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Associations of Vitamin B_{12}, Iron Deficiency and Inflammatory Markers with Crohn's Disease Patients in Gaza strip, Palestine: Case-Control Study.

دراسة العلاقة بين فيتامين ب 12، نقص الحديد ومؤشرات الالتهاب مع المرضى الذين يعانون من داء كرون في قطاع غزة، فلسطين: دراسة الحالات والشواهد

Saleh N. Mwafy[(1)], Wesam M. Afana[(2)] , Ahmad M. Tabash[(3)]

[1]Department of Biology, Faculty of Science, Al-Azhar University-Gaza, Gaza Strip, Palestine.
[2]European Gaza Hospital, Ministry of health, Gaza Strip, Palestine.
[3]European Gaza Hospital, Ministry of health, Gaza Strip, Palestine.

smwafy@hotmail.com

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Abstract:

Objective: *we aimed to investigate the associations of vitamin B_{12}, iron deficiency and inflammatory markers with Crohn's disease patients in the Gaza strip, Palestine.*

Materials and Methods*: This case-control study included 90 adult (18-50 years old) hospitalized Crohn's disease patients and 90 apparently healthy individuals as a control group. Parameters measured, statistically analyzed and compared with control.*

Results: *The mean levels of hemoglobin, red blood cell, hematocrit and mean cell hemoglobin concentration significantly decreased, while the white blood cell, red distribution width and platelets levels significantly increased in Crohn's disease patients compared to the control ($P<0.001$). Serum vitamin B_{12} and iron showed a significant decrease while serum ferritin and C-reactive protein showed significant increase in Crohn's disease patients compared to controls ($P<0.01$). About 26.7% of cases had high level of C-reactive protein compared to 3.3% of the control. Vitamin B_{12} and ferritin significantly increased (402.9±84.5, 306.3±111.6 vs. 276.0±118.9, 79.8±4.9 respectively, $P\leq0.01$), while the level of serum iron significantly decreased in Crohn's disease patients with high C-reactive protein (>5.0 mg/L) compared to patients with normal C-reactive protein (29.8±4.0 vs.*

58.2±17.0, percentage of change=-48.8 P=0.001). Some statistically significant correlations reported between different parameters.

Conclusions: *Crohn's disease was associated with vitamin B_{12}, iron deficiency and inflammatory markers. Vitamin B_{12}, iron, ferritin and C-reactive protein are useful laboratory index suitable in the assessment and management of Crohn's disease. Routine screening of complete blood count, vitamin B_{12}, iron deficiency and inflammatory markers in patients with Crohn's disease are necessary.*

Keywords*: Vitamin B_{12}, Iron deficiency, Inflammatory Markers, Crohn's disease, Gaza strip.*

الملخص:

هدفت الدراسة إلى معرفة العلاقة بين فيتامين ب $_{12}$، نقص الحديد ومؤشرات الالتهاب مع المرضى الذين يعانون من داء كرون في قطاع غزة، فلسطين: دراسة الحالات والشواهد.

المواد والأدوات: تكونت عينة الدراسة من 90 مريضاً بداء كرون يتراوح أعمارهم بين 18–50 سنة (الحالات) بالإضافة إلى عدد مساوٍ من الأفراد الأصحاء (المجموعة الضابطة). حيث تم قياس الفحوصات المختلفة ومقارنتها إحصائياً مع المجموعة الضابطة.

