ORIGINAL RESEARCH

Association between Serum Iron, Serum Ferritin Levels, and Severe Early Childhood Caries: A Case–Control Study

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Abstract

Aim: The presence of extensive dental caries leads to pain, inflammation, and discomfort and hence interferes with their nutritional intake, which includes iron deficiency anemia. This study was undertaken to determine whether any correlation exists between severe early childhood caries (S-ECC), serum iron, and serum ferritin levels in children.

Materials and methods: A total of 688 children were examined in the age-group of 2–6 years, and 82 children who fulfilled the selection criteria were equally divided into group I, that is, case group (carious group $n = 41$) and group II, that is, control group (caries-free group $n = 41$), on the basis of decayed, missing, and filled primary teeth (dmft) scores. All the selected children in both groups underwent blood investigations through phlebotomy for assessment of serum iron and serum ferritin levels.

Results: The mean values of variables, that is, hemoglobin (Hb), serum iron, serum ferritin, total iron-binding capacity (TIBC), and unsaturated iron-binding capacity (UIBC), are lower in the case group when compared to control group. The differences observed were statistically significant in case of dmft and UIBC values at $p < 0.05$ but not significant in cases of other variables like Hb, serum iron, serum ferritin, and TIBC values.

Conclusion: An inverse relationship was found between S-ECC, serum iron, and serum ferritin levels, but the evidence is still inconclusive.

Keywords: Serum ferritin, Serum iron, Severe early childhood caries.

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Introduction

Dental caries may be defined as an infectious disease with a variety of causative factors. It is caused by the combined effect of plaque and bacteria, as a consequence of their metabolism, of fermentable carbohydrates, which diffuses inside the dental hard tissues and break down their mineral contents.[1] Severe early childhood caries (S-ECC) etiology differs according to the country's level of development. Poverty is a condition that is associated with S-ECC.[2] The mechanisms involved can be associated with differences that were found to be related to the social, family, and socioeconomic factors that influence the well-defined disposition of practices.[3–7] Breastfeeding at will with frequent or prolonged day or night use of baby bottles which contain fermentable liquids,[8–11] continuous use a sweetened pacifiers,[12,13] and diet[14] are one of the most common habits that can have an influence on this kind of pathologies to arise.

Severe early childhood caries (S-ECC) may give rise to symptoms that might originate due to aversion from eating as a result of toothache that may occur[15,16] or high sucrose level intake that can lead to compromised intake of all other kinds of nutrients.[15–17] Additionally, components causing inflammation and cytokines that are released from injured tissues during the course of pulpal inflammation as well as chronic ailments such as dental abscess are known to subdue the activity of erythropoiesis and formation of hemoglobin (Hb). Similar inflammatory mediators have been identified in cases with S-ECC, which may be possible risk factors for anemia related to iron deficiency.[15]

The presence of widespread dental caries may lead to problems in mastication, which in turn may have a negative impact on the absorption of nutrients in the digestive tract. Extensive untreated caries result in cavitation and pitting, causing pain, inflammation as well as discomfort, leading to poor mastication of food. This interferes with their nutritional intake, which leads to iron deficiency anemia.[18]

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Iron deficiency constitutes almost 90% of all different types of anemia and is most common type in children between the ages of 2 and 6 years.[19] Serum ferritin is an intracellular protein that accumulates and reserves iron and releases it slowly in increments. Serum ferritin levels indicate the level of stored iron in the body and are influenced by the process of inflammation.[18] Normal levels of serum ferritin do not necessarily exclude iron deficiency anemia, which may still be present.[20]

In the findings by Sadeghi et al.,[18] early childhood caries is described as a severe form of dental caries with an inverse association with serum iron levels. According to Koppal et al.,[21] both ECC and iron deficiency are multifactorial, but direct relation between the two could not be drawn; however, ECC and iron deficiency anemia are definitely related to it. To our foremost knowledge, there are hardly any studies[15,18,19,21] existing in the literature correlating the relationship between S-ECC, serum iron, and serum ferritin levels, with inconclusive evidence. Hence, this study was undertaken to determine whether any correlation exists between S-ECC, serum iron, and serum ferritin levels in children.

