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STUDY THE EFFECT OF HELICOBACTER PYLORI INFECTION ON SERUM GHRELIN IN HAEMODIALYSIS PATIENTS

SHAIMAA MOHAMMED M. SALEH EL SHEMI
Internal Medicine Department, Faculty of Medicine, Tanta University, Egypt.

NELLY DESOUKY EL SHALL
Internal Medicine Department, Faculty of Medicine, Tanta University, Egypt.

AMAL SAEED EL BENDARY
Clinical Pathology Department, Faculty of Medicine, Tanta University, Egypt

AHMED FAWZY SELIM
Internal Medicine Department, Faculty of Medicine, Tanta University, Egypt.

MOHAMED ELSAYED SARHAN
Internal Medicine Department, Faculty of Medicine, Tanta University, Egypt.

Abstract

Background: Ghrelin metabolism is affected by variations in residual renal function and one of the most important factors affected on serum ghrelin concentrations was found to be Helicobacter pylori (H. pylori) infection in gastric mucosa. **Aim of the study:** The aim was to assess the effect of H. pylori infection on serum Ghrelin in hemodialysis cases **.Methods:** This prospective study including 90 participants, 70 CKD patients who received hemodialysis three times per week and 20 healthy volunteers. Group (1):35 CKD patients on hemodialysis with a positive H. Pylori infection. Group (2): 35 CKD Patients on hemodialysis with negative H. Pylori Infection. Group (3):20 apparently healthy age and gender matched volunteers as a control group. All eligible cases were evaluated for CBC, renal function tests, H. pylori stool Ag test and serum Acylated Ghrelin using ELISA technique **.Results:** Ghrelin levels were significant difference among the three groups (P<0.001). Ghrelin level was significantly decreased in group 1 than group 2 and 3(P<0.001) and insignificantly between group 2 and group 3. **Conclusion:** In patients with a positive H. Pylori infection, Ghrelin levels were much lower than those of patients with a negative H. Pylori infection and healthy persons.

Keywords: Ghrelin levels: Helicobacter Pylori: Hemodialysis: Chronic Kidney Disease

INTRODUCTION

The number of end-stage kidney disorder cases obtaining hemodialysis (HD) is more than 1.1 million global, and the size of this population is increasing at a rate of 7% per year. [1]

The HD cases frequently suffer from gastrointestinal disorders like bleeding, peptic ulcer and gastric cancer. Helicobacter pylori (H. pylori) infection produces atrophic gastritis, peptic ulcer and gastric cancer, and is believed to be one of the most risk factors for gastrointestinal morbidity in HD cases. [2-4]

Risk factors for death in HD patients include typical cardiovascular risk factors as well as chronic inflammation and dietary disruption. [5]

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Orexigenic peptide ghrelin, secreted predominantly by stomach endocrine cells, might play a role in the occurrence of protein energy wasting in HD cases.[6-8]

In addition to enhancing orexigenic effects, protein anabolism, anti-inflammatory properties, and cardiovascular protection, ghrelin has other beneficial roles. Cases with heart failure who have low ghrelin have an improved risk of cardiovascular death and morbidity. [9-10]

H. pylori, which is a gram-negative spiral rod which lives in mucus adhering to stomach mucosa, is the most prevalent infection in the world. Helicobacter pylori has been attached to insulin resistance and the metabolic syndrome in epidemiological research. [11-12]

Infection with Helicobacter pylori in the gastric mucosa has been identified as one of the most influential variables on blood ghrelin levels. [13]

Our aim was to assess the influence of H. pylori infection on serum Ghrelin in hemodialysis Patients.

PATIENTS AND METHOD

Our research was done in line with the Helsinki Declaration and was approved by the local institutional ethics committee of our faculty of medicine (32220/04/18). An informed consent was taken from all cases.

