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SERUM FERRITIN AND IRON PROFILE IN HELICOBACTER PYLORI INFECTED YOUNG ADULT MALE REPORTING AT A TERTIARY CARE HOSPITAL.

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ABSTRACT... Determination of serum ferritin and iron profile in Helicobacter pylori infected young adult male reporting at a tertiary care hospital of Sindh. **Study Design:** Case control study. **Setting:** Department of Medicine, Layari General Hospital Shaheed Muhtrama Benazir Bhutto Medical College **Period:** January 2015 to February 2016. **Materials and Methods:** 100 cases (H. pylori stool specific antigen positive) and 100 controls (H pylori negative) were selected and studied. 5 ml blood was collected in a disposable syringe by venesection. 2 ml was put in EDTA tubes and 3 ml was centrifuged (3000 x rpm for 10 minutes). Sera were used for the estimation of iron profile. Elisa assay method (Fortress diagnostics) detected the H. pylori stool specific antigen (HpSA). Data was analyzed on SPSS 22.0 (USA) at 95% CI (P ≤ 0.05). **Results:** Age of control and cases was noted 35.48±4.79 and 33.60±3.96 years (P=0.053). Hb, Hct and RBC counts were low in cases (P=0.0001) significantly. Serum iron (Fe++), ferritin and TIBC in controls and cases were noted 152.72±6.08 and 118.79±43.30 µg/dl, 394.34±136.50 and 529.87±101.0 ng/dl, & 140.80±19.99 and 130.88±28.46 µg/dl respectively (P=0.0001) (Table-I). **Conclusion:** Helicobacter pylori infection causes iron malabsorption as detected by serum iron and ferritin and total iron binding capacity in young adult male.

Key words: Helicobacter pylori, Ferritin, Iron, TIBC, Male.

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INTRODUCTION

One of the most important human pathogen of current era is a gram negative bacterium that inhabits the acidic gastric environment; called the Helicobacter pylori (H pylori). It is a gram negative helix shaped microaerophilic bacteria. Currently, it infects >50% human population of world. It is capable of survival against the acidic medium of stomach. It colonizes the gastric mucosa.¹ H. pylori have been implicated in the etiology and pathogenesis of gastric ulcers, gastric carcinomas, gastric lymphoma and atrophic gastritis.^{2,3} Extra gastric disorders have also been linked with H. pylori infection.³ Few of extra-gastric disorders associated with H. pylori infection include the chronic idiopathic thrombocytopenic purpura (CITP), chronic cholecystitis, etc. Iron deficiency anemia (IDA) has been reported in the H. pylori infected patients. Eradication of H. pylori ameliorates the IDA of unknown cause,

CITP, etc. Previous meta-analysis suggested the association of H. pylori infection with depletion of iron stores and its eradication replete the iron store.^{4,5} Further evidence suggests the eradication of H. pylori also replete the blood hemoglobin (Hb) and serum ferritin.⁶ Patients with IDA must be eradicated from the H. pylori eradication, this has been strongly recommended by the Western medical guidelines.³ Few reports from other geographical regions of World have negated the association of H. pylori infection and IDA.⁷ Pathological link of H. pylori infection and iron metabolism is not clearly and needs further investigations at the molecular levels for better understanding and planning for the remedy.^{8,9}

A few studies reported strong association of H. pylori infection, Iron deficiency and IDA. In Japan, a study reported on the improvement of iron metabolism after H. pylori.⁹ In South East

Asian countries including Pakistan, majority of population is infected with *H. pylori* with low gastric acidity and gastric atrophy. Hence the possibility of *H. pylori* infection with iron malabsorption needs further research. Acid secretion within stomach keeps the gastric mucosa healthy.¹⁰ However, mechanism of iron malabsorption and deficiency caused by *H. pylori* infection is not fully understood.¹⁰ Suggested mechanisms implicated in the pathogenesis of *H. pylori* induced iron malabsorption are; Iron consumption by *H. pylori* with expression of iron transporters,¹¹ and impairment of iron chelation with lactoferrin.¹² *H. pylori* utilizes iron and ferritin for growth and proliferation.¹³

With this background, and prevalent *H. pylori* infection in Pakistan, it needs more research on iron metabolism and serum ferritin. Keeping this scenario of prevalent *H. pylori* infection in country, the present research analyzed the serum ferritin, iron and total iron binding capacity (TIBC) and serum ferritin levels at our tertiary hospital. The present study hypothesized such relationship does not exist until proved otherwise.