النتائج: أظهرت نتائج الدراسة انخفاضاً ذا دلالة إحصائية في مستويات كل من الهيموجلوبين، كرات الدم الحمراء، الهيماتوكريت ومتوسط تركيز خضاب الدم، بالإضافة إلى زيادة ذات دلالة إحصائية في متوسط كرات الدم البيضاء، جاء عرض التوزيع للخلايا الحمراء والصفائح الدموية لدى مرضى داء كرون مقارنة مع المجموعة الضابطة عند مستوى الدلالة (P<0.001). كما لوحظ انخفاضاً ذا دلالة إحصائياً في مستوى فيتامين ب $_{12}$ والحديد في حين ارتفع مستوى الفيريتين والبروتين التفاعلي–س ارتفاعاً ذا دلالة إحصائية لدى مرضى داء كرون مقارنة مع المجموعة الضابطة عند مستوى الدلالة (P <0.01). بينت النتائج أن 26.7٪ من مجموعة الحالات يعانون من ارتفاع في مستوى البروتين التفاعلي–س مقابل 3.3٪ من مجموعة الأصحاء الضابطة. وارتفع مستوى فيتامين ب $_{12}$ والفيريتين (402.9 ± 84.5، 306.3 ± 111.6 مقابل 276.0 ± 118.9، 79.82 ± 4.9 على التوالي (P≤0.01)، في حين أظهر مستوى الحديد انخفاضاً ذا دلالة إحصائية لدى مرضى داء كرون المصاحب بارتفاع في مستوى البروتين التفاعلي–س (<5.0ملليجرام/ليتر) مقارنة بمرضى داء كرون طبيعيي قيمة البروتين التفاعلي–س (29.8 ± 4.0 مقابل 58.2 ± 17.0، نسبة التغير =– 48.8، P=0.001). كما وجدت علاقات ذات دلالة إحصائية بين مقاييس الدراسة المختلفة.

الاستنتاجات: خلصت الدراسة إلى أن مرض داء كرون مرتبط بتغييرات ذات دلالة إحصائية في فيتامين ب $_{12}$، نقص الحديد ومؤشرات الالتهاب. ويعتبر قياس مستوى فيتامين ب $_{12}$، الحديد،

الفيريتين والبروتين التفاعلي–س مؤشراً مخبرياً هاماً يساعد في التقييم والتحكم في داء كرون. بالإضافة إلى ضرورة القياس الدوري لفيتامين ب $_{12}$، نقص الحديد، ومؤشرات الالتهاب لدى هؤلاء المرضى.

الكلمات المفتاحية: فيتامين ب $_{12}$، نقص الحديد، مؤشرات الالتهاب، داء كرون، قطاع غزة

1. Introduction

Crohn's disease is an inflammatory bowel disease (IBD) characterized by chronic infection of the gastrointestinal tract (Hugot et al., 2001), with a globally increased prevalence reaching up to 0.5% in the Western world (Kaplan, 2015). Local and regional estimates showed a considerable incidence of IBD; in Saudi Arabia it was 0.5 /10^5 cases in year (El Mouzan et al., 2005), in Egypt it was 22 patients with Crohn's disease (14% of the total 157 patients) (Esmat et al., 2014) and in Algeria it was 5.87 /10^5 person in year. Additionally, its prevalence reached 5 cases/10^5 populations in Saudi Arabia and 19.02 cases/10^5 populations in Algeria (Ng et al., 2017), while no records were found for the Gaza strip of Palestine. Crohn's disease is a multifactorial disease which may disturb the gastrointestinal tract (Sartor, 2006). Anemia is a severe complication of Crohn's disease that triggers hospitalization and, if not interfered with, may lead to death. The prevalence rates of anemia in IBD are widely varying from 6 to 74% (S Kulnigg & Gasche, 2006). Inflammatory bowel disease anemia is a combination of iron deficiency and anemia of inflammation (Wickbom et al., 2018). The etiopathogenesis of Crohn's disease remains unclear (Shivashankar et al., 2017). Crohn's disease is usually recognized via clinical symptoms of diarrhea (with blood or/and mucus), fever, weight loss and abdominal pain. The body has an expansive store of vitamin B_{12}, when expended standard vitamin B_{12} injections will be required to anticipate improvement of anemia (Kuroki et al., 1993). Therefore, iron deficiency anemia (IDA) remains a significant clinical health problem, which requires careful assessment and management in IBD. Anemia and iron deficiency are common in our community and considered as one of the most important health problems among the Gaza strip patients. This study focused on this risk health problem. The results of this research may draw the attention of physicians to transfer the current knowledge on Crohn's disease associated anemia into the daily management. To the

best of our knowledge, the present work could be the first that directly investigates the associations of vitamin B_{12}, iron deficiency and inflammatory markers with Crohn's disease patients in the Gaza strip, Palestine.