Materials and Methods

The study protocol was approved through the Institutional Ethics Committee before the start of this study. Parents or legally responsible persons of selected subjects received detailed information about the study protocol, investigations being carried out, and the purpose of these diagnostic tests. They were made to sign an informed consent form permitting the participation of their children. The subjects were selected from those visiting the Department of Pediatric and Preventive Dentistry and those admitted under the Department of Pediatrics for medical ailments at the affiliated medical hospital.

Out of a total of 688 children examined in the age group of 2–6 years, 82 children fulfilling the selection criteria were equally divided into group I—case group, that is, the carious group (those suffering from S-ECC) (n = 41) and group II—control group, that is, the caries-free group (n = 41). All the selected children were reviewed by a pediatrician to rule out underlying diseases and conditions affecting the serum iron and ferritin levels.

- Inclusion criteria for case group: (1) Children between 24 and 71 months of age classified under S-ECC category with minimum of five carious teeth requiring dental management under general anesthesia due to significant behavioral problems; (2) children between 24 and 71 months of age classified under S-ECC category with minimum five carious teeth admitted in the Department of Pediatrics requiring blood investigations.
- Inclusion criteria for control group: (1) Caries-free children between 24 and 71 months, admitted to the Department of Pediatrics requiring blood investigations; (2) caries-free children between 24 and 71 months, visiting the Department of Pedodontics and Preventive Dentistry for reasons other than dental caries and requiring blood investigations.

Uncooperative parents, mentally retarded children, known patients of iron deficiency, and disorders related to Hb, serum iron, and ferritin were not included in the study. A trained and appraised examiner (YA) examined the oral cavity and evaluated dental caries experience using decayed exfoliated filled teeth (deft) index for primary teeth as given by Gruebbel[22] in 1944. Dental examination of the subjects was performed under adequate lighting using mirror and explorer. Sterile cotton was used during the procedure so as to clean the tooth during examination.

All the selected children in both groups underwent blood investigations through phlebotomy by a trained nurse early in the morning. The patients were taken to the sample collection room where 2 mL of blood was withdrawn for the estimation of serum iron and was then stored in a sterile test tube. Then another 2 mL was withdrawn for the estimation of serum ferritin and Hb, collected in two different test tubes, and put on the test tube rotator. All samples of blood were immediately sent to the Department of Hematology and Biochemistry for estimation of Hb, ferritin, serum iron levels, total iron-binding capacity (TIBC), and unsaturated iron binding capacity (UIBC). For the comparison of the values of Hb, TIBC, and UIBC between case and control groups, independent t-test was used. Mann–Whitney U test was done to compare the serum iron and ferritin values between the two groups. To evaluate the association between S-ECC, serum iron and serum ferritin levels, Spearman's correlation was used. The significance level was predetermined at $p \leq 0.05$ for all the statistical tests performed in this study.

Results

The mean age of the children included in this study was observed to be group I was observed to be 3.69 ± 1.31 years and 3.48 ± 1.48 years for group II. A total of 24 males and 17 females were included in groups I and II, respectively. Table 1 represents mean values of variables, that is, decayed, missing, and filled primary teeth (dmft), Hb, serum iron, serum ferritin, TIBC, and UIBC scores for case and control groups. These values are lower in the case group and higher in the control group. Table 2 represents the mean differences, standard error, and 95% confidence interval of factors in case and control groups. The differences observed between the case and control groups were statistically significant in case of dmft and UIBC values $p < 0.05$ but statistically not significant in cases of other variables like Hb, serum iron, serum ferritin, and TIBC $p > 0.05$. Table 3 represents intergroup comparison of mean ranks of dmft, Hb, serum iron, TIBC, and UIBC between case and control groups. It is evident from the table that the average rank of dmft, serum iron, and serum ferritin is higher in case group compared to the control group. Table 4 represents the Spearman's rank correlation between dmft, serum iron, TIBC, UIBC, and serum ferritin in case group. This signifies that there is weak positive correlation of Hb with TIBC, UIBC,

Table 1: Mean values of variables, that is, dmft, Hb, serum iron, serum ferritin, TIBC, and UIBC for case and control group

