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Is ferritin estimation and optimisation important in cerebral palsy children undergoing single event multilevel surgery?☆

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1. Introduction

Cerebral palsy is defined as a syndrome characterised by a non-progressive insult to the developing central nervous system.[1] As a result, the gross motor function will get compromised, and musculoskeletal deformities are common in cerebral palsy children. The prevalence of cerebral palsy is static or increasing in most parts of the world.[2] Maintaining adequate nutrition in these children is difficult due to several reasons including poor appetite, inadequate intake, feeding difficulty, anti-epileptic medication as well as socioeconomic factors.[3]

Iron deficiency anaemia is commonly due to gastrointestinal or genitourinary blood loss.[4] Poor iron intake is extremely rare in the paediatric age group except for children with severe hookworm infection or low intake in the vegetarian population. It is reported that poor iron intake is possible in cerebral palsy children due to feeding difficulty and it may lead to iron deficiency anaemia in these children.[5]

In children with spastic CP, orthopaedic surgery has an important role to play, for example, the correction of hip migration, pelvic osteotomy, joint contractures, abnormal bony torsion or muscle shortening.[6] Recently there is an increasing trend to perform single event multilevel surgeries. As a result, there can be an increased risk of blood loss leading to postoperative anaemia. Although acute anaemia may not necessarily lead to overt organ dysfunction, it may lead to reduced exercise capacity, fatigue, dizziness, disorientation, indigestion and loss of appetite.[7,8] Symptomatic anaemia can result in delayed postoperative recovery, longer hospital stays and increased morbidity and mortality[9,10].[11]

It is proven that cerebral palsy children with high GMFCS score have a higher risk of iron and other nutrient deficiency.[12] Intraoperative blood loss in an iron-deficient child may require a blood transfusion. Transfusion guidelines recommend children should not be transfused unless their Hb decreases below 70 g/l.[13] Bearing in mind the risks of transfusion like infection, immunosuppression and alloimmunisation, it is reserved only for life-threatening anaemia.[14] It would make sense to estimate and optimise the iron stores level well in advance of the operation.[15] The literature suggests Ferritin has a positive correlation with haemoglobin,[16] but no study ever assessed their relationship in the cerebral palsy children. Additionally, the literature reports low ferritin in neurologically impaired children.[17] Consequently, our study aimed to assess the importance of ferritin estimation along with haemoglobin in cerebral palsy children undergoing single-event multilevel surgery and to study the correlation between them in these children.

2. Patients and methods

Our study is a retrospective case series of 35 consecutive patients who underwent single-event multilevel surgery at our tertiary paedia-

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tric orthopaedic hospital between January 2011 and July 2013. Age group of these patients were in between 2 and 16. These children were classified according to the Gross Motor Function Classification System (GMFCS) at the time of their first presentation to our unit.[18] As the GMFCS score increases, it corresponds to severity of the disease and hence attracts multilevel surgeries causing the risk of intraoperative blood loss.[18,19] We included all cerebral palsy children who underwent single-event multilevel surgery and excluded those with obvious reasons of iron deficiency like genitourinary and gastrointestinal blood loss and gastrointestinal infections or inflammations.

We identified that the study group children underwent an estimation of ferritin and haemoglobin levels as part of their pre-operative assessment, approximately six weeks before the planned surgery. Thousand patients who were investigated for nonsurgical reasons with haemoglobin and ferritin estimation where used as the control. The children in the control group did not have cerebral palsy or related neurological conditions. The control group was used to compare the average haemoglobin and ferritin values of the two groups. The Spearman correlation coefficient is used to test the correlation between the ferritin and haemoglobin values in the cerebral palsy group because of the small sample size. A scatter plot diagram is drawn to see if any pattern exists between haemoglobin and Ferritin among the cerebral palsy children.

3. Results

The age and sex distribution and GMFCS levels are summarised in Table 1. The average age of the study group was 13, and the majority were females. 32 out of the 35 patients belong to GMFCS 4 or 5 indicating the severity of the deformities and hence complexity of the surgery and intraoperative blood loss.

Table 2 shows the average haemoglobin and ferritin levels in the study and control group. The range of normal ferritin and Hb in our hospital laboratory is 29–371 ng per ml and 13–17 g per decilitre respectively. This table reveals that, the average Ferritin value was much lower than the required range in the cerebral palsy group compared to the control. The average haemoglobin level was in the low normal range.

