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Negative health indices indicated by neonatal hematology of cesarean section deliveries in rural India: A concern

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Abstract

Increase in Caesarean Section deliveries in rural India has been observed in last couple of years. The study was carried out to see effect of Vaginal Delivery (VD) and Caesarean Section (CS) delivery on haematology of neonates born in rural India. The newborns were categorized into two groups, Group I included those delivered by vaginal delivery and Group II by caesarean section. From each newborn venous cord blood was collected and used for hematological analysis. Newborn having abnormal haemoglobin were exclude from this study. It was found that neonates delivered by CS have an overall low blood cell counts and therefore, may be more prone to infections. Mean WBC, LYM, RBC, MCV, HCT, Hb, MPV, PDW, and Hb F was noticeably higher among the neonates delivered by vaginal delivery as compared to caesarean section deliveries. As the neonate from rural India are exposed to infections prevalent in rural regions, an overall reduction in blood cell counts in caesarean delivered neonates makes them more vulnerable to these infections. Therefore, un-necessary CS deliveries should be avoided specifically in the regions from rural India where mortality due to infections in high.

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Introduction

Mode of delivery is one of the causes of morbidity in infants (Cardoso *et al.*, 2010). It has been found that caesarean section is associated with higher morbidity and mortality (Kamath *et al.*, 2009). It increases the chance of infection to the mother and its transmission from mother to the neonate, under unhygienic conditions (Elrazek *et al.*, 2017). It has been also shown that babies delivered by elective cesarean section develop bronchial asthma, type 1 diabetes mellitus or allergic rhinitis in childhood (Bager *et al.*, 2008; Sevelsted *et al.*, 2016; Cardwell *et al.*, 2008; Lee *et al.* 2015; Thavagnanam *et al.*, 2008;). Apart from that, cesarean section delivery has excessive financial burden on rural households (Sahu and Bharti 2017).

Caesarean deliveries (CD) are on the increase worldwide (with nearly 50% of the world's CD is not indicated) and this trend varies from country to country and with socio-economic status (Betrán *et al.*, 2016; Khan *et al.*, 2017). In India, the rate of caesarean delivery has increased from 3 per cent to 10 per cent between 1992-93 and 2005-06 (IIPS, 2007). Compared to rural areas, caesarean section delivery is more likely to occur at urban areas. Increase in Caesarean Section deliveries in rural India from 4.7% to 7.4% (Kalahandi District hospital data) has been observed in the last five years.

The mode of delivery had been shown to influence white blood cells, haemoglobin, haematocrit, red blood cell distribution, platelets count and nucleated red blood cells (Glasser *et al.*, 2015; Redzko *et al.*, 2005). However, no study has been conducted on Indian rural population which varies in nutrition and hygiene condition from its urban population. It is documented that infants with acute respiratory infection has been seen more in rural area as compared to urban (Prajapati *et al.*, 2012). This is also because of high prevalence of malnutrition, illiteracy, overuse/misuse of antibiotics and poverty along with lack of awareness on hygiene (Goel *et al.*, 2012). Can mode of delivery itself be the cause of negative health indices in rural region of India? In-order to get first-hand information on this extent, variation in haematological parameters due to mode of delivery was studied.

As caesarean sections are becoming more popular in rural India due to increased medical facility and establishment of District hospitals, Primary Health Care and Community Health Care facilities, effect of mode of delivery on neonatal health in this population needs to be studied. Poor hygiene along with low blood counts may adversely affect immunity to infections.

Previous studies by our group reported a low lymphocytes and granulocytes counts in cord blood of neonates from Urban and rural region (Dixit *et al.*, 2016) which could be due to various reasons other than mode of delivery. The present study was undertaken to know difference between haematological profile of cord blood of neonates delivered by vaginal and caesarean section in the rural area of Odisha, Kalahandi district, where lymphocytes and granulocytes are low and infection rates are high.

Materials and methods

Ethics Statement

The study was approved by the institutional ethical committee. Informed written consent was taken from the parents of all the neonates.