	Group	*N*	*Mean*	*Standard deviation*	*Standard error mean*
Dmft	Case	41	8.17	3.29	0.51
	Control	41	0.00	0.00	0.00
Hb (gm/dL)	Case	41	8.99	2.38	0.37
	Control	41	9.34	2.56	0.40
Serum iron (µg/dL)	Case	41	75.77	27.97	4.37
	Control	41	77.90	66.10	10.32
TIBC (µg/dL)	Case	41	312.83	40.49	6.32
	Control	41	312.70	43.15	6.74
UIBC (µg/dL)	Case	41	215.03	32.78	5.12
	Control	41	232.77	43.65	6.82
Serum ferritin (ng/mL)	Case	41	87.10	184.74	28.85
	Control	41	92.99	214.63	33.52

Table 2: Mean differences, standard error, and 95% confidence interval of variables in case and control groups

	t-value	*Degrees of freedom*	*p-value*	*Mean difference*	*Standard error difference*	*95% confidence interval of the difference*	
						Lower	*Upper*
Dmft	15.88	80	0.00	8.17	0.51	7.14	
Hb (gm/dL)	–0.63	80	0.53	–0.34	0.54	–1.43	0.73
Serum iron (µg/dL)	–0.18	80	0.85	–2.12	11.20	–24.43	20.18
TIBC (µg/dL)	0.01	80	0.99	0.13	9.24	–18.25	
UIBC (µg/dL)	–2.08	80	0.04	–17.73	8.52	–34.70	–0.77
Serum ferritin (ng/mL)	–0.13	80	0.89	–5.88	44.22	–93.90	82.12

Table 3: Intergroup comparison of mean ranks of dmft, Hb, serum iron, TIBC, and UIBC between case and control groups (result of Mann–Whitney *U* test)

	Group	*N*	*Mean rank*	*Sum of ranks*
dmft	Case	41	61.50	2521.50
	Control	41	21.50	881.50
Serum iron (µg/dL)	Case	41	45.26	1855.50
	Control	41	37.74	1547.50
Serum ferritin (ng/mL)	Case	41	44.18	1811.50
	Control	41	38.82	1591.50
		dmft	Serum iron	Serum ferritin
Mann–Whitney *U*		20.500	686.50	730.50
Wilcoxon W		881.500	1547.50	1591.50
z-value		–8.202	–1.42	–1.02
p-value		<0.001	0.15	0.30

Table 4: Spearman's rank correlation between dmft, serum iron, TIBC, UIBC, and serum ferritin in case group

		Hb	*Serum iron*	*TIBC*	*UIBC*	*Serum ferritin*
Dmft	Correlation coefficient	–0.11	–0.07	–0.07	–0.20	0.10
	p-value	0.48	0.63	0.63	0.19	0.49
	N	41	41	41	41	41
Hb (gm/dL)	Correlation coefficient		–0.11	0.08	0.19	0.07
	p-value		0.47	0.62	0.23	0.62
	N		41	41	41	41
Serum iron (µg/dL)	Correlation coefficient			0.35	–0.24	0.40
	p-value			0.02	0.11	0.009
	N			41	41	41
TIBC (µg/dL)	Correlation coefficient				0.54	0.29
	p-value				0.00	0.7
	N				41	41
UIBC (µg/dL)	Correlation coefficient					–0.21
	p-value					0.2
	N					41

serum iron, and serum ferritin in the case group. Table 5 represents the Spearman's rank's correlation between TIBC, UIBC, serum iron, and serum ferritin in control group. This table signifies that in control group, there is a weak positive correlation of Hb with serum iron, TIBC, UIBC, and serum ferritin. Serum iron has weak positive relation with TIBC and serum ferritin but weak negative relation with UIBC. Hence, TIBC and UIBC are weakly positively related.

Discussion

Despite a dramatic fall in prevalence of S-ECC in children of the Western world, it is commonly seen in preschool children in both developed and developing countries that are unevenly distributed throughout the population.[23] It is usually observed that children with symptomatic dental caries, especially in primary dentition,

Table 5: Spearman's rank correlation between serum iron, TIBC, UIBC, and serum ferritin in control group

		Serum iron	*TIBC*	*UIBC*	*Serum ferritin*
Hb (gm/dL)	Correlation coefficient	–0.30	–0.33	–0.213	–0.18
	p-value	0.05	0.05	0.18	0.26
	N	41	41	41	41
Serum iron (µg/dL)	Correlation coefficient		–0.248	–0.27	0.16
	p-value		0.118	0.089	0.31
	N		41	41	41
TIBC (µg/dL)	Correlation coefficient			0.37	–0.05
	p-value			0.016	0.77
	N			41	41
UIBC (µg/dL)	Correlation coefficient				0.01
	p-value				0.95
	N				41

prefer soft, sticky, and refined carbohydrate-rich diet. This unusual liking may be due to various reasons. Firstly, it may lead to reduced functional ability to chew, which may reduce the intake of balanced diet and thereby influence the nutritional status. Nutritional imbalance develops as a result of S-ECC and may also affect the general status of health besides dentition.

