Correlation of IDA severity with endoscopic, histopathological and serological findings in CD patients at AL-Anbar district, [west of Iraq]: A Comparative cross-sectional study

Correlación de la gravedad de la IDA con hallazgos endoscópicos, histopatológicos y serológicos en pacientes con EC en el distrito de AL-Anbar, [oeste de Irak]: una comparación estudio transversal

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Abstract

Celiac disease (CD) is an autoimmune disorder described as a chronic inflammatory reaction due to gluten ingestion, which induces a particular degree of villous atrophy & possible -nutrient -malabsorption. Multi etiological factor of Anemia in CD patients; at the same time, iron deficiency anemia (IDA) may also be the most frequently recorded characteristic in children and adults with CD perhaps it is a unique finding existing. No previous study regarding the correlation of endoscopic, histopathological, and serological features of CD patients with IDA at Al-Anbar province. To find the correlation between the severity of IDA with endoscopic, histopathological, and serological features of CD patients. Hospital-based comparatives cross-sectional study was conducted in the Gastroenterology Clinic of AL-Ramadi teaching hospital attached to Anbar Medical College, Ramadi, Iraq from August 2017 through June. 2020. A total of 108 consecutive new CD cases with iron-deficiency anemia, 70 of them were females, and 38 were males. CBC, blood films, ferritin level, endoscopic findings had been registered for all CD patients. In every CD case, gastro¬intestinal biopsies in addition to lgA (AntitTG levels) had been recorded. Histo¬pathology outcomes had been separated through the use of "taxonomy of modified¬ Marsh". A proper suitable statistical analysis had observed results. A total of 108 CD patients with iron deficiency anemia the mean age was 28.86 with a range from 15 -66 years; the female was 64.8% and male 35.2%. There was a weak negative significant correlation Corr. Coef (r) (R=-0.003, p=0.000& R=-0.0180.161, p=0.000) amongst endoscopic and histopathological findings with IDA severity (HB gr%) respectively of CD patients using spearman's correlation coefficients (r). Negatively non-significant correlation of Anti- tTG level with IDA severity of CD (HB gr%) patients as detected through the use of Pearson's correlation (R=-149; P values 0.123). A weak negative significant correlation was found between the severity of IDA with endoscopic, histopathological finding, and but there was a negatively non-significant correlation between anti- tTG lgA level and IDA severity in CD.

Keywords: Iron deficiency anemia, celiac disease, Endoscopy, histopathology, lgA anti tTG, Cross-sectional study, Ramadi district, Iraq.

Resumen

La enfermedad celíaca (EC) es un trastorno autoinmune descrito como una reacción inflamatoria crónica debida a la ingestión de gluten, que induce un grado particular de atrofia vellositaria y posible malabsorción de nutrientes. Factor etiológico múltiple de la anemia en pacientes con EC; Al mismo tiempo, la anemia ferropénica (AIF) también puede ser la característica más frecuentemente registrada en niños y adultos con EC. Quizás sea un hallazgo único existente. No hay ningún estudio previo sobre la correlación de las características endoscópicas, histopatológicas y serológicas de los pacientes con EC con AF en la provincia de Al-Anbar. Encontrar la correlación entre la gravedad de la AF con las características endoscópicas, histopatológicas y serológicas de los pacientes con EC. Se realizó un estudio transversal comparativo basado en hospitales en la Clínica de Gastroenterología del hospital universitario AL-Ramadi adjunto al Colegio Médico de Anbar, Ramadi, Irak, desde agosto de 2017 hasta junio. 2020. Un total de 108 nuevos casos consecutivos de EC con anemia ferropénica, 70 de ellos mujeres y 38 hombres. Se había registrado hemograma completo, frotis de sangre, nivel de ferritina y hallazgos endoscópicos para todos los pacientes con EC. En todos los casos de EC, se registraron biopsias gastrointestinales además de IgA (niveles de AntitTG). Los resultados histopatológicos se habían separado mediante el uso de "taxonomía de pantanos modificados". Los resultados se habían observado mediante un análisis estadístico adecuado. De un total de 108 pacientes con EC con anemia ferropénica, la edad media fue de 28,86 años con un rango de 15 a 66 años, la mujer 64,8% y el hombre 35,2%. Hubo una correlación significativa negativa débil Corr. Coef (r) (R=-0.003, p=0.000 & R=-0.0180.161, p=0.000) entre los hallazgos endoscópicos e histopatológicos con severidad IDA (HB gr%) respectivamente de pacientes con EC usando los coeficientes de correlación de Spearman (r). Correlación negativamente no significativa del nivel de Anti-tTG con la gravedad de la IDA de los pacientes con EC (HB gr%) detectada mediante el uso de la correlación de Pearson (R=-149; valores de P 0,123). Se encontró una correlación negativa significativa débil entre la gravedad de la IDA con el hallazgo endoscópico e histopatológico, pero hubo una correlación negativa no significativa entre el nivel de IgA anti-tTG y la gravedad de la IDA en la EC.

