ASSOCIATION OF SERUM FERRITIN WITH C −REACTIVE PROTEIN IN PATIENTS WITH IRON DEFICIENCY ANAEMIA

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ORIGINAL ARTICLE

ASSOCIATION OF SERUM FERRITIN WITH C – REACTIVE PROTEIN IN PATIENTS WITH IRON DEFICIENCY ANAEMIA

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ABSTRACT

Objective: Main objective of this study was to see association of serum ferritin as acute phase reactant with C – reactive protein in patients with iron deficiency anaemia having underlying inflammatory process.

Patients and Methods:
This was a prospective and cross sectional study, conducted at Department of Pathology, Indus Medical College Hospital Tando Muhammad Khan for period of 6 months (November 2018 to April 2019). 68 patients with iron deficiency anaemia were included in this study. Blood parameters were assessed by Automated Haematology Analyzer Mindray BC-5000. Serum ferritin was assessed using Mindray CL1000i electrochemiluminesence assay. C – Reactive protein was analyzed by Automated Chemistry Analyzer Mindray BS-240, using immunoturbidimetric method. All patients were divided into three classes as per levels of serum ferritin. Group A (serum ferritin <10 µg/L), Group B (serum ferritin 11-150 µg/L) and Group C (serum ferritin >150 µg/L). The data was analyzed by SPSS version 21.0. Pearson's correlation tests were performed for statistical analysis.

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Results: C – reactive protein (CRP) was most significantly raised in Group C (high ferritin) (34.52 ± 1.44, p-value <0.001) and was reduced in Group A (low ferritin) (5.92 ± 0.99, p-value <0.001). Haemoglobin was lowest in Group C (high feritin) (7.84 ± 1.09, p=0.003), and was highest in Group B (normal ferritin) (9.88 ± 097, p=0.003). There was strong positive relationship of ferritin with C-reactive protein (r=0.79, p <0.001) and strong negative relationship with haemoglobin (r=0.59, p<0.001).

Conclusion: Levels of serum ferritin was positively associated with C-reactive protein (CRP). In patients with underlying deficiency of iron, secondary inflammation may increase the level of ferritin in serum.

Keywords: Iron Deficiency Anaemia, Ferritin, C-Reactive Protein, Haemoglobin.

INTRODUCTION

Iron is one of the most copiously metals present globally; though iron deficiency anaemia is still emerging problem in health-related concerns globally. [1-5], and it is the most common type of deficiency of micronutrient which affect 1.62 billion individuals around the world. [6] Prevalence rate of iron deficiency anaemia in Pakistan is around 40 – 70%. [7] This condition is more prevalent in females and is taken as one of the most serious health problem to human life. [8]

Most common and essentially advised investigation for the assessment of total stores of iron in body is ferritin. [1] In state of low ferritin levels, iron deficiency anaemia is most common and obvious cause; though as an acute phase reactant, serum ferritin levels may be false normal or false high. Normal C-reactive protein (CRP) can be utilized for the exclusion of high ferritin levels caused by acute phase reaction.

Acute phase reaction is immunological mechanism which is caused in response to inflammation or infection, resulting in uphill or downhill of certain acute phase proteins, including ferritin. In inflammation, upregulation of ferritin by specific cytokines is not dependant on homeostatis of the iron. [8] Since 1970, it is known that level of ferritin in serum imitates the total iron in the body and acute phase reaction so there is difficulty in interpretation of serum ferrtin in the presence of inflammatory or infectious condition; therefore not a capable marker for status of iron and delay in diagnosis may lead to complications of iron deficiency anaemia. In these situations, the status of body iron can be measured by invasive techniques e.g. bone marrow or expensive techniques e.g. soluble transferrin (sTfR) or level of hepcidin. Haematocrit or mean corpuscular volume (MCV) is decreased in anaemia, but many factors affect their levels e.g. deficiency of vitamin B, thyroid disease, kidney disease or liver disease. It was obvious that certain investigations of acute phase reactions were needed for interpretation of concentration of ferritin to assess status of body iron, the joint Centres for Disease Control and Prevention (CDC) and World Health Organization (WHO) recommended the utility of one or two acute phase reactants e.g. C-reactive protein for correction of ferritin when inflammatory condition is evident. [9] Therefore this research was conducted to interpret the correlation between ferritin and C-reactive protein in patients with iron deficiency anaemia with normal or increased level of ferritin due to associated inflammatory status.