The probability of increased rate of production of glucocorticoids in reaction to pain, decreased production and secretion of growth hormone in response to disturbed sleep pattern, and an overall increased metabolic rate through the infectious stage may also collude to delay or slow down growth, development in patients suffering from S-ECC.

Iron deficiency anemia is the most common type of deficiency in the group of malnourished children. This deficiency can occur due to various factors, including congenital factors, dietary factors, environmental factors,[24,25] as well as any of the inflammatory processes. Children suffering from S-ECC mostly drink cow's milk, which decreases absorption of iron.[26,27] Bowen[28] studied biological mechanisms of early ECC and mentioned the effects arising due to dietary metals on ECC. Many of the children who had extensive carious lesions were found to be undernourished. This effect was found to be independent of any of the topical effects of iron that could be preventive on caries. An appropriate assessment of body's iron stores is a significant factor for the purpose of diagnosis and treatment planning in order to eradicate and remove the potential risk factor for S-ECC. Most of the techniques being utilized for the assessment of levels of iron include serum iron concentration, serum ferritin as well as levels of TIBC. Serum ferritin is a protein of acute phase, and its levels in the blood indicate iron storage levels in the body, but it is suggested to be less sensitive as its quantity in the blood is found to rise due to infection or any type of chronic inflammatory condition that might be present in a child. These conditions can alter low levels of ferritin due to inadequate iron into a value that lies within the range which is considered normal. In a recent study, an inverse relationship was found between S-ECC, levels of serum iron, and ferritin, but the evidence was inconclusive. Similar results by Sadeghi et al.[18] have been presented. The authors observed that there was no association of deft index with levels of serum ferritin, but a strong inverse association was recorded with serum iron.

Contrary to our findings, Koppal et al.[21] observed that children with S-ECC had significantly lower levels of serum ferritin in comparison to children with no caries. They observed that children with unacceptably low levels of Hb also had lower levels of serum ferritin, which could be explained by the fact that the body depletes the stored iron in order to maintain appropriate levels of Hb. Supporting their findings, Schroth et al.[29] concluded that though there was no significant difference among children with S-ECC and those without caries but, in respect to the average concentration of iron, a significant difference was found in number of children having lower levels of ferritin.

In the present study, the mean Hb levels were found to be 8.99 ± 2.38 gm/dL for S-ECC group and 9.34 ± 2.56 gm/dL for caries-free group, but the difference was statistically nonsignificant. The observations of the present experiment were similar to Bansal et al.,[30] who observed lower levels of mean Hb when compared to controls, but contrary to our results, this difference was statistically significant. They reported that 25% of the entire study sample had iron deficiency anemia, and out of these, 86.7% were from the S-ECC group. The present study was also supported by Clarke et al.,[15] who noted that there was significant proportion of children with low levels of Hb. Despite all the limitations that were present, the clinical implication of the experiment was that S-ECC has been recognized as a risk identifier for iron deficiency and anemia. As established by the present study, it can be deduced that an inverse relationship has been found between S-ECC, serum iron, and ferritin levels. Treating such patients with complete mouth rehabilitation along with diet counseling may improve the masticatory efficiency of the child, thereby reversing any nutritional deficiency present due to S-ECC.

Conclusion

The conclusions drawn from this study are the following:

- The mean values of serum iron and serum ferritin in S-ECC group were lower when compared to caries-free group, but the differences were statistically nonsignificant.
- There is an inverse relationship between S-ECC, serum iron, and serum ferritin levels, but the evidence was inconclusive.
- This study identifies S-ECC as a potential risk marker for anemia, but further studies with larger sample sizes are required to strengthen the interrelation between S-ECC and levels of serum iron and serum ferritin.

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