Subject recruitment and sample collection

A total number of 427 healthy full term newborn (both male and female) were included in this prospective study. They were delivered in district hospital of Bhawanipatana, Kalahandi district from April 2013 to May 2013. These newborns were categorized into two groups, Group I included those delivered by vaginal delivery and Group II by caesarean section. From each newborn 5 ml of venous cord blood was collected under aseptic condition in EDTA vials. It was used for haematological analysis. Haemoglobin (Hb), Mean cell haemoglobin concentration (MCHC), Red blood cell count (RBC), Mean cell volume (MCV), Mean cell haemoglobin (MCH), Haematocrit (HCT), White blood cell (WBC), Lymphocytes (LYM), Monocytes (MON), Granulocytes (GRA), Red blood cell distribution width (RDW), Thrombocytes (THR), Mean platelet volume (MPV), Plateletcrit (PCT), Platelet

distribution width (PDW) were measured by using automated cell counter MS4 (Melet schloeing laboratories, Germany). Some of the cord blood samples (30 samples) were also examined using haemocytometer to test the accuracy of the automated cell counter. All the cord blood samples were analyzed for quantification of Hb type by using Hb Variant Classic (Bio Rad, USA), β -thal short program. Those found to be having any abnormal haemoglobin like HbS, HbD etc. were excluded from the study to avoid variation in overall haematological profiles due to such conditions.

Data collection

There was no noticeable difference of sex between Group I and Group II. The mean values, range and standard deviations of the mother's age, neonatal weight and haematological values were calculated.

Difference between haemoglobin values

All the cord blood samples were analysed for quantification of Hb type by using Hb variant classic (Bio Rad, USA), β -thal short program. Based on the time of elution (or retention time) normal haemoglobin was identified. Haematological percentages for HbA₀, HbF and HbA₂ were calculated. The mean values were compared between the groups for any significant difference.

Statistical analysis

Association and correlation between various Haematological parameters of two groups was carried out using SPSS version 17. Non-normally distributed variables were subjected to univariate Mann-Whitney analysis, and for normally distributed student's t-test were applied. Multivariate regression analysis was carried out for removing the effect of confounding factors like sex on association with haematological parameters between the two groups.

Results

A Total of 427 cord blood sample i.e., 283 no. of sample from group I and 144 samples from group II were analyzed. The result of cell counts taken by haemocytometer matched with the counts taken by automated cell counter in 73% cases. There was no significant difference in mean body weight between the two groups (Table 1). WBC, LYM, GRA, RBC, MCV, HCT, MCHC, HB, Hb A₂ and HbF were found to be significantly different between groups. However, MPV and RDW were not significant on adjusting for sex. Mean WBC, LYM, RBC, MCV, HCT, Hb, MPV, PDW, and HbF was noticeably higher among the neonates delivered by vaginal delivery as compared to caesarean section deliveries (Table 2). Whereas, mean HbA₂ was found to be higher in neonates delivered by caesarean section.

Table 1. Difference between types of haemoglobin of cord blood samples of newborn delivered by VD (Group I) and CS (Group II).

Type of Haemoglobin	Group I (n=283, Mean \pm S.D)	Group II (n=144, Mean \pm S.D)	P value	95% C.I.
HBA ₀ (%)	22.46 \pm 8.51	22.16 \pm 9.49	NS	
HBF (%)	73.04 \pm 9.73	70.04 \pm 10.75	0.002	0.95 - 0.99
HBA ₂ (%)	0.40 \pm 0.34	0.51 \pm 0.45	0.007	1.21 - 1.09

Table 2. Haematological differences between cord blood samples of newborn delivered by VD (Group I) and CS (Group II).

Haematological parameter	Group I	Group II	P value	95% C.I.
WBC(thousands/mm)	9.36 \pm 3.73	7.41 \pm 4.03	3.58x10 ⁻⁰⁶	0.81 - 0.92
LYM%	75.32 \pm 10.27	68.22 \pm 12.67	1.30x10 ⁻⁰⁸	0.93 - 0.96
MON%	2.47 \pm 1.23	2.83 \pm 1.63	NS	
GRA%	22.18 \pm 9.56	28.62 \pm 10.89	7.34x10 ⁻⁰⁹	1.04 - 1.09
RBC (million/ mm)	4.69 \pm 0.67	4.31 \pm 1.05	2.5x10 ⁻⁰⁵	0.41 - 0.72
MCV (fl)	98.54 \pm 8.54	93.49 \pm 8.21	6.03x10 ⁻⁰⁸	0.91 - 0.96
HCT (%)	46.02 \pm 6.13	40.11 \pm 9.22	1.73x10 ⁻¹¹	0.85 - 0.92
MCH (pg)	29.37 \pm 4.13	29.77 \pm 5.61	NS	
MCHC (g/dl)	29.80 \pm 2.79	31.86 \pm 5.30	1.70x10 ⁻⁰⁶	1.10 - 1.24
RDW	11.70 \pm 2.66	12.19 \pm 2.58	NS	

