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RESEARCH ARTICLE

Urinary Pepsinogen Levels in Peptic Ulcer: A Subclinical Marker for Better Diagnosis and Prediction of Risk Factors of Acid Peptic Disease

Mahabubunnisa Begum[1], Baderuzzaman[1], Sandeep Kumar vishwakarma[2], Nusrath Fathima[3], Syed Rahamathulla[2] Aleem A Khan*[4]

1. Department of Biochemistry, Owaisi Hospital and Research Centre, Deccan College of Medical Sciences, Kanchanbagh, Hyderabad-500 058, Andhra Pradesh, INDIA.
2. Centre for Liver Research and Diagnostics, Deccan College of Medical Sciences, Hyderabad-58, AP, INDIA.
3. Department of Genetics, Osmania University, Hyderabad, Andhra Pradesh, INDIA.
4. Salar-E-Millat Sultan Salahuddin Owaisi Centre for Cellular and Molecular Medicine, Hyderabad, AP, INDIA.

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Corresponding Author

Dr. Aleem A Khan
Associate Professor
Salar-E-Millat Sultan Salahuddin Owaisi Centre for Cellular and Molecular Medicine, Hyderabad-500 058, Andhra Pradesh, INDIA
aleem_a_khan@rediffmail.com

Abstract

Introduction
Acid peptic disease is a common gastrointestinal disorder accounting for considerable morbidity and economic loss. Previous studies from the west have demonstrated that 5-10% of the adult population can be expected to suffer from peptic ulcer during life time. However, serum pepsinogen estimation has been predictor and clinical marker for the diagnosis of peptic ulcer disease; it needs large volume of sample for estimation. Hence there is need to search for better choice of marker to overcome the previous hurdles.
Methods
Urine samples from seven hundred and sixty (760) subjects (492 males and 268 females, ages between 15-62 years) were collected randomly from different parts of Hyderabad. For fasting and post-prandial UPG estimation, urine samples from 34 subjects (24 patients and 10 controls) were collected. UPG levels were estimated by proteolytic assay.
Results
Overall in 760 cases, 188 subjects were found symptomatic and 532 were asymptomatic. 228 subjects (138 symptomatic and 96 asymptomatic) were found to have hyperpepsinogenuria, among these 102 subjects who underwent endoscopy, 30 were proved to have acid peptic disease and remaining non ulcer dyspeptic. Mean ratio of fasting/meal stimulated UPG levels found to be significantly high in patients (p value <0.001) as compared to the controls.
Conclusion
The pepsinogen present in the urine and serum represents group-I pepsinogen which plays important role in the pathogenesis of peptic ulcer. Elevated level of urinary pepsinogen indicates the hyper gastric secretory function which may serve as a subclinical marker for ulcer diathesis.

Introduction

Acid peptic disease is a common gastrointestinal disorder accounting for considerable morbidity and economic loss. This justifies continued effort to understand its epidemiology and pathogenesis. Population based studies on the prevalence of peptic ulcer are greatly hampered due to lack of a clinical marker for ulcer diseases. Rotter et al., (1979) employed a Radio Immunoassay (RIA) for quantification of serum pepsinogen-I as a subclinical marker and

reported that elevated level not only among peptic ulcer patient but also in their sibs. However, RIA is not the test of the choice for population studies which involves large samples. Since a positive correlation observed between serum pepsinogen-I and gastric acid output quantitation of urinary pepsinogen (represents pepsinogen-I activity) by proteolytic assay provides a simple reliable and convenient test for population studies (Rotter et al., 1979; Mujahid et al., 1986). A number of studies during the past three decades have shown that serum pepsinogen levels are elevated in patients with duodenal ulcer (Samloff et al., 1975; Plebani et al., 1983). Two studies have demonstrated that an elevated pepsinogen level is associated with an increased risk for developing this disorder (Mirsky et al., 1952; Chin, 1953). This test help in the identification of hyper pepsinogenemia-I and predicting the risk such individuals have of developing peptic ulcer.

