Original Article

# Selenium levels in hospitalized preterm very low birth weight neonates in North India

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## ABSTRACT

**Background:** Most of the morbidity and mortality of very low birth weight (VLBW) neonates are due to oxidative stress and infection. Selenium can address these issues due to its antioxidant role and synthesis of glutathione peroxidase for scavenging free radicals. **Objective:** The objective of the study was to find the serum selenium levels in hospitalized preterm VLBW neonates. **Materials and Methods:** This was a prospective observational study conducted in the Neonatal Unit of Department of Paediatrics in a tertiary care hospital, Lucknow, for the duration of 1 year. A total of 126 preterm VLBW neonates admitted within 72 h of birth and having a venepuncture for any reason were enrolled, and those with major congenital abnormality, prior supplementation, and necrotizing enterocolitis on admission were excluded. Blood sample was collected after enrollment in plain vacutainer under aseptic precautions and after ½ h serum was separated by centrifugation. Selenium levels were estimated in serum by inductively coupled plasma optical emission spectrometry method (Perkin Elmer Optima 8000). **Results:** Mean birth weight was 1150±210 g and mean gestational age was 30.21±3.76 weeks in our study population. Mean levels of selenium were 9.49±3.49 µg/dl. Mean selenium levels in neonates with gestational age <30 weeks, 30–32, and >32 weeks were 8.90±3.32, 9.32±3.74, and 10.57±3.15 µg/dl (p=0.107), respectively. Thus, the selenium levels were seen increasing with an increase in the gestational age. Furthermore, serum selenium level of neonates with birth weight >1 kg (10.08±3.55 µg/dl) was found to be significantly higher than those with birth weight ≤1 kg (8.40±3.12 µg/dl) (p=0.009). No significant association was seen with birth centiles or gender. **Conclusion:** Serum selenium levels were significantly lower in preterm neonates with lesser gestational age and lower birth weight although the baseline levels were within normal limits. Thus, the significant difference in levels can be linked with most of the morbidities and mortality in preterm neonates.

**Key words:** *Neonates, Selenium, Very low birth weight*

Preterm neonates are a vulnerable population which has high morbidity and mortality. In fact prematurity is the leading cause of neonatal death in India [1]. With advancement in neonatal care more preterm neonates are being saved and morbidity is increasing. Much of the morbidity is due to oxidative stress and infection, which the preterm neonate, is ill-equipped to deal with. Antioxidant capacities are inadequate in preterm newborns, both due to placental-fetal transfer interruption of antioxidant molecules and insufficient endogenous production.

A study done in 2005 [2] suggested that preterm infant's small selenium (Se) stores are used preferentially for glutathione peroxidase (GPx) production, occurring in stable or increased GPx and decreased Se concentrations. This could explain the poor correlation between selenium and GPx concentrations observed in the studies. Another possibility is that the natural defense mechanisms such as antioxidant enzyme GPx and mature along with the gestation.

A Cochrane review [3] on selenium supplementation in preterm neonates to prevent short-term morbidity reports that selenium is also known to play a role in immune competence. Blood selenium concentrations in newborns are lower than those of their mothers and lower still in preterm infants. In experimental animals, low selenium concentrations appear to increase the susceptibility to oxidative lung disease. In very preterm infants, low selenium concentrations have been associated with an increased risk of chronic neonatal lung disease and retinopathy of prematurity. However, studies have reported that supplementation was not associated with improved survival, a reduction in neonatal chronic lung disease, or retinopathy of prematurity but it was of benefit in terms of a reduction in one or more episodes of sepsis. They suggested that supplemental doses of selenium for infants on parenteral nutrition higher than those currently recommended may be beneficial. The data, in this review, were dominated by one large trial from a country (New Zealand) with

low selenium concentrations and may not be readily translated to other populations. The reviewers concluded that higher doses of selenium supplements may be able to reduce some complications for preterm babies, but more research is needed.

Selenium levels vary in different parts of the world and are affected by the selenium levels of the soil. In a study [4] it was found that selenium levels were above normal where the soils are drier and with considerably less water availability or lesser amount of rainfall is received such as in Rajasthan and southern parts of Haryana. The soils of Punjab and Himachal Pradesh where plenty of water is available for irrigation have low to normal levels of selenium. Floods may also be responsible for low levels as in Rohtak and Sonipat districts of Haryana.

No studies have been conducted on levels of selenium in neonates in the north region of India yet. It can be suggested that supplementation with Se in early weeks of life may prevent morbidities and promote growth and development. Thus, selenium supplementation in parenteral nutrition and formula is recommended. However, the ideal dose remains undefined. Maternal milk may be considered the gold standard for term newborns. Considering that mature human milk has low selenium levels and that preterm infants have a decrease in plasma selenium in the first postnatal month, it is convenient to use fortifiers with added selenium. Whether supplementation prevents diseases in newborns still requires further investigation. It must be considered that the main diseases of very low birth weight (VLBW) infants are multifactorial and selenium deficiency is only one of the risk factors.