The histograms (Figs. 1 and 2 respectively) shows the distribution of haemoglobin and ferritin in the cerebral palsy group. Both of them are not normally distributed.

Normal ferritin levels were present only in 4 out of the 35 (11%) children in the study group whereas the Hb levels were normal in 22 out of the 35 (63%) subjects. In the control group, 818 children (81.8%) had normal serum ferritin.

The Pie diagram (Fig. 3) illustrates the relationship of Ferritin and haemoglobin values in the study group. 31 out of the 35 cerebral palsy children had low ferritin. However, 19 children of the low ferritin group had normal haemoglobin.

The Spearman correlation analysis between the haemoglobin and ferritin levels in the cerebral palsy group demonstrated a correlation coefficient of 0.128, which indicate a poor correlation between them in

Table 1
Demographic data of the patients.

Variable	Cerebral Palsy Group	Control group
Mean age	13	14
Gender		
Male	16	446
Female	19	554
GMFCS level[a] (no of patients)		
3	03	
4	14	
5	18	

[a] GMFCS = Gross motor function classification system.

Table 2
Results of ferritin and haemoglobin levels in the cerebral palsy group and the control group.

	Cerebral palsy group [n-35]	Control group [n-1000]
Mean Haemoglobin[a]	13.28	15
Mean Ferritin[b]	19.41	160.3

[a] Normal range 13–17 gm/dl.
[b] Normal range 29–371 ngm/ml.

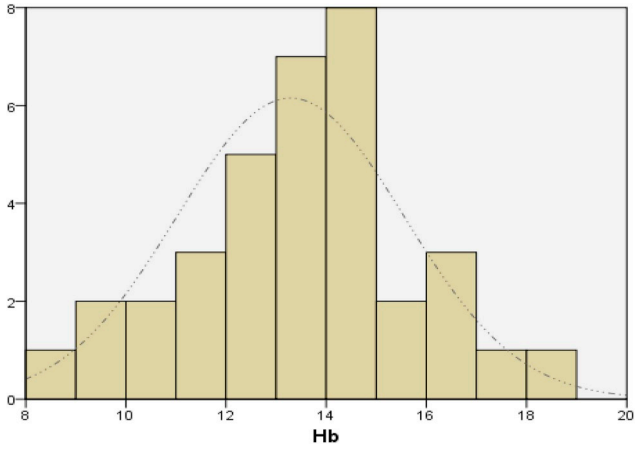

Fig. 1. Showing the distribution of haemoglobin levels in the cerebral palsy group.

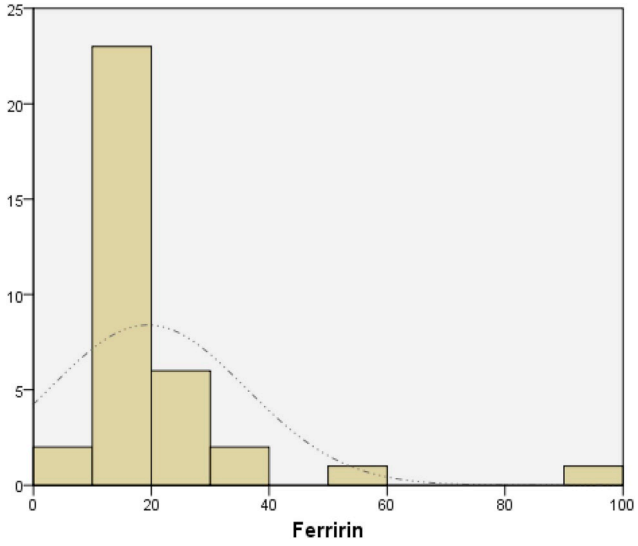

Fig. 2. Showing the distribution of ferritin levels in the cerebral palsy group.