PATIENTS AND METHODS

This was cross-sectional, observational study, carried out at Department of Pathology, Indus Medical College Hospital Tando Muhammad Khan for the period of 6 months (November 2018 to April 2019). This study included patients of both genders i.e. males and females. Patients aged between 10 to 50 years having

hypochromic microcytic anaemia were included in this study. Patients already on iron replacement treatment and patients with iron overload syndromes were excluded from the study. Patients with co-morbid conditions e.g. alcoholism, pregnancy, bleeding disorders or haemoglobinopathies were also excluded from the study.

After informed consent, 5mL venous whole blood was obtained; 3mL was transported in gel-containing tubes for assessment of serum ferritin and C-Reactive protein and 2mL was transported to EDTA-containing tube to perform complete blood count. Blood parameters were assessed by Automated Haematology Analyzer Mindray BC-5000. Serum ferritin was assessed using Mindray CL1000i electrochemiluminesence assay. C – Reactive protein was analyzed by Automated Chemistry Analyzer Mindray BS-240, using immunoturbidimetric method. All patients were then divided into 3 groups: Group A containing patients with low level of ferritin (<10 µg/L), Group B containing patients with normal level of ferritin (11-150 µg/L) and Group C containing patients with high level of ferritin (>150 µg/L). All data was analyzed using SPSS 21.0. Pearson's correlation test was used for the establishment of association between iron deficiency anaemia with serum ferritin and C-reactive protein. P – value of <0.05 was considered ass statistically significant.

RESULTS

Among 68 patients, 29 (42.64%) were males and 39 (57.35%) were female (Figure 1). Low ferritin levels (36/52.94%) were found more common followed by normal ferritin levels (28/41.17%) and high ferritin (4/5.88%) (Figure 2). Mean age of patients in Group A, B and C were 29.21 ± 6.32, 28.87 ± 6.01 and 29.89 ± 5.89 years respectively with no statistical significant value (Table 1). Mean age, haemoglobin, red blood cell count, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, ferritin and C-reactive protein in all three groups are summarized in Table 1. C-reactive protein was highest in Group C (high ferritin level) with mean level of 34.52 ± 1.44 mg/L, followed by Group B (normal ferritin level) with mean level of 25.94 ± 2.33 mg/L and Group A (low ferritin level) with mean level of 5.92 ± 0.99 mg/L. P-value was statistically significant (<0.001) showing strong correlation between serum ferritin and CRP.

Pearson's correlation demonstrated statistically significant variation between three groups in relation to ferritin and CRP. In the end, a test for correlation was performed dependant variables and iron deficiency anaemia (Table 2). Ferritin revealed strong positive correlation with C-reactive protein, but negative correlation with haemoglobin (Table 2).

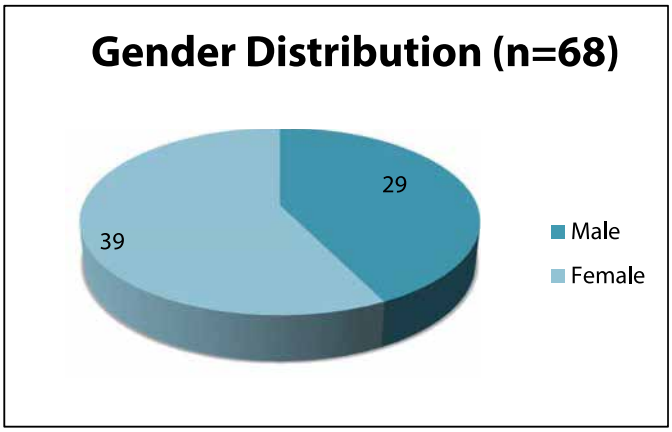

Figure 1: Gender Distribution (n=68)