2. Materials and methods

2.1. Study population and Experimental design

This study used case-control design and performed on randomly selected participants from the major general hospital at the Gaza strip governorate: Al Shifa hospital in Gaza, Nasser hospital and European Gaza hospital in Khanyounis, and Najar hospital in Rafah during the period from January to October 2016. The population of the study includes patients suffering from Crohn's disease aged (18-50) years who referred to the general hospitals for medical treatment. Cases comprised of 90 patients (36 M & 54 F) of both sexes. Additionally, 90 apparently healthy individuals of the same population and same age group used as a control group for baseline comparisons. Exclusion criteria included pregnant women, vegetarian people, those received cyanocobalamin or iron treatment, patients with malabsorption syndrome, resection stomach or small bowl surgery and patients under 18-year-old and over 50-year-old. For ethical consideration, the necessary official approval to conduct this study obtained from the Helsinki ethical committee at the Palestinian Health Research Council with approval number PHRC/HC/33/15. All participants freely signed the informed consent form of the study and freely participated in the study.

2.2. Specimen collection and testing: All stool samples collected in a plastic container and sent to the laboratory within 2 hours. About five milliliters of venous blood were collected from each subject (cases and control, then divided equally (2.5 ml) into K_3-EDTA tubes to perform complete blood count (CBC) using a Cell Dyne 1800 electronic counter (Sequoia-Turner Corporation, California, USA), (2.5 ml) into serum tubes to achieve a quantitative determination of the study parameters. Serum iron was determine quantitatively using DiaSys reagent kits (Thomas, 1998). Ferritin concentration was determined by enzyme immunoassay (ELISA) (Siimes et al., 1974). Serum vitamin B_{12} concentration was determined quantitatively using a solid phase, competitive chemiluminescent enzyme immunoassay (Immulite/Immulite 1000) (Allen, 1981). Calprotectin quantification in feces was done by enzyme immunoassay reagent kits (Røseth et al.,

1992). While CRP was determined using enzyme-linked immunosorbent assays (ELISA) (Thompson et al., 1992).

2.3. Data analysis: Data were tabulated, encoded and statistically analyzed using the IBM SPSS Statistics software V21.0 for windows. Means compared by independent-samples t-test, and percentage change was also calculated. P-value < 0.05 considered as statistically significant cutoff.

3. Results

3.1. Socio-demographic characteristics of study population

The sample size of the study population was 180 participants, 90 of them were controls while 90 participants were patients suffering from Crohn's disease. There was no statistically significant relationship between Crohn's disease and gender (χ^2=0.66, p>0.05), where 30% of control group were males and 70% were females. Thirty-six (40%) males and 54 (60%) females were Crohn's disease group. In addition, the age of the study population ranged from 18 to 50 years with mean age of control was 30.0±5.2 whereas that of cases was 30.0±3.0 years (χ^2=0.72, p>0.05) Table (1).

Table (1): Socio-demographic characteristics of study populations

Variable	Category	Case n (%)	Control n (%)	Chi Square	*P*-value [a]
Gender	Male	36 (40)	27 (30)	0.659	0.417
	Female	54 (60)	63 (70)		
Age (years)	18 – 28	30 (33.3)	33 (36.7)	0.721	0.697
	29 – 39	33 (36.7)	24 (26.7)		
	40 – 50	27 (30)	33 (36.5)		
	Mean ± SD	30 ±3.0*	30 ±5.2*		
Level of education	Primary	6 (6.7)	12 (13.3)	2.803	0.246
	Secondary	42 (46.7)	24 (26.7)		
	University	42 (46.7)	54 (60)		
Place of residency	City	39 (43.3)	45 (50.0)	0.297	0.862
	Camp	36 (40.0)	33 (36.7)		
	Village	15 (16.7)	12 (13.3)		

* Values expressed as mean ± standard deviation (SD) of 90 participants.

