ORIGINAL RESEARCH PAPER

Medical Biochemistry

THE ROLE OF SERUM FERRITIN IN ANAEMIA – A KEY DIAGNOSTIC MARKER OF IRON DEFICIENCY

KEY WORDS: Anemia, Ferritin, Immunoassay.

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ABSTRACT

Background and Objectives: Anaemia is a serious global public health problem. It is among the top leading causes of disability-adjusted life years lost among adolescents. The WHO has recognized Iron deficiency anemia as the most common nutritional deficiency in the world with 30% of the population being affected. Anemia has significant implications in terms of mortality as well as impaired work capacity and economic development. Serum ferritin plays a major role in diagnosis as well as management of anemia. **Objectives:** 1. To study and interpret the iron parameters in patients of anemia of Iron deficiency and anemia of chronic diseases. 2.To evaluate the role of serum ferritin over serum iron in early detection of iron deficiency. **Material and Methods:** A cross-sectional study was undertaken during February 2017 to August 2018. A total of 65 patients of anemia were included in the present study comprising 31 cases of Iron deficiency anemia and 34 cases of anemia of Chronic diseases. Serum ferritin was analyzed by chemiluminescent microparticle immunoassay technique in Abbott instrument. All other biochemical measurements were performed as per standard procedures. SPSS version 2.0 was used, Descriptive and inferential statistical analysis was done. **Results:** There was a high prevalence of anemia among the age group 21 to 40, that is 38.7%. In Iron deficiency anemia median and interquartile range values of serum Iron and serum ferritin were 45 and 51.0, 13 and 13.80 respectively. Spearman's correlation with serum ferritin was found to be significant in patients of iron deficiency anemia. The r value being 0.537 and the p value 0.002. Spearman's correlation of serum ferritin with serum iron was found to be more significant in females. **Conclusion:** Serum ferritin can be used as an early marker in diagnosis of Iron deficiency anemia as well as in screening risk population, thus preventing associated morbidity and mortality.

INTRODUCTION:

Anaemia is a serious global public health problem. Anaemia is defined as hemoglobin concentration below a specified cutoff point that depends on age, gender, physiological status, smoking habits and altitude. The WHO defines anaemia as blood Hemoglobin level below 130 g/L(13g/dL) in men, <120 g/L(12g/dL) in women, <110 g/L(11g/dL) in children aged under 5 years and pregnant women at sea level.[1]

Iron deficiency and anemia of chronic diseases are the most common causes of anemia worldwide. WHO estimates that 40% of children 6 to 59 months of age, 37% of pregnant women and 30% of women 15 to 49 years of age worldwide are anemic. [1,2] The WHO has recognized Iron deficiency anemia as the most common nutritional deficiency in the world with 30% of the population being affected.[1]

Anaemia is among the top leading causes of disability-adjusted life years lost among adolescents.[3]

Prevalence of anemia among pregnant and non-pregnant women are included as primary outcome indicators in the core set of indicators for the global nutrition monitoring framework. These indicators are used to monitor progress towards achieving global nutrition target 2 which is a 50% reduction in anemia among women of reproductive age by 2025.[4]

- In absence of inflammation, serum ferritin is representative of body iron stores and serves as a sensitive and specific biochemical marker for iron deficiency even in early stages.[5]
- Anemia has significant implications in terms of mortality as well as impaired work capacity and economic development.[6] Serum ferritin plays a major role in diagnosis as well as management of anemia.

OBJECTIVES:

- To study and interpret the iron parameters in patients of anemia of Iron deficiency and anemia of chronic diseases.
- To evaluate the role of serum ferritin over serum iron in early detection of iron deficiency.

MATERIAL AND METHODS:

- A cross-sectional study was undertaken during February 2017 to August 2018. The study was approved by the ethical committee of the institute and an informed consent was obtained from all the patients who took part in the study.
- A total of 65 patients of anemia were included in the present study, comprising 31 cases of Iron deficiency anemia (IDA) and 34 cases of anemia of Chronic diseases (CD).
- Diagnosis of anemia was made based on clinical features, interpretation of hematological profile and iron parameters.
- Patients of hemoglobinopathies, hemolysis, hypogonadism, hypothyroidism, myelodysplastic syndromes, history of drug intake and pregnant women were excluded from the present study. 5ml of venous blood sample was obtained by venipuncture under aseptic precautions.
- Hematological parameters were analyzed in Horiba instrument by fluorescent flow cytometry and photometry. Serum ferritin was analyzed by chemiluminescent microparticle immunoassay technique in Abbott analyzer. [7,8]

- All other biochemical measurements were performed as per standard procedures.

Reference range:

- Hemoglobin (Hb): 11.5 - 16.5 g/dl, Serum Iron in Men: 60 – 160 µg/dl, Women: 35 – 145 µg/dl. Serum Ferritin; Men: 22 – 274 ng/ml, Women: 10 – 204 ng/ml

Total Iron Binding Capacity (TIBC): 250 – 400 µg/dl, Transferrin saturation (TS): 20 – 40%.