SUBJECTS AND METHODS

A case control study was designed to analyze the serum ferritin and iron profile in *H. pylori* infected subjects. Ethical permission was sought from the institution's review committee. Participants for the study purpose were selected from the Department of Medicine, Layari General Hospital Shaheed Muhtrama Benazir Bhutto Medical College from January 2015 to February 2016. A sample of 100 *H. pylori* infected (*H. pylori* stool specific antigen positive) subjects were labelled as cases and 100 normal healthy subjects (*H. pylori* negative) were taken as control.

Study participants were selected by non-probability (purposive) sampling according to strictly exercised criteria of inclusion and exclusion. *H. pylori* stool specific antigen (HpSAg) positive, young adult male, age 20- 40 years, presenting with gastric dyspeptic symptoms were included. Female subjects and subjects with concomitant systemic disease such as diabetes mellitus, inflammatory bowel disease, chronic diarrhoea,

etc were excluded. Control and cases taking betel nuts, pan, gutkha, manipuri, etc were also excluded. Cases and control were interviewed and informed purpose of research study, gain and loss, and merits and demerits. They were free to ask questions about the loss or damage to them if they are thinking of it. They were informed that the charges laboratory investigation will be paid by the researcher. Research will cause no harm to them and will be beneficial to the community against the *H. pylori*. Over the duration of study, many subjects were examined, interviewed and communicated. Finally, only volunteer participants qualified for the entry into research protocol who gave a signed informed consent. All of volunteers were informed if they have any query or problem, they are free to ask and even can withdraw from the study protocol without telling the reason, and this will not affect their medical therapy. Willing participants were requested to comply with research protocol voluntarily. All volunteers were examined by a medical officer and a consultant physician.

Volunteers were asked for sampling of blood and stool. HpSAg was assayed by Elisa kit (Fortess Diagnostics). A 5 ml disposable syringe was used for blood sampling from ante cubital vein. Area was clean and sterilized by alcohol swab. Of 5 ml blood, 2 ml was put into EDTA tube, remaining 3 ml was centrifuged to separate out sera. Sera were obtained by centrifugation of 3000 x rpm for 10 minutes. EDTA samples were used for the estimation of hematocrit (Hct), hemoglobin (Hb) and Red blood cell (RBC) counts. Iron profile parameters were estimated from the sera. Serum ferritin was detected by Immulite immunoassay kit (Chemiluminescent system, UK). Rang of assay kit was 7- 149 ng/ml. Biochemical estimation of parameters was conducted on the Cobas e 411 analyzer (Roche Diagnosis GmbH, Mannheim, Germany). Data was noted in a pre-designed pre structured proforma. Confidentiality was maintained and signing of consent form by volunteers was mandatory. All data variables were analyzed on SPSS 22.0 (USA). Statistical comparisons of continuous variables was performed by the Student's t-test (Independent samples). Data analyzed at 95% Confidence

interval ($P \leq 0.05$).

RESULTS

Age (mean \pm SD) of control and cases was noted 35.48 ± 4.79 and 33.60 ± 3.96 years ($P=0.053$). Hb, Hct and RBC counts were found significantly low in cases ($P=0.0001$) (Table-I). Serum iron (Fe^{++}), ferritin and TIBC in controls and cases were noted 152.72 ± 6.08 and 118.79 ± 43.30 $\mu\text{g/dl}$, 394.34 ± 136.50 and 529.87 ± 101.0 ng/dl , & 140.80 ± 19.99 and 130.88 ± 28.46 $\mu\text{g/dl}$ respectively ($P=0.0001$) (Table-I). Serum iron is shown in Figure-1, serum TIBC in Figure-2 and serum ferritin levels in Figure-3.