[a] The significance of difference was checked by chi square test (compare all vs. control), significant at $P \leq 0.05$.

3.2. Hematological parameters:

Table (2) illustrates the hematological parameters of Crohn's disease patients compared to controls. The mean levels of hemoglobin (Hb – 10.6±1.6 g/dL vs. 13.4±0.9 g/dL), red blood cell count (RBC – 3.5 ± 0 .9×10^6/ µL vs. 4.9 ±0 .1×10^6/ µL), hematocrit (Hct – 35.9±3.9% vs. 43.3±1.3%) and mean cell hemoglobin concentration (MCHC – 32.5±2.0 g/dL vs. 33.9±1.0 g/dL) significantly lower among cases compared to controls. The percentage differences was -20.9 %, -28.6%, -17.1% and -4.13%, respectively (*p*-value <0.01). White blood cell (WBC – 9.1±3.8×10^3/µL vs. 6.6±1.6×10^3/µL), red distribution width (RDW – 16.3±3.10 % vs. 13.0±0.72%) and platelets (PLT – 365.2±160.6×10^3/µL vs. 257.8±65.0×10^3/ µL, *p*-value <0.01) significantly increased in cases compared to controls. On the other hand, no significant differences found for mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) between cases and controls.

Table (2): Hematological parameters of the different study groups

Parameters	Case	Control	% Change	*P*-value [a]
Hb (g/dl)	10.6±1.6	13.4±0.9	-20.9	0.002
RBCs (×10^6/µL)	3.5 ± 0 .9	4.9 ±0 .1	-28.6	0.001
WBC×10^3/µL	9.1 ±3.8	6.6 ±1.6	37.9	0.002
Hct (%)	35.9±3.9	43.3±1.3	-17.1	0.001
MCV (fl)	85.5 ±9.5	84.9 ±3.0	0.71	0.754
MCH (pg)	28.9±3.1	29.7 ±1.1	-2.7	0.191
MCHC (g/dl)	32.5±2.0	33.9±1.0	-4.13	0.001
RDW (%)	16.3 ±3.1	13.0 ±0.72	25.4	0.001
PLT×10^3/µL	365.2 ±160.6	257.8 ±65.0	41.7	0.002

RBC; Red blood cell, WBC; White blood cell, PLT; Platelet, Hb; hemoglobin, Hct; Hematocrit, MCV; mean corpuscular volume, MCH; mean corpuscular hemoglobin; MCHC; mean corpuscular hemoglobin concentration; red cell distribution width. Values expressed as mean ± standard deviation (SD) of 90 participants.

[a] The significance of difference was checked by independent sample T test (compare all vs. control), significant at $P \leq 0.05$.

3.3. Biochemical parameters:

The mean levels of serum vitamin B_{12} and iron showed significant decreases with differences of (-27.1%, -38.2%, *P*=0.001) among cases compared to controls (table 3). In contrast, serum ferritin and C-reactive protein showed a significant elevation with percentage differences of (87.7%, 60.5% *P*<0.01) in cases compared to controls. Table (4) reveals that 26.7% of Crohn's disease patients and 3.3% of controls had a high level of CRP (>5.0 mg/L**)**. On the other hand, 73.3% of Crohn's disease patients and 96.7% of controls had a normal level of CRP (*P* <0.001). Crohn's disease patients are 10.6 times at a higher risk of having high CRP level compared to apparently healthy individuals (OR 10. 6% CI (3.1– 36.5), *P*<0.001).

Table (3): Serum iron, ferritin, and Vitamin B12 levels of the study population.

