

Predicting serum gastrin levels among men during Ramadan fasting

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التكهّن بمستويات غاسترين المصل عند ستة رجال أثناء صيام رمضان

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الخلاصة: إن ازدياد حموضة المعدة أمر شائع أثناء صيام رمضان. وقد هدفت هذه الدراسة إلى استنباط معادلة تحوّل للتكهّن بمستويات غاسترين المصل أثناء الصيام، باستخدام متغيرات parameters تُجرى تحليلاتها بكثرة في المختبرات السريرية. وقد تم أخذ عينات دم أثناء الصيام من 6 رجال في الأيام 1، 10، 19، 26 و 28 من رمضان. وتم تحليل عينات غاسترين المصل والكوليسترول الكلي واليوريا وحمض اليوريك. وتم تضمين العينات الخمس من كل رجل في التحليل التحوّلي المتعدد مما أدّى إلى الحصول على معادلة التكهّن التالية: غاسترين المصل مقدراً بالبيكوغرام لكل مل = $198.27 - 0.199 \times \text{مقدار الكوليسترول الكلي (مغ/دل)} + 2.525 \times \text{مقدار اليوريا (مغ/دل)} - 103.238 \times \text{مقدار حمض اليوريك (مغ/دل)} + 3.983 \times \text{مَنسَب كتلة الجسم}$. وهي معادلة يُعتدُّ بها جداً من الناحية الإحصائية ($P < 0.001$, $r^2 = 0.75$)، بحيث يمكن أن تستخدم هذه المعادلة لتقدير مستويات الغاسترين وللتخطيط للتدابير القوتية والدوائية بما يكفل تجنب الحموضة المعدية العالية في رمضان.

ABSTRACT Increased gastric acidity is common when fasting during Ramadan. Our study aimed to develop a regression equation to predict fasting serum gastrin levels using parameters commonly analysed in clinical laboratories. Fasting blood samples from six men were taken on days 1, 10, 19, 26 and 28 of Ramadan. Serum gastrin, total cholesterol, urea and uric acid were analysed. All 5 samples from each man were included in multiple regression analysis and the prediction equation obtained was: serum gastrin, pg/mL = $198.27 - 0.199 \text{ total cholesterol (mg/dL)} + 2.525 \text{ urea (mg/dL)} - 103.238 \text{ uric acid (mg/dL)} + 10.923 \text{ uric acid (mg/dL)}^2 + 3.683 \text{ body mass index}$, $r^2 = 0.75$, $P < 0.001$. This equation might be used to estimate gastrin levels and plan dietary and medicinal measures to avoid high gastric acidity during Ramadan.

Prédiction du taux de gastrine sérique chez des hommes pendant le jeûne du ramadan

RÉSUMÉ Une augmentation de l'acidité gastrique est courante pendant le jeûne du ramadan. Notre étude visait à établir une équation de régression pour prédire le taux de gastrine sérique à jeun en utilisant les paramètres couramment analysés dans les laboratoires cliniques. Des prélèvements sanguins à jeun ont été effectués chez six hommes au 1^{er}, 10^e, 19^e, 26^e et 28^e jour de ramadan. La gastrine sérique, le cholestérol total, l'urée et l'acide urique ont été analysés. Les cinq échantillons de chaque homme ont tous été inclus dans l'analyse de régression multiple et l'équation de prédiction obtenue était la suivante : gastrine sérique, pg/mL = $198,27 - 0,199 \text{ cholestérol total (mg/dL)} + 2,525 \text{ urée (mg/dL)} - 103,238 \text{ acide urique (mg/dL)} + 10,923 \text{ acide urique (mg/dL)}^2 + 3,683 \text{ indice de masse corporelle}$, $r^2 = 0,75$, $p < 0,001$. Cette équation pourrait être utilisée pour estimer le taux de gastrine et prévoir des mesures médicamenteuses et diététiques permettant d'éviter une forte acidité gastrique pendant le ramadan.

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Introduction

Several reports have indicated the problem of increased gastric acidity and episodic peptic ulcers during the fasting month of Ramadan [1,2]. During Ramadan changes in total cholesterol, uric acid and urea have been observed as well [3–9].