DISCUSSION

The present observed low serum ferritin and serum iron in young male with H.pylori infection (H. pylori stool specific antigen positive). It is first study which reports on the serum iron profile in young adult male with active H. pylori infection.

Age (mean \pm SD) of control and cases was noted 35.48 ± 4.79 and 33.60 ± 3.96 years ($P=0.053$), this shows the study included young population.

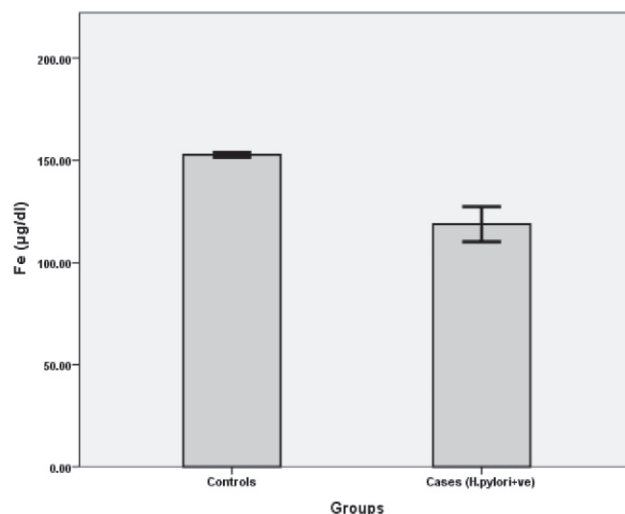


Figure-1. Serum iron levels in controls and cases

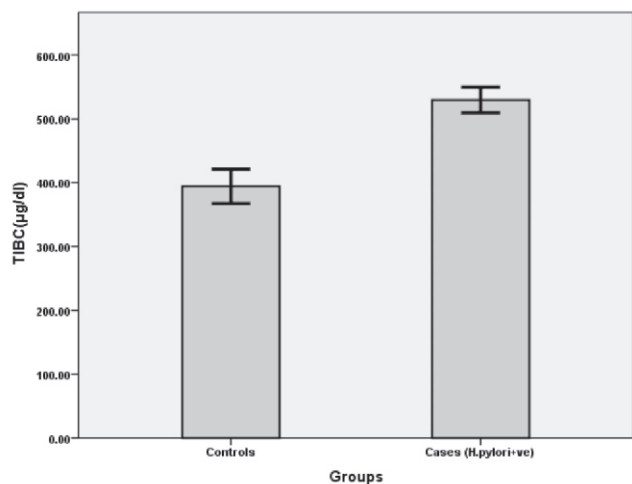


Figure-2. Serum TIBC levels in controls and cases

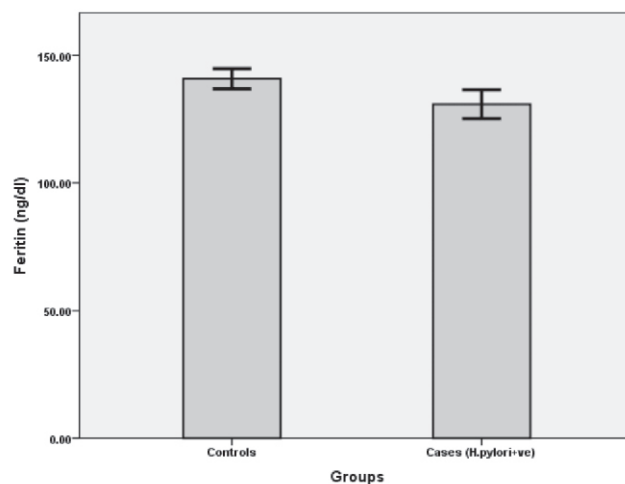


Figure-3. Serum ferritin levels in controls and cases

	Control (H.pylori -ve)	Cases (H.pylori +ve)	P-value
Age (years)	35.48 \pm 4.79	33.60 \pm 3.96	0.053
Hemoglobin (g/dl)	13.15 \pm 2.49	11.81 \pm 4.62	0.0001
Hematocrit (%)	41.92 \pm 5.26	35.95 \pm 9.40	0.0001
RBC counts ($\times 10^6/\mu\text{L}$)	4.25 \pm 0.22	3.95 \pm 0.49	0.0001
Serum Fe^{++} ($\mu\text{g/dl}$)	152.72 \pm 6.08	118.79 \pm 43.30	0.0001
Serum Ferritin (ng/dl)	394.34 \pm 136.50	529.87 \pm 101.0	0.0001
Serum TIBC ($\mu\text{g/dl}$)	140.80 \pm 19.99	130.88 \pm 28.46	0.005