Parameters	Case	Control	% Change	*P*-value [a]
Vitamin B_{12} level (pg/ml)	309.8±123.4	425.1±64.8	-27.1	0.001
Iron level (µg/dl)	50.6±19.4	81.9±5.6	-38.2	0.001
Ferritin (ng/ml)	140.2± 115.7	74.7± 2.7	87.7	0.003
CRP (mg/L)	6.1± 1.1	3.8± 0.84	60.5	0.001

Vitamin B_{12} Low level < 174 pg/ml, Normal 174-878 pg/ml, High > 878 pg/ml,
Serum iron in men; low < 35 µg/dl, Normal 35-168 µg/dl, High > 168 µg/dl, in women: low < 23, Normal 23-134 µg/dl and High > 134 µg/dl, Serum ferritin in men; 20-250 ng/ml and in women 10-120 ng/ml and C-reactive protein (CRP); Normal CRP <5 mg/L, High CRP >5 mg/L.
Values expressed as mean ± standard deviation (SD) of 90 participants.
[a] The significance of difference was checked by independent sample T test (compare all vs. control), significant at $P \leq 0.05$.

Table (4): Association between Crohn's disease and CRP

Category	Case N (%)	Control N (%)	CI (95% interval)	*P*-value [a]
High CRP	24 (26.7)	3 (3.3)	10.6 (3.1– 36.5)	< 0.001
Normal CRP	66 (73.3)	87 (96.7)		

C-reactive protein (CRP); Normal CRP <5 mg/L, High CRP >5 mg/L

Values expressed as mean ± standard deviation (SD) of 90 participants.
[a] The significance of difference was checked by chi square test (compare all vs. control), significant at P ≤ 0.05.

In addition, table (5) demonstrates that the mean level of vitamin B_{12} (402.9± 84.5 pg/ml vs. 276.0±118.9 pg/ml) and serum ferritin (306.3±111.6 ng/ml vs. 79.8±4.9 ng/ml) significantly increased in Crohn's disease patients with a high CRP (>5.0 mg/L**)** compared to normal CRP patients (*p*-value ≤0.01). Meanwhile, serum iron levels in Crohn's disease patients with a high CRP (>5.0 mg/L**)** significantly decreased compared to normal CRP patients (29.8±4.0 µg/dl vs. 58.2±17.0 µg/dl, percentage of change = -48.8, *P*=0.001). Analyses using the Pearson correlation coefficient shown in table (6) revealed significant correlations between vitamin B_{12}, serum iron, ferritin and C-reactive protein levels with other hematological and biochemical parameters. Among these important correlations are a positive correlation between vitamin B_{12} levels with Hb, Hct, RBC, WBC and PLT and a negative correlation with MCV and MCH (*P*≤0.01). The iron levels show a positive correlations with CRP, Hb, Hct, RBC, PLT, MCH and MCV (P≤0.05) and a negative correlations with WBC, and RDW (r=-0.72, -0.82, P≤0.01). Statistically significant positive correlations were reported between serum ferritin levels with CRP, WBC and PLT (P≤0.01) and negative correlations with iron, Hb, Hct, MCV and MCH (r = -0.62, -0.28, -0.28, -0.40 and -0.48 respectively, P≤0.05).

Table (5): Association between CRP in Crohn's disease patients with Vitamin B12, iron and ferritin levels.

Parameters	Crohn's disease patients		% Change	*P*-value [a]
	High CRP (>5 mg/L)	Normal CRP (<5 mg/L)		
Vitamin B_{12} level (pg/ml)	402.9± 84.5	276.0± 118.9	46.0	0.010
Iron level (µg/dl)	29.8± 4.0	58.2± 17.0	-48.8	0.001
Ferritin (ng/ml)	306.3± 111.6	79.8± 4.9	283.4	0.001

Vitamin B_{12} Low level < 174 pg/ml, Normal 174-878 pg/ml, High > 878 pg/ml,

Serum iron in men; low < 35 µg/dl, Normal 35-168 µg/dl, High > 168 µg/dl, in women: low < 23, Normal 23-134 µg/dl and High > 134 µg/dl and Serum ferritin in men; 20-250 ng/ml and in women 10-120 ng/ml

Values expressed as mean ± standard deviation (SD).

