phosphate, and other serum anions [3]. Also, maternal hypomagnesaemia in diabetic mothers often results in functional hyperparathyroidism in the newborn that further increases the risk of early calcium disorder in the population at risk [8]. The impairment is especially applicable to infants of diabetic mothers where the loss of urinary magnesium under the impact of maternal glycosuria and consequent foetal hypomagnesaemia, which cause the suppression of parathyroid hormone levels since the mid-gestational period [9]. As a result, such infants usually exhibit a temporary failure to properly raise the level of secretion of parathyroid hormone due to the sudden withdrawal of placental calcium at birth [2]. This sudden change in physiology compels the newborn infant to depend on the autonomous homeostatic processes, such as secretion of parathyroid hormone and reabsorption of calcium into the blood by the kidneys, which, during the early postnatal stage, is usually functionally inadequate [10].

In Iraq, several studies have been conducted to indicate the prevalence of hypocalcaemia or frequency in accordance with various conditions [12], [13], [14], [15], [16]. Hence, this study aims to evaluate risk factors of neonatal hypocalcaemia.

2. Materials and Methods

Samples

The final sample size obtained was 50 neonates were admitted to the neonatal care unit in Al-Zahraa Teaching Hospital, as well as Al-Kut Hospital for Gynecology and Pediatrics in Wasit (Iraq). Neonates with serum calcium levels less than 8.8 mg/L were involved in this study with no exclusion criteria. Data were collected for approximately 6 months, starting from February 2023 until August 2023.

Data collection

The data collected depends on the statistical department of hospitals by checking admission cards and getting some information such as: sex, gestational age, history of phototherapy, history of diabetes in the mother, and level of calcium concentration.

Ethical approval

The agreement was approved by the directors of hospitals. Special codes were used instead of the names of the patients.

Statistical analysis

Data were organized using Microsoft Office Excel and analyzed statistically by the GraphPad Prism Software Through calculation of descriptive (frequency), mean, compare means (ANOVA). The minimum significant level was set at $p < 0.05$ [17].

3. Results

Socio-demographic characteristics

Among 50 infants enrolled in the study, 33 (66%) of them were males and 17 (34%) were females at a significance of $p < 0.0197$ (95%CI: 153.3 to 253.3), (Figure 1); 42 (84%) of them are term gestational age and 8 (16%) are preterm gestational age at a significance of $p < 0.0082$ (382.0 to 482.0), (Figure 2); 4 (8%) of them were delivered by NVD and 46 (92%) by CS at a significance of $p < 0.0064$ (483.7 to 583.7), (Figure 3). Regarding maternal ABO, 24 (48%) of them were group A, 3 (6%) group B, 2 (4%) group AB, and 21 (42%) were group O at a significance of $p < 0.0125$ (11.98 to 61.98) (Figure 4).

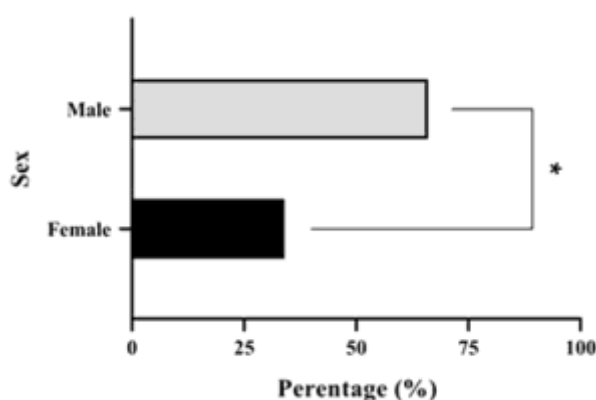


Figure 1. Association of neonatal hypocalcaemia with the sex of the study population.

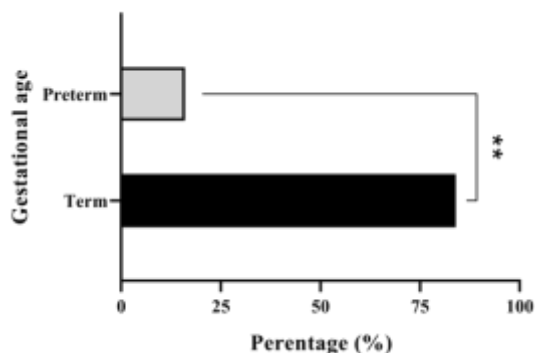


Figure 2. Association of neonatal hypocalcaemia with the gestational age of the study population.

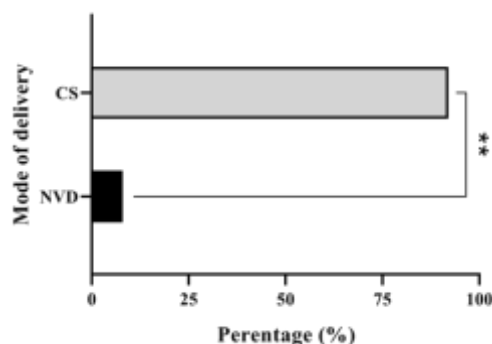


Figure 3. Association of neonatal hypocalcaemia with the delivery mode of the study population.

