CORRELATION OF SERUM FERRITIN WITH C-REACTIVE PROTEIN IN IRON DEFICIENCY ANAEMIA

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ABSTRACT

Objective: To find the correlation of serum ferritin as an Acute Phase Reactant with C-Reactive Protein in Iron deficiency Anaemia with underlying inflammatory condition.

Study Design: Comparative cross-sectional study

Place & Period of Study: Department of Chemical Pathology, and Endocrinology CMH Malir Karachi from August 2017 to December 2017.

Method and Material: One hundred and fifty subjects with Iron Deficiency Anaemia (IDA) were enrolled in study. Blood Complete Picture (CP) was analysed on Sysmex Haematology autoanalyzer, Serum Ferritin was analyzed by third generation electrochemiluminescence assay using "Roche autoanalyzer Cobas e-411 and Serum CRP was measured by immunoturbidimetric method. All Participants were divided into three groups on the basis of serum ferritin, Group A had low ferritin (<10 ug/l) n=84(56%), Group B with normal ferritin (11-150 ug/l) n=51(36%) and Group C with high ferritin (>150 ug/l) n=15(10%). All data was analyzed through SPSS version 20. Statistical analysis was performed by Pearson's correlation tests.

Results. CRP was the highest in group C (mean±SD = 26.34± 0.34, p< 0.001) and the lowest in group A, (mean±SD = 5.70±0.98, p< 0.001). Contrarily to CRP, Hb was the lowest in group C, (mean± SD=8.2±0.31, p < 0.001) and the highest in group A, (mean±SD = 10.0±0.73, p < 0.001). Ferritin had a strong positive correlation with CRP (r = 0.87, p< 0.001) and strong negative correlation with Hb, (r = -0.67 p < 0.001).

Conclusion. High ferritin level secondary to inflammation may mask an underlying iron deficiency. Serum ferritin was found to be positively correlated with CRP.

Key Words: Serum ferritin, APR, CRP.

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INTRODUCTION

Iron is the most abundant metal in the world however; Iron Deficiency Anaemia (IDA) is an emerging health related concern worldwide [1-5] and the most prevalent form of micronutrient deficiency affecting 1.62 billion people worldwide [6]. In Pakistan, prevalence of IDA is 40-70% [2]. In Larkana district the prevalence was (30.73%) [7]. This is more common in women and is being considered as the most serious threat to human health [8].

Serum Ferritin is an important and most frequently advised test for the assessment of total body iron stores [1]. If ferritin is low, there is no cause other than IDA, but in IDA S. ferritin may be falsely normal or high because of its rise as an Acute Phase Reactant (APR). A normal CRP can be used to exclude elevated ferritin caused by APR.

The APR is an immunologic process in response to infection or inflammation, that results in rise or fall of some APR proteins. Ferritin is one of the APR protein. Ferritin is upregulated by certain cytokines in inflammation that is independent of iron homeostasis [8]. This is a known fact since 1970 that serum ferritin can reflect the status of total body iron and an APR so it is difficult to interpret the concentration of serum ferritin alone in the presence of inflammatory condition hence not a promising marker for iron status and due to delayed in diagnosis, patient may progress to complication of IDA like organ ischemia specially ischemic heart disease, intellectual dysfunction, impaired memory and poor cognitive function etc. In this situation body iron status can either be assessed by invasive procedure like bone marrow or costly investigations like truncated soluble

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transferrin (sTfR) or Hepcidine. Mean corpuscular volume (MCV) or haematocrit, which is low during anaemia, but it can also be changed by a multiple condition like Vit B deficiencies, Kidney, liver and thyroid disease and so was not a good choice. It became clear that some tests of the APR were required to interpret Ferritin concentration for assessment of body iron status, the joint WHO/ Centers for Disease Control and Prevention (CDC) also recommended the use of one or two APR like CRP to correct ferritin in the presence of inflammation [9]. Therefore, this study was plan to find out the correlation of serum ferritin with easily available APR test like CRP in subjects of IDA having normal or high ferritin due to underlying inflammatory condition.