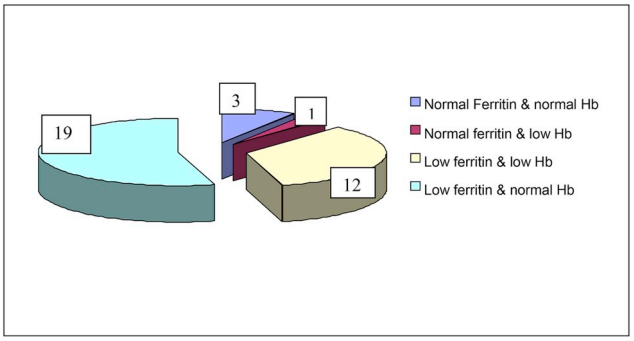

Fig. 3. Comparative analysis of ferritin and hemoglobin in the study group.

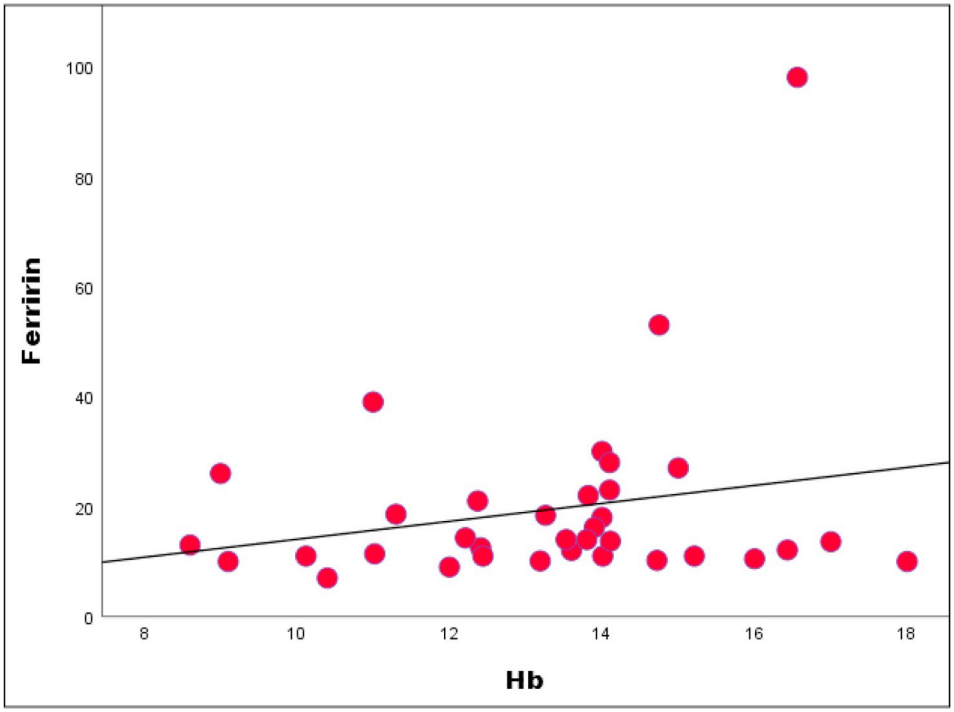

Fig. 4. Scatterplot diagram showing the relation between haemoglobin and ferritin in the cerebral palsy group.

the cerebral palsy children.

The scatterplot diagram [Fig. 4] plotting the haemoglobin and ferritin shows an insignificant linear association between them in the study group. Both correlation analysis and the scatterplot diagram demonstrate a poor association between haemoglobin and ferritin in cerebral palsy children.

4. Discussion

Biochemical deficiency of several micronutrients are well documented in children with neurological impairment.[3,12,20] Deficient intake of iron and other minerals have been reported in this group. The diet of children with neurological disability is quantitatively and qualitatively deficient for several reasons. Nutritional causes of iron deficiency include poor appetite, inadequate intake, feeding difficulty and gastrointestinal dysfunctions like a motor abnormality, gastroesophageal reflux and constipation. Non-nutritional factors include the severity of cerebral palsy affecting ambulation and cognitive function as well as antiepileptic medication.[17] This may be compounded by socioeconomic factors.[3]

Inadequate iron stores can cause high morbidity and mortality, growth retardation, poor school performance, cognitive and motor dysfunction.[21] Literature states poor iron supplementation is an important cause for the deficient iron stores and iron deficiency anaemia in children.[21] Ferritin is the suitable marker of iron stores, and haemoglobin is the established marker for anaemia.[22] Most of the hospitals measure haemoglobin as the marker of anaemia assuming adequate iron stores. However, Cerebral palsy is one of the diseases where we must consider measuring the iron stores as well. Penagini et al., in 2015 suggested ferritin estimation along with full blood count in neurologically impaired children[17] however, they did not assess the correlation of ferritin and haemoglobin in these children. To our knowledge, this could be the first study in English literature which demonstrated the importance of ferritin estimation and optimisation specifically in cerebral palsy children.