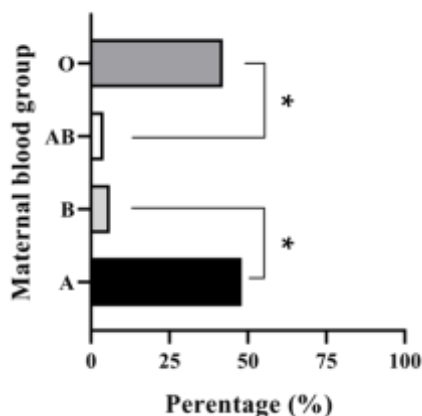


Figure 4. Association of neonatal hypocalcaemia with the maternal blood group of the study population.

Association between maturity and mode of delivery with mean calcium

Regarding the association between maturity and serum calcium, the results showed a significant decrease ($p < 0.0185$; 95%CI: 0.2069 to 13.51) in preterm ($6.3357 \pm 0.77520 \text{ mg/dL}$) when compared to term ($7.3828 \pm 0.63041 \text{ mg/dL}$) (Figure 5). In addition, the findings of delivery mode showed a significant decrease ($p < 0.0141$; 95%CI: 0.8565 to 13.73) in serum calcium among the CS cases ($6.7857 \pm 0.74405 \text{ mg/dL}$) when compared to NVD cases ($7.7987 \pm 0.47632 \text{ mg/dL}$) (Figure 6).

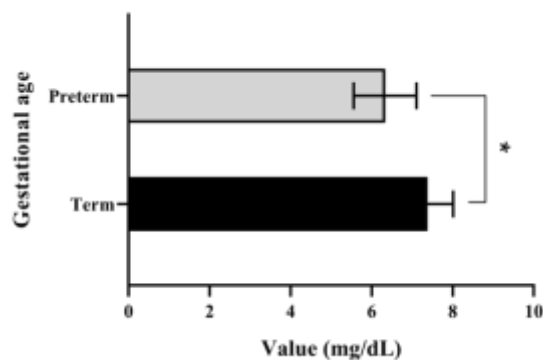


Figure 5. Association of neonatal hypocalcaemia with maturity (gestational age).

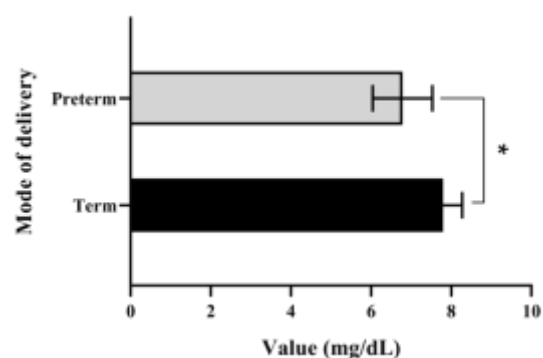


Figure 6. Association of neonatal hypocalcaemia with the mode of delivery.

Association between mean calcium and maternal ABO

Regarding maternal blood group, the findings shown a significant decrease ($p < 0.0191$; 95%CI: 6.826 to 7.712) in serum calcium among the A group ($6.95 \pm 0.95143 \text{ mg/dL}$) when compared to AB group ($7.6 \pm 0.28284 \text{ mg/dL}$); however, insignificant variation ($p > 0.05$) was seen in B ($7.3667 \pm 0.65064 \text{ mg/dL}$) and O ($7.161 \pm 0.69643 \text{ mg/dL}$) blood groups (Figure 7).

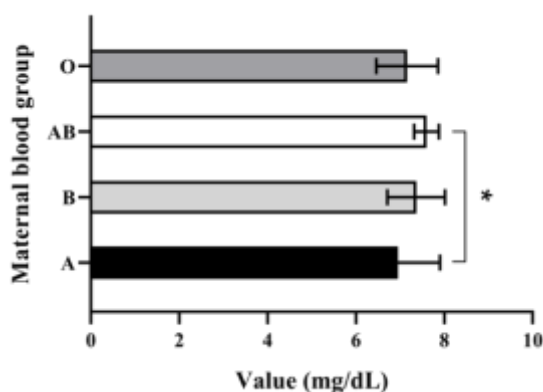


Figure 7. Association of neonatal hypocalcaemia with maternal blood group.

Association between calcium and neonatal sex

No significant association ($p < 0.0903$; 95%CI: 5.667 to 8.586) was observed between the levels of serum calcium among the male ($7.0115 \pm 0.88952 \text{ mg/dL}$) and female ($7.2412 \pm 0.65485 \text{ mg/dL}$) neonates (Figure 8).