Haematological parameter	Group I	Group II	P value	95% C.I.
HB (g/dl)	13.69±1.89	12.59±2.67	4.39x10 ⁻⁰⁶	0.72 – 0.88
THR (million/ mm ³)	262.86±274.42	292.21±397.61	NS	
MPV (fl)	8.55±0.65	8.47±0.67	NS	
PCT%	0.21±0.18	0.22±0.23	NS	
PDW	9.23±2.36	8.97±3.08	NS	

P-values stand multiple correction.

Discussion

With the increasing incidence of elective pre labour caesarean section, it is important to understand the effects of mode of delivery on normal development of the neonate. This study was carried out to estimate the difference in health implications as indicated by haematological parameters of CS deliveries and VD in rural region of India. CS deliveries are becoming more common in urban as well as rural regions of India and in most of the second CS deliveries irrespective of region. As Cord blood haematology is a good source of health summary of an individual over the perinatal period and beyond, we compared the cord blood haematology in VD and CS deliveries among neonates from a rural region of Odisha, India. A significant higher mean leucocyte counts (WBC) in VD neonates has been reported which is speculated to be the consequences of physical stress and periodic hypoxia, which are more frequent and prolonged with VD compared with CS delivery (Almanzar *et al.*, 2015; Hasan *et al.*, 1993). In concurrence in the present study too we observed a statistically significant increase in WBC and LYM counts in VD cases than in CS. RBC, MCV, HCT and Hb, HbF were also found to be significantly high in VD than in CS like in many other studies (Glasser *et al.*, 2015; Redzko *et al.*, 2005). Along with mode of delivery gestational age and sex is also one of the major factor effecting cord blood parameter (Glasser *et al.*, 2015; Alur *et al.*, 2005). Therefore, the preterm neonates were not included in our study and the regression analysis was adjusted for sex.

Underdeveloped immune mechanisms, due to insufficient haematopoiesis, in a neonate may lead to infections in perinatal stage. It has been reported that labour in VD may up-regulate the two innate immune system markers TLR2 and TLR4 on the cord blood monocytes of newborns (Shen *et al.*, 2009) which is essential for prevention of infection in neonates.

In addition, recent reports also suggest effect of mode of delivery on the epigenetic state of neonatal hematopoietic stem cells. White blood cells from infants delivered by CS were reported to be globally more DNA methylated than DNA from infants delivered vaginally (Schlinzig *et al.*, 2009). This suggests an under-expression of neonatal immune system in CS deliveries which might result in a poor tolerization to the antigens and allergens to which a neonate is exposed after birth. From our study it is suggested that there is an overall up regulation of haematopoietic pathways including HbF levels in VD neonates than in CS, which could be due to exposure to hypoxic stress to foetus during VD. Therefore, in case of CS the neonatal immune system may not be functional enough to tackle some of the environmental infections. On the other hand vaginally delivered neonates, due to higher levels of HbF may be better oxygenated.

As CS are becoming more common in rural India due to improvement in medical facility it is important to know the effect of CS on neonatal and perinatal infections in babies born in rural India. It is well known that neonatal mortality rate due to infection is very high in India when compared to developed countries and is skewed towards rural regions of India (Upadhyay *et al.*, 2012).

Our study shows under representation of most of the white blood as well as red blood parameters in CS deliveries as also seen in many earlier studies; this may make the neonate more vulnerable to infections prevalent in rural regions due to malnutrition, illiteracy and un-hygienic conditions and practices. Therefore, we must take care of unnecessary CS deliveries especially in rural region of India. The study recommends that prevention of un-necessary

CS deliveries may reduce morbidity/mortality due to infection in the neonates of rural India. As also recommended by WHO (Lumbiganon *et al.*, 2010), in order to improve perinatal health outcomes, caesarean section should be done only when there is a medical indication.

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