Palabras clave: Anemia por deficiencia de hierro, enfermedad celíaca, endoscopia, histopatología, lgA anti tTG, estudio transversal, distrito de Ramadi, Irak.

Introduction

Celiac disease (CD) is an autoimmune disorder described as a chronic inflammatory reaction due to gluten ingestion, which induces a particular degree of villi atrophy & possible -nutrient –malabsorption[1].

Its identification depending on the existence of duodenal villous ¬atrophy that appear histologically, in addition to +ve ABs against specific target antigens, especially tissue "transglutaminase" with "gliadin" or endomysium and also biopsies examination[2]. Villous ¬atrophy findings on superior Endoscopy may appear for example "scalloped folds" or some time a mosaic pattern[3]. It has a wide variety of clinically silent cases from overt malabsorption or standard gastrointestinal symptoms[4]. IDA is a predominant sign of CD extra intestinally & was defined as the sole- sign of the CD disease[5,6].

Multi etiological factor of Anemia in CD patients; at the same time, iron deficiency anemia (IDA) may also be the most frequently recorded characteristic in children and adults with CD perhaps it is a unique finding existing[7]. Stimulatingly, in the CD, IDA is not only linked to damage of gluten driven in the intestinal mucosa, because IDA has also been described in serology positive CD patients earlier the duodenal atrophy progress[8].

This confirms that there is a need for IDA testing in patients with CD, with the recommendation and in the early stages to give a gluten-free diet to these patients who display the so-called "celiac trait" (with manifestations outside the intestine)[9].

IDA might also be the most frequently recorded characteristic in children &adults with CD; perhaps it is unique finding existing[10-12].

The chief mechanism for IDA in CD is linked to malabsorption because the iron absorption location in the proximal duodenum is virtually permanently involved[13].

No previous study regarding the correlation of endoscopic, histopathological, and serological features of CD patients with IDA at Al-Anbar province.

Patients and methods

Of 108 consecutive fresh patients aged over 15 years identified in the Gastroenterology Clinical department in ALRamadi teaching hospital during a period from August 2017 to June 2020 had been involved through using a retrospective cross-sectional epidemiological study. Seventy of them were females & other males. ELISA registered CBC, blood films, ferritin levels, lgA Anti tTG levels.

During the present study, gastrointestinal tract bleeding with patients with thalassemia had been excluded. Basically, IgA anti tTG< 10 IU/ml measured as a negative, whereas IgA anti tTG 10.1-20 IU/ml measured as suspicious even in the clinical- symptoms nonappearance CD patients. Whoever, IgA anti tTG >20 IU/ml were considered measured as a positive as described by the manufacturer & it had a calibration- a variety of 3 to 100 IU/ml.

Endoscopy of the upper gastrointestinal tract with four duodenum biopsies from D2 was carried out for all patients with the estimate of endoscopic markers of the duodenum that include, “reduction in duodenal folds”, scalloping of duodenal folds, the presence of mucosal fissures, and nodularity of the mucosa. Results of histopathology were categorized according to the “modified¬Marsh arrangement”[14,15].