Our prospective research was performed at the outpatient clinic of internal medicine department at our university hospitals, from August 2021 to April 2022. 90 participants were recruited, 70 CKD patients who received hemodialysis three times per week and 20 healthy volunteers. The following groups were studied:

Group (1):35 CKD patients on hemodialysis with a positive H. Pylori infection

Group (2):35 CKD Patients on hemodialysis with negative H. Pylori Infection

Group (3):20 apparently healthy age and gender matched volunteers without any risk factors or chronic diseases were recruited as control group

We excluded any patient with past history of H.pylori eradication, patient with Gastrectomy and patients with malignant tumors. All participants were subjected to full History taking: There was a record of each patient's demographic and clinical data such as age and gender, main renal illness, comorbid diseases, drugs used during the last three months and previous medical history .All eligible participants were evaluated for CBC, renal function tests, H.pylori stool Ag test and serum Acylated Ghrelin using ELISA technique

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STATISTICAL ANALYSIS

SPSS v28 (IBM, Chicago, IL, USA) was utilised for statistical analysis. The Shapiro-Wilks test and histograms were employed to determine whether or not the distribution of data was normal. The mean and standard deviation (SD) of quantitative parametric variables were presented and analyzed by the ANOVA (F) test with post hoc tests (Tukey). To compare the two groups, Kruskal-Wallis and Mann Whitney tests were utilized to compute the median and interquartile range (IQR). The Chi-square test was utilized to analyze the frequency and proportion (percentage) of qualitative data. P-values less than 0.05 were deemed statistically significant. [14]

RESULTS

No significant differences founded among all groups related to age and sex, however there was significantly different in BMI among the studied groups (P value = 0.002). BMI was significantly increased in group 1 and 2 than group 3 (P=0.002, 0.026 respectively) and insignificantly different between group 1and group 2. The occurance of DM or HTN were insignificantly different among three groups, but the occurance of both DM and HTN were significant difference among studied groups (P=0.032). (Table 1)

(Table 2) Hemoglobin and hematocrit were significantly lower in group 1 and 2 than group 3 (P=0.003, 0.042, <0.001, <0.001 respectively). WBCs were significantly increased in group 1 and 2 than group 3(P<0.001) and insignificantly between group 1 and group 2. Platelets were insignificantly different among the three groups.

Albumin and glucose were significantly different among the three groups (P<0.001, P=0.006 respectively). Albumin was significantly decreased in group 1 and 2 than group 3 (P<0.001) and non-significant between group 1 and group 2.

Creatinine and urea were significant difference among the studied groups (P<0.001). Creatinine and urea were significantly increased in group 1 and 2 than group 3 (P<0.001) and insignificantly between group 1 and group 2.

(Table 3) Median of Ghrelin was 1.599 ng/ml with inter quartile range (IQR) of (0.39- 8.03) ng/ml in group 1, 2.602 ng/ml with IQR of (1.08- 6.13) ng/ml in group 2 and 3.256 ng/ml with IQR of (1.87-11.11) ng/ml in group 3. Ghrelin levels were significantly different among the studied groups (P<0.001). Ghrelin level was significantly decreased in group 1 compared to group 2 and 3(P<0.001) and insignificantly among group 2 and group 3.

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Table 1: The Main evaluated participants' demographic and clinical criteria

		Group 1 (n = 35)	Group 2 (n = 35)	Group 3 (n = 20)	P value		
Age (years)	Mean ± SD	54.74 ± 7.13	54.20 ± 6.21	52.20 ± 6.37	0.397		
	Range	45 – 66	45 – 66	45- 66			
Sex	Male	22 (62.86%)	17 (48.57%)	14 (70.00%)	0.248		
	Female	13(37.14%)	18 (51, 43%)	6(30.00%)			
BMI (kg/m^2)	Mean ± SD	29.31 ± 1.53	28.91 ± 1.52	27.90 ± 1.33	0.002*	P1	0.500
	Range	27 – 33	26 -32	26- 30		P2	0.002
						P3	0.026
co-morbidities	DM	7(20%)	6 (17.00%)	0(00.00%)	0.108		
	HTN	8(23%)	7(20.00%)	0(00.00%)	0.073		
	HTN and DM	8(23%)	3(9.00%)	0(00.00%)	0.032*		

BMI: body mass index, * significant as p value <0.05, P1: P value between groups 1 and 2, P2: P value between groups 1 and 3, P3: P value between groups 2 and 3.DM: Diabetes Milletus, HTN: Hypertension

Table 2: Distribution of CKD patients on hemodialysis and controls according to laboratory investigations