A negative association between fasting serum gastrin level and gastric acidity has been observed [10]. Others have also noted low plasma gastrin concentrations and increased intragastric acidity [11,12]. The possibility of using fasting blood gastrin level to predict gastric acidity has been suggested [10]. The objective of our study was to develop a prediction equation for fasting serum gastrin level during Ramadan using blood parameters routinely analysed in clinical laboratories such as cholesterol, urea and uric acid. Screening for gastrin for those who fast during Ramadan or for other reasons may help to define dietary and medicinal measures to prevent episodes of peptic and duodenal ulcer.

Methods

The study was approved by the Institutional Review Board of West Virginia University, United States of America, for the protection of human subjects. Six healthy male college students and faculty members participated in the study from November through December 2000. The mean and standard deviation (SD) for age, weight and body mass index [BMI, body weight in kilograms/(height in metres)²] were 33.5 (SD 17.9) years, 81.1 (SD 10.5) kg and 26.5 (SD 1.4) kg/m² respectively.

The subjects broke their fast at sunset by consuming 3 dates and 240 mL of orange juice or cow's milk (3% fat). Immediately after *maghrib* prayer, they ate dinner,

which mainly consisted of 240 mL of vegetable or pasta soup, 2 cups (410 g) of rice and one and a half servings (160 g) of a lamb and chicken combination. The meal also included either 3/4 cup of *tabouli* (chopped parsley, lettuce, green onion leaves and bulgar with olive oil or corn oil and lemon juice or vinegar dressing) or salad (lettuce, tomato and cucumber with olive oil or corn oil and lemon juice or vinegar dressing). To be sure that the subjects consumed sufficient dietary fibre, they ate an apple [171.6 (SD 7.6) g] and a tangerine [123.9 (SD 6.1) g] immediately after each dinner. At *sahur*, the predawn meal, a bowl of vegetable salad (33 g each of lettuce, shredded carrot, tomato and oil dressing) and a sandwich (two slices of bread, 58g, and lamb/beef meat or chicken, 50 g) or bran cereal (56g), and one and half cups of milk (366g) were consumed. Sweet desserts were consumed sparingly, such as 1–2 pieces of baklava on Fridays at dinner. Diet analysis software (*Food processor for Windows*, version 7, ESHA Research, Salem, Oregon, USA) was used to estimate energy [2072 (SD 307) kcal/day], protein [9.6 (SD 17.5) g], fat [70.6 (SD 14.8) g], carbohydrate [305.9 (SD 41.1) g] and dietary fibre intake [24.2 (SD 7.6) g]. Blood samples were drawn at 16:00–16:15, i.e. approximately one hour before *iftar* (breaking of the fast at sunset) on days 1, 10, 19, 26 and 28 of Ramadan. Total fasting hours per day were approximately 11.5 hours (predawn to sunset) and blood samples were taken after 10.5 hours of fasting. Serum gastrin, total serum cholesterol, urea and uric acid were analysed by enzymatic methods [13–15]. Serum gastrin was analysed by radioimmunoassay (ION Pharmaceuticals, Orangeburg, New York, USA). The data were statistically analysed with *Statistica* software.

Results

There was no significant difference in mean serum gastrin levels with day of fasting: day 1 [57.3 (SD 22.1) pg/mL], day 10 [62.7 (SD 19.0) pg/mL], day 19 [54.5 (SD 15.2) pg/mL], day 26 [54.7 (SD 13.5) pg/mL] and day 28 [59.3 (SD 20.3) pg/mL]. Therefore, all 30 observations were considered as a single set of data for regression analysis. The mean (SD) for serum gastrin, total cholesterol, urea, uric acid and BMI for the whole experimental period was [57.7 (SD 17.3) pg/mL], [203 (SD 28) mg/dL], [14.1 (SD 3.2) mg/dL], [5.01 (SD 0.65) mg/dL] and [26.5 (SD 1.4) kg/m²] respectively.

A single predictor serum variable was first used to predict the serum gastrin variable. Gastrin (pg/mL) was negatively associated with serum total cholesterol level (mg/dL): Gastrin 127.25 – 0.3419 total cholesterol (correlation coefficient, $r = -0.55$, coefficient of determination, $r^2 = 0.3$, $P < 0.01$).