Two expert pathologists have observed the specimen. Gender had been identified as a CD using “Gastroenterology ¬WHO¬ criteria”[16]. CD identification frequently depending on “serological EMA¬IgA¬antibodies” as well as “anti-tTG antibodies” positivity[17], &/or[18], plus anti¬tTG specific Abs targeting intestinal- mucosa histopathological antigens[19].

Severity of IDA was classified according to Hb gr% level in non-pregnant female (15 years of age and above) [normal >=12 gr% mild anemia 11-10.9gr%, moderate 10.9-8 gr%, sever <8gr%.and in male (15 years of age and above) normal Hb >=13gr%, mild 12.9-11 gr%, moderate 10.9-8gr%, sever <8 gr%[20,21].

CD patients with missing medical data have been excluded from the current study. Family recorded consent was taken from a total of patients. Ethical approval of the current study was taken from the Anbar medical faculty ethics approval Committee, Iraq.

Statistical- Examination: Statistical- investigation of our data was through using- the SPSS/software 24.0. Correlation of endoscopic, histopathological, and serological features of CD patients with IDA was calculated according to Pearson and spearman correlation. The variance in the concordance output was verified using the chi-square test.

Results

Of108 CD examinations patients during a year of study, 35.2% of them were male, and 64.8% were females giving a male/female 1:1.8. The range of age was from 15 years to 66 years. The mean age was (28.86±12.597 years). Most of the patients with CD presented in Hb% group 8-10.9 (48; 44.4%) followed by 11 and over (45;13.9%), while the remaining 15 [13.9%], was with Hb < 8gr shown in Table 1. A statistically significant between- different Hb % groups of CD patients (P-Value 0.000) (Table 1).

Regarding the Endoscopy, the study showed that 23 (21.3), 58 (53.7), 4 (3.7) and1 (0.9) of CD patients were with a reduction in duodenal folds, scalloping, mucosal fissures, and atrophy with visible vessels respectively while the other 22 (20.4) of CD patients were normal Endoscopy. There was statistically significant between different endoscopic features of CD patients (P-Value 0.000) (Table 1)

Regarding the histopathological features, the study showed that 41(38.0%), 33(30.6%), 26(24.1%), 5 (4.6%) and1 (0.9%) of CD patients were with G3A, G3B, G3C, G2, and G1respectively while the other 2(1.9%) of CD patients were normal histopathological features. There was a statistically significant between different histopathological features of CD patients (P-Value 0.000) (Table 1).

Table 1. General characteristic of endoscopic, histopathology and Hb % groups findings of CD patients

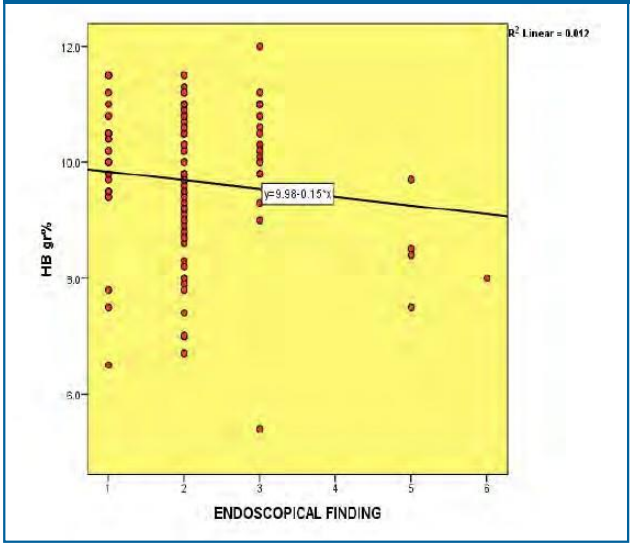
Negatively correlation (Corr. Coef (r)) of endoscopic finding with IDA severity of CD (HB gr %) of celiac disease patients as measured by using a spearman’s correlation (R-0.003; P values 0.000) (Table 2, Figure, 1B). There was a weak correlation of endoscopic finding with the IDA severity of CD (HB gr %) the determined the grade of anemia of celiac disease patients as measured by using “spearman’s correlation” (R 0.014; p-values 0.000) as shown in Table 2 and Figure 1