[a] The significance of difference was checked by independent sample T test (compare all vs. control), significant at $P \leq 0.05$.

Table 6. The correlation of vitamin B12, iron, ferritin with study parameters

Parameters	Vitamin B_{12} (µg/dl)	
	Pearson correlation (r)	***P*-value**
Hb	0.57 [a]	0.001
Hct	0.52 [a]	0.001
RBCs	0.73 [a]	0.001
WBCs	0.33 [b]	0.010
PLT	0.33 [a]	0.010
MCV	-0.62 [a]	0.001
MCH	-0.40 [a]	0.002
	Iron (µg/dl)	
CRP	0.45 [b]	0.050
Hb	0.45 [a]	0.001
Hct	0.49 [a]	0.001
RBCs	0.37 [a]	0.003
WBCs	-0.72 [a]	0.001
PLT	0.70 [a]	0.001
MCV	0.53 [a]	0.001
MCH	0.69 [a]	0.001
RDW	-0.82 [a]	0.001
	Ferritin (ng/ml)	
Iron	-0.62 [a]	0.001
CRP	0.46 [a]	0.001
Hb	-0.28 [b]	0.030
Hct	-0.28 [b]	0.032
WBCs	0.43 [a]	0.001
PLT	0.39 [a]	0.002
MCV	-0.40 [a]	0.001
MCH	-0.48 [a]	0.001
RDW	-0.54 [a]	0.001
	C-reactive protein (mg/L)	
MCHC	-0.27 [b]	0.039

RBC; Red blood cell, WBC; White blood cell, PLT; Platelet, Hb; hemoglobin, Hct; Hematocrit, MCV; mean corpuscular volume, MCH; mean corpuscular hemoglobin; MCHC; mean corpuscular hemoglobin concentration; red cell distribution width and CRP: C-reactive protein.

[a] Correlation is significant at the 0.01 level (2-tailed); [b] Correlation is significant at the 0.05 level (2-tailed).

4. Discussion

Crohn's disease disorder is a persistent gastrointestinal inflammatory condition of unknown etiology. At the turn of the 21st century, inflammatory bowel disease has become a global disease with accelerating incidence in newly industrialized countries whose societies have become more westernized (Ng et al., 2017). Anemia, a common complication associated with inflammatory bowel disease, frequently ignored in the management of IBD patients. Appropriately, anemia represents one of the major causes of both decreased quality of life and increased hospital admissions among population (Guagnozzi & Lucendo, 2014). Crohn's disease anemia is a common trouble of a multifactorial origin; intestinal blood loss along with chronic inflammation regarded as the most important mechanism in the pathogenesis of anemia in Crohn's disease (Mücke et al., 2017; Semrin et al., 2006).

Our results showed that the levels of Hb, RBC, HCT and MCHC notably fall among Crohn's disease patients compared to controls. Related observations of our findings were described elsewhere (Wilson et al., 2004). Song et al., in 2012 reported that these parameters constitute an independent indicator for predicting the disease activity in patients with CD without anemia (Song et al., 2012). Both iron deficiency and anemia of chronic disease contribute most to the development of anemia in IBD. Anemia was described by WHO as a hemoglobin concentration less than 12 g/dL in non-pregnant women and less than 13 g/dL in men (WHO, 2011). These criteria are observed in our results as the mean level of hemoglobin (Hb – 10.6±1.6 g/dL vs. 13.4±0.9 g/dL) significantly decreased among cases compared to controls with p-value <0.01 and this findings in agreement with Gasche et al. study (Christoph Gasche et al., 2007).