		Group 1 (n = 35)	Group 2 (n = 35)	Group 3 (n = 20)	P value		
Hemoglobin (g/dl)	Mean ± SD	11.23 ± 0.79	11.47 ± 0.91	12.07 ± 1.01	0.005*	P1	0.512
	Range	9.8 - 12.6	9.8 - 12.6	10.6- 13.8		P2	0.003*
						P3	0.042*
WBC (/mm3)	Mean ± SD	8071.80± 888.50	8132.09± 971.57	6260.80± 1022.85	<0.001*	P1	0.962
	Range	6780- 9800	6780- 10000	4560- 7890		P2	<0.001*
						P3	<0.001*
Platelets	Mean ± SD	217.11 ± 23.99	219.26 ± 22.79	223.60 ± 15.23	0.397		
	Range	167 – 254	167 – 254	200- 254			
Hematocrit (%)	Mean ± SD	32.34± 2.21	32.51± 2.36	35.30± 2.00	<0.001*	P1	0.994
	Range	29- 35	29- 35	32- 39		P2	<0.001*
						P3	<0.001*
Albumin (g\dl)	Mean ± SD	3.63± 0.25	3.61± 0.29	4.41± 0.31	<0.001*	P1	0.964
	Range	3.2 - 3.9	3 -3.9	4- 5		P2	<0.001*
						P3	<0.001*
Random glucose (mg\dl)	Mean ± SD	183.80± 52.18	181.51± 43.72	140.10± 30.92	0.006*	P1	0.976
	Range	100- 259	100- 256	99- 193		P2	0.007*
						P3	0.012*
Creatinine (mg\dl	Mean ± SD	5.61± 0.76	5.47± 0.79	0.89± 0.09	<0.001*	P1	0.646

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	Range	4.3 -6.7	4.3 -6.7	0.78- 1		P2	<0.001*
						P3	<0.001*
Urea (mg\dl	Mean ± SD	101.20± 10.50	100.89± 11.63	26.15± 2.25	<0.001*	P1	0.990
	Range	89-120	80-120	23.6- 29.8		P2	<0.001*
						P3	<0.001*

* Significant as p value <0.05, P1: P value between groups 1 and 2, P2: P value between groups 1 and 3, P3: P value between groups 2 and 3.

Table 3: Distribution of CKD patients on hemodialysis and controls according to ghrelin levels

		Group 1 (n = 35)	Group 2 (n = 35)	Group 3 (n = 20)	P-value		
Ghrelin (ng/ml)	Median	1.599	2.602	3.256	<0.001*	P1	<0.001*
	Range	0.39- 8.03	1.08- 6.13	1.87-11.11		P2	<0.001*
						P3	0.172

* Significant as p. value <0.05, P1: P value between groups 1 and 2, P2: P value between groups 1 and 3, P3: P value between groups 2 and 3.

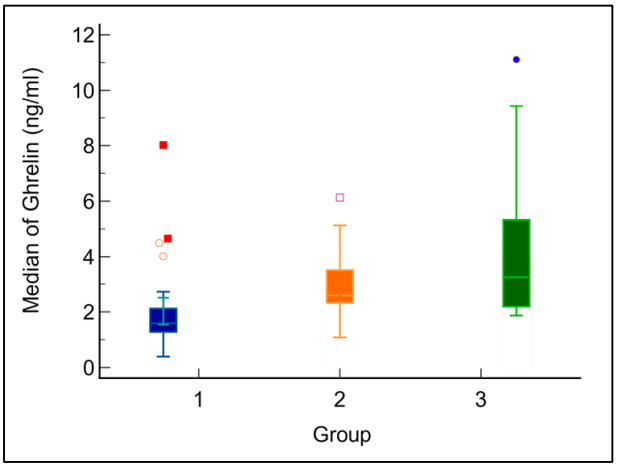

Figure 1: Distribution of CKD patients on hemodialysis and controls according to ghrelin levels

DISCUSSION

Patients with CKD may suffer from anorexia as a result of high levels of des-acyl ghrelin. Ghrelin metabolism is affected by variations in residual renal function. Ghrelin is broken down in the kidney. Decreased ghrelin breakdown in the kidney is the primary cause of an increase in total ghrelin levels in CKD. [15]

Helicobacter pylori infection of the stomach mucosa has recently been identified as a strong influence on serum ghrelin levels. Infected gastric endocrine cells produce less ghrelin when affected by H. pylori. [16]

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The purpose of this research is to assess the influence of Helicobacter pylori infection on serum ghrelin in individuals with HD