Endoscopic finding	No.(%)	Histopathology	No.(%)	Hb gr%	No.(%)
Reduction in duodenal folds	23 (21.3)	G3A	41(38.0%)	< 8gr	15(13.9%)
Scalloping	58 (53.7)	G3B	33(30.6%)	8-10.9	48(44.4%)
Normal	22 (20.4)	G3C	26 (24.1%)	>=11	45(41.7%).
Mucosal fissures	4 (3.7)	G2	5 (4.6%)		
Atrophy with visible vessels	1 (0.9)	G1	1 (0.9%)		
		Normal	2 (1.9%)		
p.value 0.000		p.value=0.000		p.value=0.000	

Table 2: Correlation between Hb count (gr%) and endoscopical finding in CD patients (n = 108)

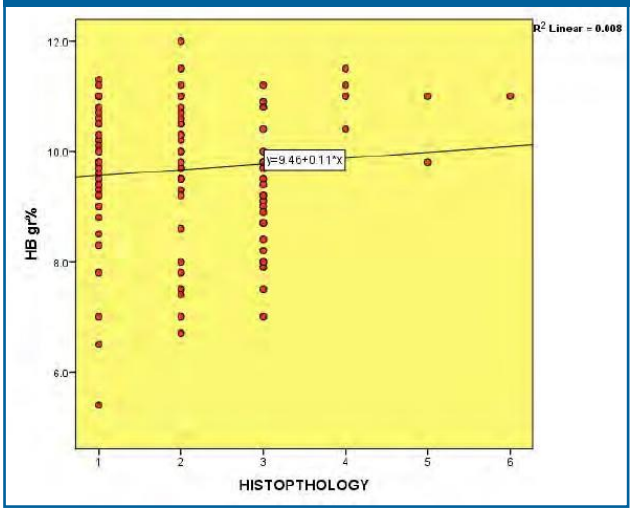
Endoscopic finding	Mean of HB gr % (No. of patients)						Spearman's Correlation
HB gr% group	<8	8-10.9	> 11	Mean of Hb	P-value	Endoscopic finding with HB gr% group	Endoscopic finding with HB gr%
Reduction in duodenal folds	7.267% (3)	9.644% (9)	10.773 (11)	9.874 (23)			
Scalloping	7.422% (9)	9.255% (29)	10.805% (20)	9.505 (58)			
Normal	5.400% (1)	9.671% (7)	10.779% (14)	10.182 (22)			
Mucosal fissures	7.500% (1)	8.867% (3)	0.0% (0)	8.525 (4)			
Atrophy with visible vessels	8.000% (1)	0.0% (0)	0.0% (0)	7.300 (1)	0.000	0.014	-0.003
Total	7.300%	9.365%	10.789%	9.671			

Figure 1: Correlation between Hb count (gr%) and Endoscopical finding in CD patients (n = 108).



Negatively Correlation (Corr. Coef (r)) of histopathological finding with IDA severity (HB gr %) of CD patients as measured by using "spearman's correlation" (R-0.018; p values 0.000) (Table 3, Figure, 2). There was a weak correlation of histopathological findings with the IDA severity (HB gr %) of CD that determined the grade of anemia of celiac disease patients as measured by using "spearman's Correlation" (R 0.030; P values 0.000) as described in Table 2, Figure 1.

Figure 2: Correlation between Hb count (gr%) and histopathology in celiac disease patients (n = 108) Correlation was significant at the 0.01 level (2-tailed).



Negatively Correlation, (Corr. Coef (r)) of Anti- tTG level with IDA severity (HB gr %) of CD patients as measured by using a "Pearson's correlation" (R-.149-; p values 0.123) as described in Table 3, Figure 2.