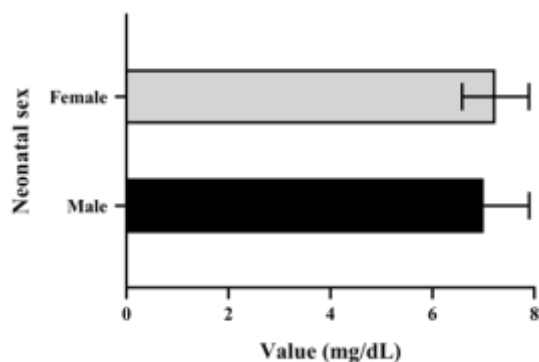


Figure 8. Association between neonatal sex and serum calcium.

Association between calcium and the infant of a diabetic mother

Regarding the association between mean calcium and infants of diabetic mothers, there is a significant association between them ($p < 0.0258$; 95%CI: 1.959 to 11.82). Infants of diabetic mothers were shown a lower value of serum calcium ($6.5 \pm 0.54772 \text{ mg/dL}$) than those of non-diabetic ones ($7.2758 \pm 0.80512 \text{ mg/dL}$) (Figure 9).

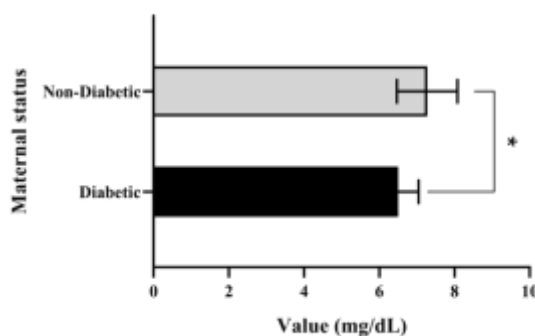


Figure 9. Association between neonatal serum calcium and the diabetic status of the mother.

Association between mean calcium and infant received phototherapy

Regarding phototherapy, the findings of exposed infants ($6.6647 \pm 0.95193 \text{ mg/dL}$) were reduced significantly ($p < 0.0117$; 95%CI: 2.896 to 11.08) when compared to non-exposed ones ($7.3085 \pm 0.65250 \text{ mg/dL}$) (Figure 10).

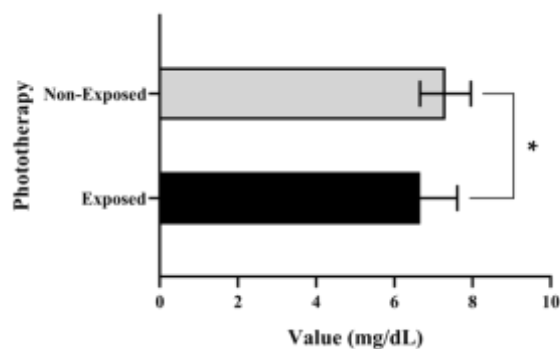


Figure 10. Association between neonatal serum calcium and exposure to phototherapy.

4. Discussion

Hypocalcaemia is one of the most frequent metabolic diseases during the newborn period and infancy [18]. The treatment of the symptomatic cases is accepted, but what is unanimously agreed is the level of calcium at which the treatment will be instituted, and the choice of treatment options is controversial in asymptomatic hypocalcaemia [19], [20], [21]. Our study showed that gestational age is significantly associated with hypocalcaemia; preterm births have a higher chance of being affected by hypocalcaemia compared to term births. Such findings are congruent with the findings of various studies [22], [23], [24] but opposite to the findings of a study by Jeong et al., which did not find any significant relationship between gestational age and hypocalcaemia, and are congruent with a study by Jain et al. that reported that preterm infants are more prone to hypocalcaemia [25].

Our findings indicate that there is a significant association between mode of delivery and the existence of hypocalcaemia in the babies. The findings align with the outcomes of other authors who endorsed the fact that hypocalcaemia is more common among infants born through caesarean delivery [26], [27].

Our findings revealed that maternal blood groups and the sex of infants had an insignificant association with the occurrence of hypocalcaemia. Known similar outcomes were demonstrated by Awan et al., who demonstrated that the sex of infants and the incidence of hypocalcaemia are insignificantly correlated [28]. There was a substantial correlation among infants of diabetic women with the existence of hypocalcaemia. Such findings can be compared with the findings of other researchers [29], [30], [31]. As our findings indicate, we have a significant correlation between phototherapy history and hypocalcaemia. The same findings were demonstrated by Beser et al., who concluded that hypocalcaemia and phototherapy have a strong relationship; children who have undergone phototherapy have a higher risk of acquiring hypocalcaemia [32].

5. Conclusion

Incidence of hypocalcaemia in neonates of Wasit remains high, with possible existence of many consequences. Therefore, further studies are necessary to investigate the more related risk factors related to hypocalcaemia in neonates, particularly asymptomatic cases. Hypocalcaemia in a neonate may be associated with many consequences that may increase the risk of neonatal mortality. Babies who are under stressful conditions must be under intensive care.

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