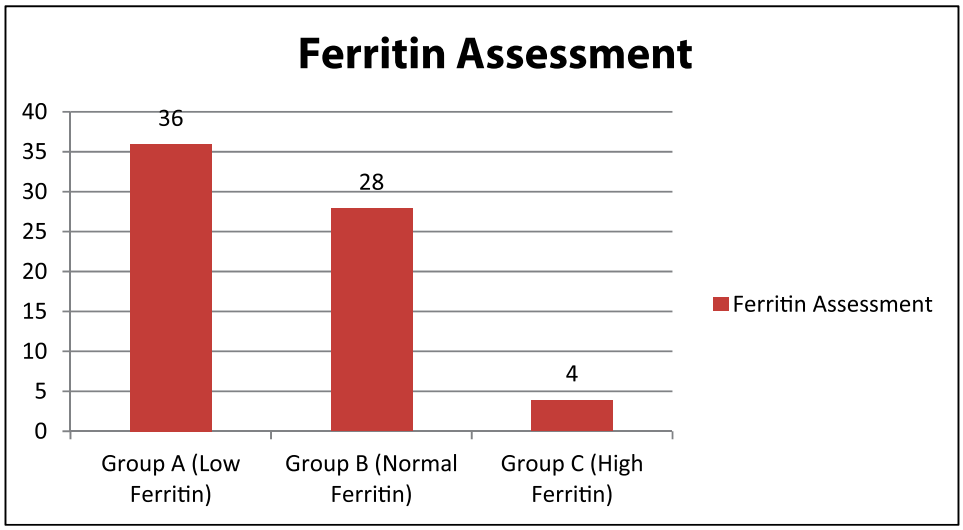

Figure 2; Pattern of Ferritin Level in Selected Population of the Study (n=68)

Table 1; Descriptive Analysis of Parameters (n=68)

Variable	Group A (Low Ferritin)		Group B (Normal Ferritin)		Group C (High Ferritin)		P-value
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	
Age (years)	29.21	6.32	28.87	6.01	29.89	5.89	0.11
Hemoglobin (g/dL)	9.42	1.02	9.88	0.97	7.84	1.09	0.003
Red Blood Cell Count (x10^{12}/L)	3.28	0.43	3.71	0.78	3.41	0.15	0.20
MCV (fL)	58.23	3.24	57.20	2.98	61.42	2.55	0.28
MCH (pg)	25.12	1.12	24.09	2.03	25.71	1.87	0.17
MCHC (g/dL)	26.87	1.79	26.03	2.21	25.87	2.19	0.29
Ferritin (µg/L)	6.31	1.80	84.22	6.42	161.42	7.88	<0.001
C-Reactive Protein (mg/L)	5.92	0.99	25.94	2.33	34.52	1.44	<0.001

Table 2: Pearson's Correlation of Iron Deficiency Anaemia with Test Variables (n=68)

Variable	Pearson's Value (r)
Hemoglobin	-0.59
Ferritin	0.79
C-Reactive Protein	0.92

DISCUSSION

Iron deficiency anaemia is major global problem of health concern. In various healthcare setups, serum ferritin is utilized as marker for iron status.[10] High or normal ferritin level is often associated with patients having underlying state of inflammation, chronic disorder or infection; hence diagnosis of iron deficiency anaemia is not accurate. This study showed high female predominance (57.35%) in comparison to males (42.64%). Similar findings were observed by Khan et al. [7] UNICEF and WHO recommends the use of additional inflammatory marker e.g. CRP for assessment of iron status in case of inflammatory condition. [2] In our results, group B and group C with normal and high ferritin levels respectively showed higher levels of CRP due to underlying inflammatory conditions and demonstrated positive correlation between CRP and ferritin. It also showed that from low to high ferritin levels, there was decline in haemoglobin levels as well as increase in levels of ferritin and CRP which was similar to findings of Khan et al. [7] Kalantar et al also showed high level of ferritin because of malnutrition inflammation complex syndrome (MICS) in patients with haemodialysis. [11] Allam et al utilized the hsCRP levels as the inflammatory marker and high level of ferritin in patients with diabetes mellitus type 2. [12] In study of nutritional health and examination survey by Gillum et al, it was observed that there was positive correlation of high ferritin levels with risk of obesity and metabolic syndrome. [13] Our results showed similar findings.

Eftekhari et al, in contrast, observed low level of ferritin in inflammatory conditions [14], while there was no influence of C-reactive protein in assessment of concentration of serum ferritin or prevalence of iron deficiency in population of Mexico by Cruzz et al. [15] In study conducted in Peshawar, high ferritin levels were observed in individuals with obesity and overweight due to presence of generalized inflammation. [15-18]

Due to these observations, the use of ferritin as novel marker for diagnosis of iron deficiency anaemia is controversial in underlying inflammatory conditions. [17-18]

In our study, ferritin was not proved to be ideal marker for assessment of body iron in underlying inflammatory conditions. Though, positive correlation was found between ferritin and inflammatory status, addition of C-reactive protein was shown to be beneficial in diagnosis of status of iron in the body and help in making early diagnosis and interventions in iron deficient patients. However, studies on larger populations are recommended to assess various factors and to get strong correlation is necessary.

CONCLUSION

High level of ferritin in patients with underlying inflammatory conditions may mask the deficiency of iron in the body. Use of inflammatory marker such as C-reactive protein (CRP) with high or normal level of ferritin can be essential in diagnosis of iron deficiency. Ferritin was shown to be positively correlated with C-reactive protein.

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