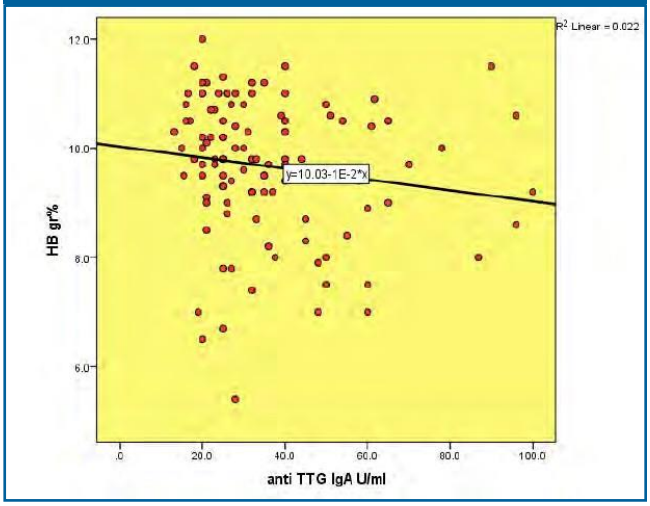
Table 3: Correlation between Hb count (gr%) and Histopathology in CD patients (n = 108)

	Mean of HB gr% (No. of patients)					Spearman's Correlation	
Hb gr% group	Hb<8 gr	Hb 8-10.9 gr%	Hb >11gr%	Mean Hb	P-value	histopathology with Hb gr% group	histopathology with Hb gr%
G3A	6.675%	9.375%	10.65%	9.644			
G3B	7.40 %	9.527	10.81%	9.767			
G3C	7.68%	9.213%	10.820%	9.227			
G2	0.0%	0.00%	11.02%	11.020	0.000	0.030	-0.018
G1	0.0%	0.0%	11.00%	11.000			
Normal	0.0%	9.800%	11.000%	10.400			
Total	7.30%	9.365%	10.789%	9.671			

Table 4: Correlation between Hb count (gr%) with anti -tTG U/ml in celiac disease patients (n = 108)

Anti- tTG level	Hb gr% <8	Hb gr% 8-10.9	Hb gr% >11	Mean Hb	P-value	Pearson Correlation
10.1-20	12 (12.9%)	41 (44.1%)	40 (43.0%)	9.713	0.123	**-.149-**
>20	3 (20.0%)	7 (46.7%)	5 (33.3%)	9.413		
Total	15 (13.9%)	48 (44.4%)	45 (41.7%)			

Figure 3: Correlation between Hb count (gr%) with anti tTG IgA U/ml in CD patients (n=108



Discussion

Our study revealed female predominance which was identical to the US, Europe, & Middle East as overall showed a female –predominance of CD patients[22-24], the causes are unknown but might due to the autoimmune-mediated illnesses generally more predominant in females[25].

The study showed a weak negative correlation between endoscopic finding and anemia severity this finding is consistent with the research done by Mauri no et al.[26] and Kalhan S, et al.[27] and inconsistent with the study done by Oxentenko et al.[28].

20.4% of our CD patients with the iron-deficiency anemia had routine Endoscopy. "Endoscopic markers" nonappearance of villous atrophy doesn't reject the identification & duodenal biopsies must be complete in cases of clinical & o, CD laboratory suspicion[29,30].

Our study showed a weak negative correlation with the severity of anemia and duodenal histopathology this finding is consistent with Zamani et al. [31] and inconsistent with Ganji et al.[32].

Our study revealed 2 cases of positive serology and normal Endoscopy and histopathology; these are considered as latent celiac[33].

Our study revealed that there is a negative non-significant correlation between anti-tTG lgA level and severity of anemia, this result was inconsistent with the result reported by Ertekin et al. who identified that Hb levels of CD patients negatively correlated with tTG titers[34].

Conclusions

Our study identified a weak negative significant correlation was registered between the severity of IDA with endoscopic, histopathological findings. A negatively non-significant correlation between anti- tTG IgA level and IDA severity in CD

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