Through this perception, urinary pepsinogen level was quantified in a randomly drawn samples from Hyderabad, India population for ascertaining the frequency of hyper pepsinogenemia and risk such individuals have for acid peptic disease. Wherever required endoscopy was also done apart from clinical examination and provisional diagnosis based on the exhaustive proforma. As such there are few studies on the role of age, sex, environmental factors in predisposition to peptic ulcer (Spiro et al., 1955; Hirchowitz et al., 1955). To our knowledge this is the only population based study in south Indian population employing urinary pepsinogen to ascertain the frequency of hyper pepsinogenemia and predisposition ulcer.

Materials and Methods

Screening of patients and sample collection

To investigate the clinical usefulness of urinary pepsinogen (UPG) as a sub clinical marker for acid peptic disease (APD), urinary pepsinogen levels were estimated in general population. Urinary pepsinogen was selected because it represents the activity of pepsinogen I, which is a major predisposing factor for acid peptic diseases. Urine samples from seven hundred and sixty (760) subjects (492 males and 268 females, ages between 15-62 with mean 30.7±13.7±9.7 respectively) were collected randomly from different parts of Hyderabad, south India representing individuals belonging to different socio-economic strata. After a detailed interview and clinical examination of each individual symptoms suggestive of peptic ulcer in the subjects or in any of his first degree relatives was recorded.

Further for the estimation of fasting/meal stimulated UPG levels, urine samples from 34 subjects (10 control and 24 patients) were collected and analyzed by proteolytic assay in post-prandial patients as compared to fasting patients.

Urinary pepsinogen estimation by proteolytic assay

Urinary pepsinogen level was estimated by the modified method of proteolytic assay described by Mirsky et al. (1952) using acidified haemoglobin (pH 1.75) as a substrate. Briefly, Urine was added to the substrate and the acidity of the mixture was adjusted to 1.5 to 2.0. After 24h of incubation at 37°C the reaction was stopped by trichloroacetic acid and the amount of tyrosine-like substances in the supernatant was determined by the Folin-Ciocalteau reaction. The density of the color developed was analyzed in a spectrophotometer. The urinary pepsinogen levels were expressed as units/mL which represents the amount of tyrosine (µg/mL) released from 80mg dehydrated urine by the enzymatic activity of 1mL urine in 24h at 37°C and pH 1.5 to 2.0. Both the fasting and post-prandial urinary pepsinogen levels were estimated. The mean levels of urinary pepsinogen levels were compared according to sex, age, endoscopic findings, and different pathologies.

Statistical analysis

Distribution of UPG were tested using Fisher's exact test. Since differences between conditional logistical regression and unconditional logistical regression were small, unconditional logistical regression was used to estimate odds ratio (OR) and 95% confidence interval (CI). All statistical analysis was performed using Graph pad prism version 5.0 (GraphPad Software, Inc., San Diego, California, USA).

Results

Overall in 760 cases, 188 subjects were found symptomatic and 532 were asymptomatic. 228 subjects (138 symptomatic and 96 asymptomatic) were found to have hyperpepsinogenuria, among these 102 subjects who underwent endoscopy, 30 were proved to have acid peptic disease and remaining non ulcer dyspeptic. Mean uropepsinogen level in males (492) was 2261+946.6 unit/mL whereas in females (268) was 2159±929.0 unit/ml (Table 1).

Table 1: Mean uropepsinogen level in males and females

Category	No.	Mean UPG+SD in unit/ml
Males	492	2261±946.6
females	268	2159±929.0

Hyper urinary pepsinogen levels were observed in 54.8% symptomatic and 18.7% of asymptomatic subject in general population where as the remaining subjects had urinary pepsinogen levels in the normal range (Table 2). Data did not revealed any statistically significant variation when compare to the Hyper UPG with normal in symptomatic cases (OR; 6.963, CI: 4.92-9.83; *p*=4.64), and in asymptomatic cases (OR; 0.14, CI: 0.10-0.20; *p*=4.64).