MATERIAL AND METHOD:

This cross-sectional, observational study was conducted in the department of Pathology CMH Malir Hospital Karachi, Pakistan, in August 2017 to December 2017. This study was approved by the hospital's ethics review committee. The study included patients from both genders in the age range of 10 to 60 years having Hypochromic microcytic anaemia. Patients already on iron therapy and those diagnosed with iron overload were also excluded. Other exclusion criteria were set on the basis of medical conditions which could potentially affect the ferritin, such as pregnancy, alcoholism, hemoglobinopathies or any bleeding disorders. After taking Informed consent, present and past medical/surgical history, 5mL of venous blood was drawn; 3mL was put in gel tubes for the determination of serum ferritin and CRP and 2 ml whole blood sample in EDTA tube for Blood CP. Serum ferritin was analyzed by the Electrochemiluminesence Immunoassay on Roche autoanalyzer Cobas e 411, Serum CRP Quantify by Immunoassay method Blood CP on Sysmex haematology autoanalyzer. Those Individuals whose blood CP showed hypochromic microcytic blood picture with normal TRBC, most probably of ID were included in the study and their ferritin and CRP was done finally they were divided into three groups, Group A low ferritin (<10 ug/l) n=84(56%), Group B normal ferritin (11-150 ug/l) n=51(36%) and Group C high ferritin (>150ug/l)n=15(10%). All the data was entered and analyzed by SPSS version 20. Pearson's correlation test was applied establishing an association Of IDA with serum ferritin and CRP, P value of <0.05 was considered as significant.

Operational definition:

IDA = Hb <10 gm/dl, TRBC <4 x10^{12}/L, MCV < 60 fl, MCH <26pg, MCHC 28 g/dl

ferritin <12 µg/L children and <15 µg/L in women.

The WHO-defined Ferritin concentration cutoff in the presence of inflammation of <30 µg/L[9].

RESULTS

Amongst all the participants, 35% were male and 65% were female (Figure-1), Low and normal ferritin was found to be more common than high ferritin 84(56%) and 31(36%) respectively (Figure-2). The mean age, Hb, MCV, MCH, MCHC and serum ferritin of all the participants were 31.74 years, 9.1 g/dl, 66.50 fl, 21.41pg, 32.0 g/dl and 131.19 ug/l respectively. Group specific descriptive statistics are given below (Table 1). To find out any impact of Inflammation on the dependent variables, namely Ferritin and CRP, CRP was the highest in group C (mean+-SD=26.34+- 0.34, P < 0.001), higher in group B (mean +-SD= 19.3+-1.4, P < 0.001), and lowest in group A (mean+-SD= 5.7+- 0.9, P < 0.001). However, despite the highest CRP level in group C, Hb was the lowest (mean+-SD 8.2+- 0.3, P < 0.001). Similarly, along with Hb both MCV and MCH were the highest in group A, intermediate in group B, and the lowest in group C (Table-1).

Moreover, one-way ANOVA showed a statistically significant difference between the three groups with regard to CRP and ferritin. Finally, a correlation test was run between the IDA and the dependent variables, namely ferritin and CRP (Table-2). It is also notable that ferritin had a strong positive correlation with CRP (r = 0.87), but a negative one with Hb(r−0.67) The detailed breakdown is given (Table-2).

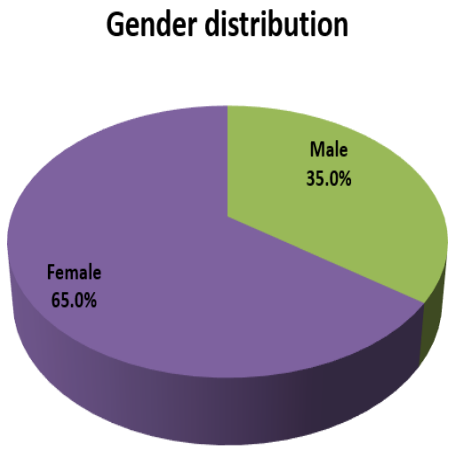

Figure-1: Gender distribution.