Table-I. Demography, physical and laboratory findings of study subjects (n=200)

The findings are in agreement with previous studies.^{14,15} We observed low Hb, Hct, RBC counts, serum Fe⁺⁺, serum TIBC and serum ferritin levels in H.pylori infected male (cases) compared to controls (P=0.0001). The findings are supported by previous studies.^{16,17}

More than 50% of World population is suffering from H. pylori infection this is true for developing countries like Pakistan. In developing countries, iron deficiency is an established public health problem and this is compounded by the H. pylori infection.¹⁸ H. pylori is suggested risk factor of iron deficiency, hypoferritinemia and iron deficiency anemia,¹⁹ this is in keeping with the present study. We found low serum iron (Fe⁺⁺) and ferritin and high TIBC. RBC counts, hemoglobin and hematocrit were also found low in cases with active H. pylori infection. In present study, serum iron (Fe⁺⁺), ferritin and TIBC in controls and cases were noted 152.72±6.08 and 118.79±43.30 µg/dl, 394.34±136.50 and 529.87±101.0 ng/dl, & 140.80±19.99 and 130.88±28.46 µg/dl respectively (P=0.0001).

These observations show the H. pylori infection is associated with iron deficiency. HpSag positive indicates the active H. pylori infection. Our these findings are supported by previous studies.²⁰⁻²² Reports²⁰⁻²² from developing countries have suggested the active H. pylori infection is associated with iron deficiency. Because of many reasons the developing countries have high prevalence of H. pylori infection. Surely, this occurs because of overcrowding, fecal water contamination, poor sanitation, poverty, unhygienic feeding, contaminated foods, and life style habits.^{22,16,17} Serum ferritin is a iron storing protein that is stored source of iron as well as circulates in the blood plasma. Serum ferritin is a reliable biological marker of iron stores of human body.²³ A fallacy of serum ferritin is that it is acute phase protein, so during infections and inflammatory processes, its circulation levels are unreliable.²⁴ Low serum ferritin and iron and raised TIBC were observed and this has been attributed to H. pylori infection that disturbs the gastric pH. Resulting hypochlorhydria adversely affects the iron absorption. H. pylori infection

causes gastric atrophy and parietal cell damage.²⁵ Our findings of low serum ferritin and iron are supported by previous studies.^{16,17} However, other studies^{26,27} had reported controversial results of no association of H. pylori infection with iron deficiency. These findings are inconsistent to present and previous studies.^{16,17,22-25}

Controversial results may be due to various reasons such as the different study population and geographical areas, life style, dietary habits, food fortification, hygienic conditions, sample size, sampling errors, laboratory errors, statistical errors, etc. We conclude that the H. pylori infection is associated with iron malabsorption; the underlying molecular mechanisms need to be elucidated. The present study has certain limitations such as the; sample size, particular ethnicity, life style, etc that might have affected the results to alternative hypothesis. However, the strength of study lies in its inclusion and exclusion criteria, active H. pylori infection, age matched control, and proper handling of data and statistical analysis.

CONCLUSION

The present study reports low serum ferritin and serum iron in young male with H. pylori infection. This point to the iron malabsorption induced by H. pylori infection. Eradication of H. pylori infection is recommended for prevention of iron deficiency anemia and related morbidities.

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
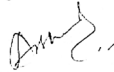



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2	Arshad Ali	Literature review, Material static analysis.	
3	Dileep Kumar	Concept introduction, Lab. Investigation.	
4	Nathu Mal	Manuscript, Hand up material.	
5	Urooj Tabassum	Material hand up proof reading.	
6	Bilawal Hingorjo	Material hand up proof reading.	