## MATERIALS AND METHODS

This was a prospective observational study conducted in Neonatal Intensive Care Unit at the Department of Pediatrics, and Neonatal Unit in a hospital, at Department of Obstetrics and Gynaecology, Lucknow. The study was conducted for the duration of 1 year, i.e., September 2016–July 2017. Ethical Committee Clearance was obtained from the institution. Preterm VLBW neonates admitted within 72 h of birth and having a venepuncture for any reason were included in the study and those with a major congenital abnormality, necrotizing enterocolitis on admission, and prior supplementation with selenium were excluded.

During the study period, 1619 neonates were admitted in the units. Out of these, 282 neonates were VLBW and 60 were extremely low birth weight. VLBW neonates were included consecutively in our study until a total of 126 neonates were enrolled. 50 VLBW neonates were excluded due to congenital anomalies, short hospital stays due to death or leaving against medical advice. Baseline characteristics such as body weight at birth, sex, gestational age, birth centiles, type of delivery, birth asphyxia, maternal risk factors for infection, antenatal steroids, date of birth, date of admission, and treatment received before admission, as well as the demographic data and details of resuscitation were noted. Detailed history and examination of the baby was done and clinical characteristics such as respiratory support (mechanical ventilation, non-invasive positive pressure ventilation, and continuous positive airway pressure), oxygen requirement, intraventricular hemorrhage, sepsis, retinopathy of prematurity, periventricular leukomalacia, necrotizing enterocolitis, Bronchopulmonary dysplasia, start of enteral nutrition (day of life), supplements given**,** days to regain birth weight, and daily weight monitoring, were noted during follow-up.

About 1 ml blood was collected after enrollment in plain vacutainer under aseptic precautions and after ½ h serum was separated by centrifugation. Selenium levels were estimated in serum by inductively coupled plasma optical emission spectrometry method (Perkin Elmer Optima 8000) in the biochemistry department. The baseline selenium levels were estimated, but we did not supplement it in the babies as we wanted to know the levels in our area so that further, the appropriate dose for supplementation can be found out. The data entry was done in an excel sheet and analysis was done using SPSS software; $p<0.05$ was considered significant. Standard deviation was calculated using the excel program and appropriate statistical tools were applied.

## RESULTS

In the present study, the mean birth weight of the study population was 1150±210 g and the mean gestational age was 30.21±3.76 weeks. It was found that the mean serum selenium level was 9.49±3.49 µg/dl in our study. Out of 126 neonates, 60 (47.62%) were females and rest 66 (52.38%) were males. Difference in selenium level of males (9.16±3.88 µg/dl) and females (9.86±2.99 µg/dl) was not found to be statistically significant. Furthermore, out of 126 neonates, 107 (84.92%) were appropriate for gestational age (AGA) and rest 19 (15.08%) were small for gestational age (SGA). Difference in serum selenium level of SGA neonates (9.45±3.91 µg/dl) and AGA neonates (9.50±3.43 µg/dl) was not found to be statistically significant.

An increase in serum selenium levels with increase in gestational age was found. The mean serum selenium levels increased from 8.90±3.32 µg/dl in <30 weeks to 10.57±3.15 µg/dl in neonates born at >32 weeks of gestational age though it was not statistically significant (Table 1). This may be because preterm neonates born before 30 weeks of gestation may receive less transfer of selenium from the mother than those born after 32 weeks of gestation since maximum transfer occurs in the latter part of gestation. Serum selenium level of neonates with birth weight >1 kg (10.08±3.55 µg/dl) was significantly higher than those with birth weight ≤1 kg (8.40±3.12 µg/dl) ($p=0.009$).

## DISCUSSION

Of the VLBW neonates admitted in our unit, on an average, only one-fourth are discharged. The rest either die or leave against medical advice primarily due to their poor general condition. A poor antioxidant defense system and blunted immune competence are responsible for much of the morbidity in VLBW neonates. Since selenium is known to have a positive effect on

**Table 1: Association of serum selenium levels with gender, birth centile, gestational age, and birth weight**

| Associated factor | Number of neonates | Serum selenium (µg/dl) Mean±SD | Statistical significance |
|---|---|---|---|
| Gender | | | |
| Female | 60 | 9.86±2.99 | t=0.234; p=0.815 |
| Male | 66 | 9.16±3.88 | |
| Birth centiles | | | |
| SGA | 19 | 9.45±3.91 | t=0.436; p=0.664 |
| AGA | 107 | 9.50±3.43 | |
| Gestational age | | | |
| <30 weeks | 44 | 8.90±3.32 | ANOVA F=2.273; p=0.107 (NS) |
| 30–32 weeks | 50 | 9.32±3.74 | |
| >32 weeks | 32 | 10.57±3.15 | |
| Total | 126 | 9.49±3.49 | |
| Birth weight (kg) | | | |
| Up to 1 kg | 44 | 8.40±3.12 | t=2.641; p=0.009 |
| >1 kg | 82 | 10.08±3.55 | |

**AGA: Appropriate for gestational age, SGA: Small for gestational age, SD: Standard deviation**

both, we decided to study their levels in preterm VLBW neonates and determine their correlation with morbidity, mortality, and growth. Several diseases of the neonate have been shown to be caused, at least in part, by oxygen-free radicals. Antioxidant capacities are inadequate in preterm newborns, both due to placental-fetal transfer interruption of antioxidant molecules and insufficient endogenous production.