Statistical software and analysis:

- SPSS (Statistical Package for Social Sciences) version 20. [IBM SPSS statistics (IBM corp. Armonk, NY, USA released 2011)] was used to perform the statistical analysis.
- Data was subjected to normalcy test (Shapiro-wilk test). Non-parametric tests were applied. Descriptive statistics of the explanatory and outcome variables were calculated by mean, standard deviation/median and interquartile range for quantitative variables, frequency and proportions for qualitative variables.
- Chi square test was applied to test the statistical association between qualitative variables. Spearman's correlation was calculated and scatter plots were drawn to calculate the correlation between serum ferritin and other iron parameters.

The level of significance was set at 5%.

RESULTS:

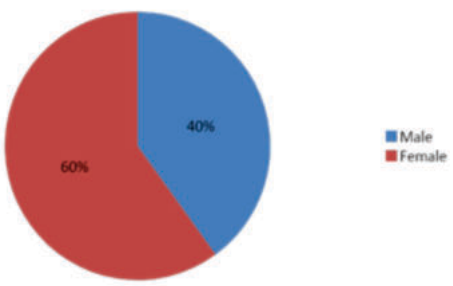
Among the age group 21 to 40 years, there was high prevalence of anemia which was found to be 38.7% in Iron deficiency anemia and 41.2% in Anemia of chronic diseases.

Table 1 shows distribution of anemia among different age group.

Graph 1 shows gender distribution of Anemia. Table 2 shows variables in Iron Deficiency Anemia. Table 3 depicts variables in Anemia of Chronic Disease. Spearman's correlation of different parameters with S. ferritin based on cause of anemia is shown in Table 4. Scatter plot depicting serum iron and serum Ferritin in IDA is in Graph 2. Spearman's correlation of different parameters with S. ferritin based on gender is shown in Table 5.

Table 1. Distribution of Anemia among different age group

Age group	Cause of anaemia		Total
	IDA	CD	
</= 20	3	6	9
	9.7%	17.6%	13.8%
21-40	12	14	26
	38.7%	41.2%	40.0%
41-60	8	8	16
	25.8%	23.5%	24.6%
61-80	8	6	14
	25.8%	17.6%	21.5%
Total	31	34	65
	100.0%	100.0%	100.0%
p value - 0.728*			



Graph 1. Gender distribution of Anemia

Table 2. Variables in Iron Deficiency Anemia

IDA (n - 31)						
Variables	Minimum	Maximum	Mean	Std. Dev	Median	IQR
Age	16.00	85.00	44.68	19.83	45	36.00
S.Iron	15.00	349.60	67.45	64.20	45	51.00
S. Ferritin	1.00	154.00	21.48	30.86	13	13.80
TS%	3.40	83.00	21.21	18.50	14.1	16.60
TIBC	150.00	616.20	337.52	108.50	327	126.00
Hb%	4.10	11.50	7.74	1.70	8	2.80

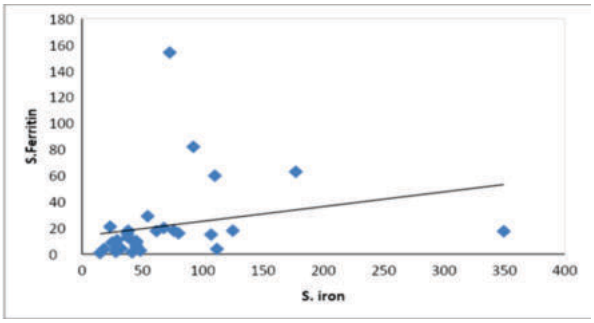
Table 3. Variables in Anemia of Chronic Disease

CHRONIC DISEASE (n- 34)							
Variables	Minimum	Maximum	Mean	Std. Dev	Median	IQR	IQR
Age	12.00	75.00	39.74	18.77	36.5	33.00	33.00
S.Iron	41.10	237.90	120.27	58.74	117.1	100.20	100.20
S. Ferritin	25.00	2,000.00	511.33	594.56	308.5	338.16	338.16
TS%	6.91	97.30	49.55	27.60	44.55	44.37	44.37
TIBC	132.90	651.00	268.88	115.42	233.5	77.87	77.87
Hb%	1.80	13.20	6.60	2.17	6.4	2.75	2.75

Table 4. Spearman's correlation of different parameters with S. ferritin based on cause of anemia.

Spearman's correlation with S. ferritin					
Anemia cause		S.Iron	TS%	TIBC	Hb%
IDA	r value	.537*	.630*	-.255	.065
	p value	.002	.000	.166	.730
	N	31	31	31	31
CD	r value	.158	.311	-.227	.131
	p value	.373	.073	.197	.460
	N	34	34	34	34

***significant**



Graph 2. Scatter plot depicting S. iron and S. Ferritin in IDA

Table 5. Spearman's correlation of different parameters with S. ferritin based on gender Table 5.