In our study, 89% of children with CP were found to have low ferritin levels preoperatively compared to 18.2% in the control group. It confirms the risk for low iron stores in cerebral palsy children. Papadopoulos et al., in 2008 reported 33% cerebral palsy children with hypochromic microcytic anaemia of which 38% were iron deficient.[5] They suggested poor iron intake due to difficult feeding as the main reason in these children. They ruled out common causes of iron deficiency like genitourinary and gastrointestinal blood loss. This study also demonstrated that the type of diet also affects the iron stores. They found 95.6% of the children on liquid diet were deficient in iron stores compared to 22.3% on the normal diet. However, this study didn't measure the correlation between the haemoglobin and ferritin in the cerebral palsy children.[5] As in this study, we also ruled out the common causes of iron deficiency like gastrointestinal or other sources of blood loss and recurrent gastrointestinal infections or inflammations.[23] Hence, we believe nutritional deficiency could be the major reason of ferritin deficiency in our study group.

There are a few published articles which assessed the correlation between Ferritin and Haemoglobin. Franchini et al., in 2007 conducted a study comparing the haemochromatosis and normal patients. They demonstrated a positive correlation between ferritin and haemoglobin[16] levels. They divided the study subjects into two groups: 523 subjects with normal serum ferritin levels and 66 patients with high serum ferritin levels (haemochromatosis). The average age of the two groups were 36.3 and 51.6 respectively, and the respective average ferritin levels were 103.8 and 658.4 μg/L. Hence, they came up with the interesting finding that the ferritin levels are age dependent and are regardless of the underlying cause. On the contrary, our study showed 61.3% of the cerebral palsy patients with low ferritin, had normal haemoglobin levels at a 6-week preoperative check-up. The correlation analysis and the scatter plot diagram confirmed the poor correlation between ferritin and haemoglobin in the cerebral palsy children as well. Hence relying on haemoglobin only, will not be a good approach in such patients. The positive correlation between haemoglobin and ferritin in the study of Franchini et al. agrees with children and adults without neurological impairment. However, there were no studies conducted to prove this correlation in cerebral palsy children. Our study showed a poor correlation between ferritin and haemoglobin in cerebral palsy children. However, this is a retrospective study with a

small number of patients. Hence, further prospective trials with more number of patients will be beneficial to assess the factors contributing to ferritin deficiency in cerebral palsy children and its poor correlation with haemoglobin levels in them.

It is recognised that the inflammatory effect of surgery alters iron metabolism and decreases the efficiency of oral iron in the post-operative period.[10] Studies have shown commencement of iron either orally, or intravenous in the postoperative period will not benefit the immediate postoperative correction of anaemia.[24] Evidence says supplementation with oral iron for patients with deficient iron stores must be initiated well in advance of any planned surgery to optimise ferritin.[24]

5. Conclusion

We conclude that preoperative haemoglobin estimation alone is not enough in cerebral palsy patients who require single-event multilevel surgery especially those with high GMFCS score. This study showed that these patients had low ferritin reserves and many of these patients with low ferritin reserves can have normal haemoglobin. Hence, we recommend ferritin estimation along with haemoglobin in the pre-operative assessment, which will help to optimise the level of ferritin with iron treatment well in advance of the operation thereby reducing the risk of postoperative anaemia. Accordingly, we made changes in our practice, and we are looking forward to publishing the outcome of the ferritin optimisation with iron treatment as a follow-up study.

Conflicts of interest

No conflicts of interest.

Author Contributions

First name, Family name	Concept	Academic Writing	Literature search	Statistics	Editing
Rahul Mohan		Yes	Yes	Yes	Yes
PN Unnikrishnan	Yes		Yes		Yes
Harvey George	Yes		Yes		
Alfie Bass	Yes		Yes		
Satish Vinayaka Rao Dhotare				Yes	Yes
Jayanth S Sampath	Yes		Yes		

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