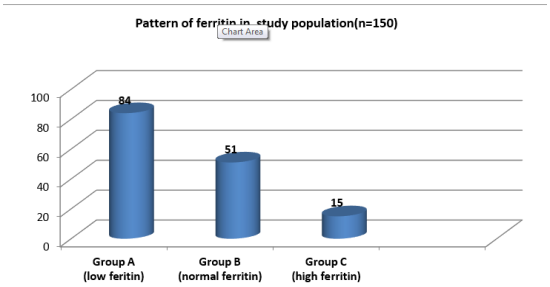

Figure-2: Pattern of ferritin in three group

Similarly, High ferritin due to malnutrition Inflammation complex Syndrome (MICS) was also observed by Kalantar K, et al in their study done on Hemodialysis patients [11]. While Allam F *et al* used hsCRP as marker of inflammation and high ferritin in Type 2 Diabetes [12], similarly a positive correlation of high levels of ferritin with the risk of metabolic syndrome and obesity was observed by Gillum RF in the study of Nutritional health and examination survey [13]. Our findings are consistent with these results.

Table-1: Descriptive statistics of different study variables in each group.

Variable	Group A		Group B		Group C		*p*-value
	Mean	SD	Mean	SD	Mean	SD	
Age(years)	31.7	5.1	31.6	5.1	31.6	5.1	
Hb (gm/dl)	10.0	0.7	9.8	0.3	8.2	0.3	<0.001
TRBC(x10^{12}/l)	4.0	0.2	3.8	0.2	3.1	0.1	
MCV (fl)	60.1	2.0	52.2	2.1	50.1	2.0	
MCH (pg)	26.1	1.3	23.2	1.2	20.0	1.4	
MCHCg/dl	27.2	2.3	25.1	2.1	22.0	0.8	
Ferritin (ug/l)	5.2	1.7	78.5	1.2	132.7	0.6	<0.001
CRP(mg/l)	5.7	0.9	19.3	1.4	26.3	0.3	<0.001

Table-2: Pearson's correlation of IDA with test variables *(note a strong positive correlation with ferritin and CRP)*

Variable	Pearson's value(r)
Hb	-0.67
Ferritin	0.87
CRP	0.88

DISCUSSION

IDA is global health problem and ferritin is used as a marker of ID in various healthcare facilities across the globe [10]. Patients with underlying inflammatory conditions, infections or chronic diseases are usually missed to diagnose IDA due to normal or high serum ferritin. Our study showed high ratio of IDA among female (65%) as compared to male (35%) and same was also observed by Khan A et al [7] As per WHO/UNICEF recommendation, use of inflammatory marker like CRP to assess the actual body iron status [2]. In our study group B and C with normal and high ferritin due to underlying inflammatory condition diagnosed by high CRP, showed a positive correlation between ferritin and CRP also found that falling values of IDA as on moves upwards from group A to group C, there was a not only a corresponding decline in the level of hemoglobin (Hb), but also a significant increase in the level of ferritin and CRP which is consistent with the result of Khan A et al [7].

However, in contrast to our results, low ferritin in inflammation was observed in a study by Eftekhari et al [14]. while no effect of CRP in estimation of SF concentration or ID prevalence in Mexico population that was concluded by Cruzz La De [15]. However, in a study of Peshawar Pakistan high serum ferritin level is found in overweight and obese people, because of generalized inflammation in them [15-18] Similarly due to this fact, using serum ferritin as a marker of IDA in people with inflammatory condition is controversial [17,18].

Ferritin was not a true indicator of an underlying IDA in our study population of IDA. Rather, ferritin correlated positively with the inflammatory status, CRP along with serum Ferritin, was found `to be helpful in diagnosis of body iron status and make it early diagnosis and management of ID and prevent the further sequel of IDA. However, we recommend further studies with bigger sample size, in order to arrive at a more logical conclusion.

CONCLUSION

High ferritin level secondary to inflammation may mask an underlying iron deficiency. CRP in subjects with normal or high ferritin can be helpful in diagnosing iron deficiency. Serum ferritin was found to be positively correlated with CRP.

AUTHORS CONTRIBUTION

Shagufta Yousaf: Planned research work, sample collection, analysis and write-up.
Muhammed Younas: Literature review and critical analysis.
Fahim Akhtar: Literature review and critical analysis.
Amir Ijaz: Planned research work and literature review.
Ghulam Murtaza, Muhammad Yasir Rafiq, Syed Raza Jaffar, Irfan Najam Sheen, Zulfiqar Ali Kango: Literature review

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