Spearman's correlation with S. ferritin					
Gender		S.Iron	TS%	TIBC	Hb%
Female	r value	.660*	.703*	-.397*	.051
	p value	.000	.000	.012	.757
	N	39	39	39	39
Male	r value	.482*	.566*	-.598*	-.652*
	p value	.013	.003	.001	.000
	N	26	26	26	26

***significant**

DISCUSSION

- Anemia has significant consequences on human health, as well as for social and economic development. In 2010, anemia accounted for 68.4 million years of life lived with disability or 9% of the total global disability burden from all conditions. [9]

- Anemia is associated with increased morbidity and mortality in women and children, poor birth outcomes, decreased work productivity in adults and impaired cognitive and behavioral development in children. [10,11,12]
- Prevalence of Iron deficiency anemia among the age group 21 to 40 years, found to be more 38.7%, this is in agreement with previous observation by Milman N et al.[13] conducted in European women.
- In Iron deficiency anemia median and interquartile range values of serum Iron and serum ferritin were 45 and 51.0 and 13 and 13.80 respectively. These findings are in accordance with the study of Michelle L Parker et al.[14] and Laura Tarancon-Diez et al [15] showed a median of serum ferritin of 8, interquartile range of 5–14.25.
- Study by Laura Tarancon-Diez et al [15] results suggest that a ferritin level < 50 ng/mL is the clinical threshold to redefine and consider ferropenia, in order to achieve an early diagnosis and initiate treatment for iron deficiency.
- Spearman's correlation of serum ferritin with serum Iron was found to be significant in patients of iron deficiency anemia. The r value being 0.537 and the p value 0.002. Spearman's correlation of serum ferritin with serum iron was found to be more significant in females r value being 0.660 and negative correlation with TIBC with r value .397.
- These findings are in accordance with study done by Sei Woo Chung et al.[16]concluding as serum ferritin is a useful survey tool for the initial assessment and prospective monitoring of iron stores.
- Iron is required for various cellular functions, including but not limited to enzymatic processes, DNA synthesis, oxygen transport and mitochondrial energy generation. [17]
- The storage form of iron is ferritin with molecular weight of 450,000D. Concentrations may increase in the event of inflammation and certain metabolic syndromes. Of note, the only cause of low ferritin serum concentration is Iron deficiency. Reference values for serum ferritin also vary depending on age and sex, especially in children and pregnant women.[5]
- Patients with IDA deserve urgent investigation, since 8–15% of these patients will be diagnosed with a gastrointestinal cancer.[18]
- Iron deficiency anemia is associated with some rather striking neurological sequelae. Some subjects possess the compulsion to move their lower extremities while at rest. The restless leg syndrome is now recognized as a reversible symptom of reduced brain iron levels that is particularly prevalent during pregnancy.[19]
- According to some studies, Iron deficiency anemia is significantly more prevalent among obese than normal weight people.[20,21]
- There is a rapid turnover of transferrin-bound iron and circulating iron concentration can be affected by dietary intake; as a result, there is significant variation in iron concentration within each day and between days. For this reason, assessment of serum iron alone provides little helpful clinical information.
- The concentration of serum iron does not fall until the body's iron stores are exhausted. As the stores are depleted, the concentration of transferrin rises while the concentration of ferritin falls. Estimation of serum iron alone in the investigation of anemia is consequently inadvisable. [22,23]
- Subnormal levels of ferritin can be detected when iron stores are exhausted, but before the serum iron level has become affected. Ferritin thus represents the most sensitive index of early iron deficiency.[24]

SUMMARY AND CONCLUSION:

- Iron deficiency is the most common anemia and nutritional disorder worldwide. Despite of effective treatment strategies there is high prevalence of iron deficiency anemia, could be due to economic status, cultural barriers and infectious diseases.
- It is crucial to note that iron deficiency should not be excluded in the presence of a normal Hb as a significant amount of iron must be lost before the Hb levels begin to decline. Thus, a low mean corpuscular Hb with a normal Hb or an increase in red cell distribution width signifies mild iron deficiency without anemia.[25]
- The commonly reported threshold of 15µg/L is likely specific but can be expected to miss many cases of Iron deficiency(ID) perhaps as many as half.[25]
- There is variation in recommendations for Serum Ferritin cutoffs indicative of ID among different expert organizations and even laboratories, which impairs the development of recommendations to implement screening programs. This complicates clinical guidelines for diagnosis and treatment of ID. [26]
- As in iceberg phenomenon of iron deficiency anemia only the tip of the iceberg is reported. To achieve WHO global nutrition target 2, which is 50% reduction in anemia among women of reproductive age by 2025, nutrition programme of Weekly Iron Folic acid Supplemenation (WIFS) has to be generalized globally in large scale.
- Limitations of present study were small sample size and the circulatory levels of acute phase reactants were not assessed.

CONCLUSION:

- Serum ferritin can be used as an early marker in diagnosis of Iron deficiency anemia as well as in screening the risk population, thus preventing associated morbidity and mortality.
- Further large scale, long term prospective, comparative research studies are required to develop new strategies, an evidence-based cutoffs of serum ferritin in early diagnosis and management of Iron Deficiency anemia.
- Prevention is better than cure, so we need to do Screening of risk population, fortification of foods, creating awareness, early diagnosis and effective treatment, maintain physical and mental wellbeing of adolescent girls and pregnant women.

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