Table 2: Urinary pepsinogen level in symptomatic and asymptomatic individuals

Category	Total No.	Urinary pepsinogen	
		Hyper	Normal
Symptomatic	228	138 (3068±752.0*)	90 (1734±430.8)
Asymptomatic	532	96 (2947±712.8*)	436 (1689±442.7)
Total	760	234 (3019±722.0*)	526 (1699±430.8)

p>0.05 (4.64)

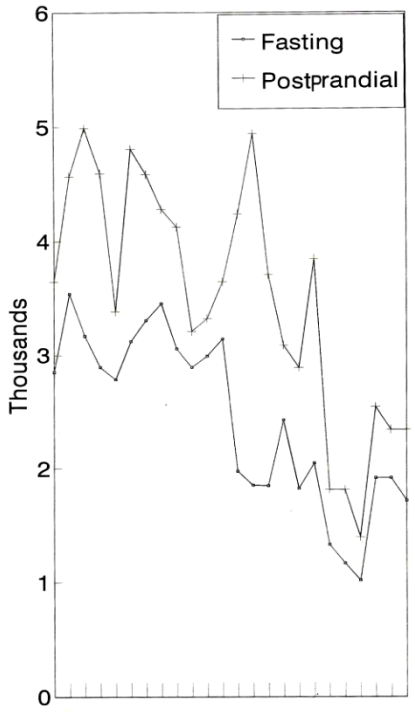
Mean ratio of fasting/meal stimulated UPG levels was calculated for total 34 subjects (10 control and 24 patients) which was found to be significantly high in patients (p value <0.001) as compared to the controls (Table 3). Proteolytic assay performed in fasting and postprandial patients for UPG levels is provided in figure 1 showing higher in post-prandial patients as compared to fasting patients.

Table 3: Urinary pepsinogen level post-prandial cases found significantly high as compared to the fasting cases.

Category	No.	Fasting UPG (Mean±SD)	90 days after meals UPG levels (Mean±SD)
Control	10	1896.11±275.00	2205.44±212.80
Patients	24	2420.77±785.80	3612.65±1141.80

P<0.001

Figure 1: UPG levels in fasting and postprandial patients



Discussion

The pepsinogen present in the urine and serum represents group-I pepsinogen which plays important role in the pathogenesis of peptic ulcer. Detection of group–I pepsinogen in the serum samples is difficult since it can only be detected by a RIA which is not a method of choice to estimate pepsinogen in general population. In urine the group-I pepsinogen can be estimated by simple, colorimeteric, proteolytic assay. Hence, urinary pepsinogen can be a better choice of subclinical marker for the prediction of peptic ulcer in general population.

In the present study we observed relatively lower mean urinary pepsinogen level in females compared to males. The peptic secretory mass is influenced by the sex (Hanley, 1964). The pepsinogen levels reported to reflect the size of the gastric cell mass. This is generally smaller in females; hence pepsinogen levels are relatively lower in females.

A previous report from our centre has shown a high degree of correlation between serum pepsinogen and urinary pepsinogen (Habibullah et al., 1985). Based on the prevailing concept that the concentration of pepsinogen in serum as well as urine reflects the capacity of the gastric mucosa to secreted hydrochloric acid, it is generally accepted that an elevated serum pepsinogen level indicates gastric hyper secretion and that a low level predicts hypochlorohydria or achlorohydria (Shanchez et al., 1996; Haruki et al., 1993; Fishermann et al., 1975; Cubberly et al., 1955).

It has been suggested that pepsinogen secretion has an endocrine as well as exocrine components (Cubberly et al., 1955). The high level of serum and urinary pepsinogen result from an increased chief cell mass (Samloff et al., 1975) which is genetically determined. Therefore, the exocrine component tends to keep the levels of pepsinogen elevated in these individuals. In the absence of overt diseases this elevated level serves as a genetic as well as subclinical marker for an ulcer diathesis. The measurement of urinary pepsinogen can be recommended as an indirect assay for ascertaining achlorohydria, hypochlorohydria and hyperchlorohydria as well supported by previous study (Cubberly et al., 1955).

In conclusion an elevated level of urinary pepsinogen is seen in 35.4% of general population. Since the high level of urinary pepsinogen also indicates the hyper gastric secretory function which may serve as a subclinical marker for ulcer diathesis.

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