Serum selenium levels have been studied in various parts of the world, and wide variations have been seen. Since maximum accretion of Se occurs in the last trimester of pregnancy, we carried out this study to gauge the levels in VLBW neonates in our part of the country. This will help us in deciding if active supplementation is required for these neonates and may give us some idea of the dose required for the same.

The mean selenium level in our study population was 9.49±3.49 µg/dl **(**range - 4–16.8 µg/dl). There is a wide variation in serum Se levels in different parts of the world and even different parts of the same country. The Se levels in neonates in Iran were similar to our data as demonstrated in a study [5] that the mean selenium concentration in term infants was higher than in preterm infants and the levels were 124.80±13.72 µg/L and 100.30±11.72 µg/L, respectively. Furthermore, it found the mean umbilical cord Se levels in normal and low birth weight neonates to be 73.8 µg/ml and 77.32 µg/ml, respectively [6]. Studies within Iran reported adequate Se intakes in the general population. It was also found that the concentration of Se in water is excessive in parts of Jordan [7].

A study on preterm VLBWs from Rohtak, Haryana [8] found low mean Se levels of 31.1±14.8 µg/L at birth. Se supplementation at 10 µg/day increased serum Se levels significantly (63.9±13.9 µg/L on day 28 in selenium group vs. 40.9±17.3 µg/L on day 28 in placebo group [p<0.01]) but even these post supplementation levels were less than our baseline levels. Levels of even neonates <30 weeks and <1000 g birth weight in our unit were more than those found after 28 days of supplementation in their study. This may be primarily because Rohtak is a selenium deficient area.

As discussed earlier, selenium levels are higher in the Punjab and Himachal Pradesh area due to the availability of water for irrigation [9]. A number of studies have been conducted in European countries and a wide variation in the selenium levels is seen in them as well. In a study in Germany [10-12] on VLBW neonates, selenium levels of 17.8±8.1, 19.9±2.2, 34.2±11.7 µg/L, respectively, were found. In a study at Hungary [13], a Se low area the impact of selenium supplementation on preterm VLBW neonates was studied. Twenty eight preterm infants were randomized into two groups at birth with respect to selenium supplementation. In the supplemented group, the serum selenium concentration increased from 32.1±8.5 µg/L to 41.5±6.5 µg/L and in the un-supplemented group, it decreased from 25.9±6.8 µg/L to 18.2±6.4 µg/L within 2 weeks. Thus, European countries were found to be selenium deficient and their baseline and post supplementation levels were considerably lower than the baseline levels found in our study.

Similarly, an RCT on VLBWs in New Zealand [13] found low mean plasma Se concentration of 0.33 µmol/L before randomization in both groups and 0.56 µmol/L at 28 days in the supplemented group but 0.29 µmol/L in the control group (p<0.0001). An Australian study also found low plasma selenium of 0.3±0.1 µmol/L in VLBW neonates (1 µmol/L=6.583 µg/dl) [14]. Thus, these nations were found to be selenium deficient.

"A review of dietary Se intake and Se status in Europe and the Middle East" [15] states that Se intake and status are suboptimal. They quoted that government surveys indicate low Se intake across a wide age range of the UK population both Caucasian and Asian [16]. A Polish study [17] documented that Se content of the consumed foods was 4-time lower than in Spain; studies in France [18] and Belgium [19] reported intakes equivalent to the recommended dietary allowance (RDA), while those from Slovenia [20] and Italy [21] found intakes below the RDA. The nutritional status of Se has been difficult to assess through food intake data

alone, because many factors influence its presence in the food chain. Although its distribution in soil is uneven a number of other factors affect its concentration in various foods, including varying uptake into plants due to soil pH, rainfall, land contour, and microbial activity and importation of food from higher Se areas [22].

In our study, we found Se levels to increase with gestational age and birth weight. This is due to progressive accretion of Se in the last trimester. The results of our study correlate with the study [23] that reported that cord blood Se levels correlated significantly with birth weight and gestational age. Similar association was found earlier also [24,25]. Studies on Se concentration in VLBW preterm infants showed a correlation between selenium, GPx, and birth weight [26,27].

## CONCLUSION

In this pilot study of selenium levels in VLBW preterm neonates, the selenium levels in neonates with lower birth weight and lesser gestational age were significantly low. Therefore, suggesting that supplementation with selenium in VLBW neonates in our region may help in preventing morbidity and mortality; however, further research is advocated for deciding the appropriate dose of supplementation since our baseline levels are higher than those in many other parts of the world.

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