There was insignificantly different in age and sex among any of the groups examined in our research

BMI was significantly increased in group 1 and 2 than group 3 (P=0.002, 0.026 respectively) and insignificantly different between group 1and group 2

Ichikawa et al., (2019) conducted pilot research on 21 patients who undergo HD, maintain HD for four hours three times a week, and have H. Pylori in order to assess ghrelin serum concentrations prior and following eradication treatment. H. pylori eradication did not alter BMI significantly (P = 0.715), according to the findings. Their research's small sample size might be the cause of the discrepancy among their outcomes and those of the other studies.[17]

In our research we discovered that hemoglobin and hematocrit concentrations were significantly decrease in group 1 and 2 than control group.

GÜRSU et al. (2013) undertook an investigation on H. Pylori's effect on ghrelin levels in uremic individuals. There were 91 participants in the study: 29 in the control group (CG), 21 in HD, 12 in the peritoneal dialysis group (PD), 29 in the pre-dialysis group. According to the findings, uremic H. pylori-infected individuals had significantly lower hemoglobin levels and hematocrit levels than those in the control group.[18]

Our study results revealed that Albumin was significantly decreased in group 1 and 2 than group 3 (P<0.001) and non-significant between group 1 and group 2.

GÜRSU et al. (2013) found that albumin was considerably decreased in uremic individuals with H. Pylori than the control group (P=0.01) [18]

We found significantly different in ghrelin levels (P<0.001) in the three groups in this research. Group 1 had considerably lower ghrelin levels than groups 2 and 3 (P0.001), however there was insignificantly different between groups 2 and 3 (P>0.05)

Ichikawa et al., (2019) noticed insignificant change in ghrelin serum levels among cases before and after H. pylori eradication. Ghrelin levels rose significantly in the healthy group.[16]

Research published by Ichikawa et al., (2016) discovered that ghrelin concentrations were low in both the group that had been previously infected and those who had recently been infected. However, the control group had a significantly higher level (P= 0.001).[19]

One hundred sixty-three patients were studied in cross-sectional research by Mantero et al., (2018) Patients with H. Pylori had decrease concentrations of serum ghrelin than those had no infection.[20]

Although GÜRSU and colleagues, (2013), observed that ghrelin serum concentrations were significantly increased in the uremic group, whether infected or uninfected,

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compared to the healthy group. The patients in both trials were suffering from uremia, which explains the discrepancy. [18]

It has been reported by Osaka et al., (2016) that ghrelin acyl and des-acyl levels were identical in both present H. pylori positive and negative individuals, regardless of whether they were on dialysis or not. The discrepancy between the two studies may be explained by the fact that one research included individuals who had not undergone HD, while the other did.[21]

CONCLUSION

In patients with a positive H. Pylori infection, Ghrelin levels were much lower than those of patients with a negative H. Pylori infection and healthy persons.

There are still a number of questions that need to be answered about the effect of H. Pylori infection and its eradication on serum ghrelin levels and their relationship to hunger, weight, protein energy wasting and cardiovascular changes in CKD cases on Hemodialysis.

Abbreviations

CKD: chronic kidney disease; HD: hemodialysis: **H.pylori**; helicobacter pylori; **BMI**: body mass index; **CBC**: complete blood count; **WBCs**: white blood cells; **ELISA**: enzyme-linked immunosorbent assay; **DM**: Diabetes mellitus; **HTN**: hypertension; **CG**; control group; **PD;** peritoneal dialysis.

Ethics approval and consent to participate; the study was done based on the ethical standards of the 1975 Declaration of Helsinki and was approved by the local institutional ethics committee of our faculty of medicine (32220/04/18).

Conflict of interest disclosure statement: The authors report having no competing interests.

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Authorship (Authors' Contribution): Study concept and design: Mohamed E. Sarhan and Shimaa M. Elshemy. Data acquisition: All authors. Data analysis and interpretation: Amal S. El Bendary, Ahmed F.Selim and Nelly D. El shall. Drafting of the manuscript: Mohamed E. Sarhan, Shimaa M.El shemy and Ahmed F.Selim. Critical revision of the manuscript for important intellectual content: All Authors. Statistical analysis: All Authors. Final revision and manuscript approval for submission: All Authors.

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Availability of data and materials: Data that support the outcomes of this research are involved in the article.

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