Anemia is a key symptom in IBD that involves more than one pathogenic mechanisms resulting in low hemoglobin levels, endless blood loss from chronically inflamed intestinal mucosa and micronutrient deficiency (iron and B_{12}) (C Gasche et al., 2004). A

review by Stein et al. revealed that the cause of anemia in patients with IBD is multifactorial; resulting from iron deficiency secondary to blood loss through the ulcerations of the intestinal mucosa, reduced iron absorption and reduced iron intake (Stein et al., 2010).

The results indicate that CD patients have a low level of iron in comparison to apparently healthy individuals. This finding was in agreement with other studies in other settings (Annibale et al., 2001). Semrin et al. proposed that inflammatory cytokines released by the inflamed bowel inhibit intestinal iron absorption as it correlates with the disease activity and the markers of inflammation in Crohn's disease (Semrin et al., 2006). These findings may reveal that intestinal blood loss and chronic inflammation are regarded as the greatest important mechanisms in the pathogenesis of anemia in Crohn's disease (C Gasche et al., 1994). Intestinal inflammation is mediated by overproduction of cytokines, which contribute to the generation of anemia in chronic diseases، followed by insufficient production of erythropoietin, consequently IBD anemia is an example of chronic iron deficiency and anemia of chronic diseases combination (Ebinger et al., 2004).

In contrast, the results revealed that serum ferritin showed significant increase in CD patients compared to controls. Similar records were described by Kulnigg et al. (Stefanie Kulnigg et al., 2008). Serum ferritin, the gold standard test for iron deficiency (Goddard et al., 2011), can be normal or even elevated in response to inflammation, as it is an acute phase reactant even in the presence of severe iron deficiency. Even though, serum ferritin is generally considered as the most efficient indicator of iron deficiency (Oldenburg et al., 2001).

Vitamin B_{12} level was significantly lower among Crohn's disease patients compared to apparently healthy controls. Similar observation of our results was reported elsewhere (Yakut et al., 2010). Vitamin B_{12} abnormalities are common in CD, and patients with a prior ileal or ileocolonic resection are at particular risk (Headstrom et al., 2008). Multiple probable mechanisms that might lead to B_{12} deficiency. These include inflammation of the distal ileum, development of fistulas, a small intestinal bacterial overgrowth, and resection of the distal ileum. The possible contributors of anemia include CD Patients, impaired absorption of vitamin B_{12}, and extensive bowel resection (Yakut et al., 2010).

Diagnostic standards for iron deficiency need to be adjust to the level of inflammation. The mean levels CRP showed a significant increase in cases compared to apparently healthy individuals. The CRP is generally considered the best laboratory marker of inflammation (Koon et al., 2017). CRP is the classical acute phase of plasma protein that increases dramatically in concentration in response to many forms of tissue injury, inflammation and malignant neoplasia (Hedlund, 1961). In addition, a marked elevation of CRP levels exist in some patients with CD, and other patients showed normal levels of CRP. Similar findings were obtained in Click et al., study (Click et al., 2015). The increase in CRP among CD patients may probably indicate occult inflammatory activity though genetic differences in the capacity to produce CRP. It is therefore possible that the varying CRP responses are seen in CD patients and may be in part a reflection of individual genetic factors (Fagan et al., 1982). The quantitative determination of serum CRP provides an objective criterion of inflammatory activity, which may be useful in the assessment, management, and study of Crohn's disease.

5. Conclusions

The mean levels of Hb, RBC, HCT, MCHC, serum vitamin B_{12} and iron showed significant decreases while ferritin and CRP showed significant increases in Crohn's disease patients than in healthy controls. Crohn's disease was associated vitamin B_{12}, iron deficiency and inflammatory markers. C-reactive protein, ferritin, iron and vitamin B_{12} are useful laboratory index, which may be convenient in the assessment and management of Crohn's disease. Routine screening for complete blood count, vitamin B_{12}, iron deficiency and inflammatory markers in Crohn's disease patients are necessary. Further, in depth researches are need.

Conflicts of interest: The authors declare no conflicts of interest.

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