With regard to serum urea and uric acid (mg/dL), there was a curvilinear increase in increasing order in serum gastrin levels with these variables.

$$\text{Gastrin} = 136.68 - 15.0896U + 0.6419U^2 \quad (r^2 = 0.44, P < 0.01)$$

$$\text{Gastrin} = 210.34 - 77.1039UA + 9.16UA^2 \quad (r^2 = 0.34, P < 0.01)$$

where: U = urea and UA = uric acid.

An association between gastrin and BMI was noted as well ($r^2 = 0.45$, $P < 0.05$). Serum gastrin level increased with increasing BMI.

In the next step of the analysis, multiple regression equations were developed that included BMI in the model. Inclusion of BMI improved r^2 values in all 3 equations by more than 10% as compared with earlier equations with one predictor variable only.

$$\text{Gastrin} = 13.065 - 0.2875TC + 3.893BMI \quad (r^2 = 0.4, P < 0.001)$$

$$\text{Gastrin} = 8.53 - 13.561U + 0.5814U^2 + 4.5BMI \quad (r^2 = 0.58, P < 0.001)$$

$$\text{Gastrin} = 155.067 - 103.189UA + 11.514UA^2 + 4.753BMI \quad (r^2 = 0.48, P < 0.001)$$

where: TC = total cholesterol, BMI = body mass index, U = urea and UA = uric acid.

The equation with total cholesterol, urea and BMI as predictors was:

$$\text{Gastrin} = -24.6048 - 0.5205TC - 0.0018TC^2 - 7.988U + 0.383U^2 + 3.2171BMI \quad (r^2 = 0.67, P < 0.001)$$

where: TC = total cholesterol, U = urea and BMI = body mass index.

The data were further analysed with a stepwise forward multiple regression analytical model (Table 1). In the model, the variance in serum gastrin was a good fit ($R^2_{\text{gastrin}} = 75.3\%$, i.e. the percent coefficient of determination). Total cholesterol contributed the most to the variance (30.3%), followed by urea (25.5%), uric acid and its square (11.8%) and BMI (7.5%). Partial regression coefficients for the predictor variables were significant at $P < 0.05$ or $P < 0.01$ levels as well. The multiple regression equation derived was:

$$\text{S. gastrin} = 198.27 - 0.199TC + 2.525U - 103.238UA + 10.923UA^2 + 3.883BMI \quad (r^2 = 0.753, P < 0.001)$$

where: S. gastrin = serum gastrin, TC = total cholesterol, U = urea, UA = uric acid and BMI = body mass index.

Discussion

Often because of changes in meal and sleep patterns people who fast experience irregularity in bowel movements during the

Table 1 Summary of stepwise forward multiple regression analysis, serum gastrin as dependent variable

Predictor variable	Step in	Multiple R	Multiple R ²	R ² change	F to enter	P-value	Variables included
Total cholesterol	1	0.551	0.304	0.304	12.2	0.002	1
Urea	2	0.747	0.559	0.255	15.6	0.001	2
Body mass index	3	0.796	0.633	0.075	5.3	0.03	3
Uric acid ²	4	0.82	0.672	0.039	3.0	0.09	4
Uric acid	5	0.868	0.753	0.081	7.8	0.01	5

month of Ramadan. In our study, subjects had regular bowel movements and had no flatus or constipation. Furthermore, the men did not experience any feelings of heaviness or discomfort in the chest or of acidity in the mouth, i.e. acid reflux. This indicates that the intake of good sources of dietary fibre such as fruits after dinner and salad in *sahur* helped to maintain the normal transit time of food in the gastrointestinal tract (GIT). Total mean dietary fibre intake was 24.2 (SD 7.6 g/day) [20.5 (SD 6.4) g insoluble fibre and 3.7 (SD 1.3) g soluble fibre]. Fibre, especially insoluble fibre, through GIT distension, contributes to motility of gastrointestinal tract churning, mixing of content and emptying of chyme [16].

Serum cholesterol, urea and uric acid association with gastrin can be explained through the regulatory role of duodenal hormone, cholecystokinin, and the role of dietary protein, fat and fibre in inducing hormonal and gastric secretions and gastric emptying [16–23].

Dietary protein first buffers, then triggers gastrin secretion that stimulates gastric juice secretion [19]. Cholecystokinin is secreted in response to the emptying of fat and other digesta (chyme) from stomach into the duodenum; the hormone triggers emptying of gallbladder content [17,18].

The gallbladder content is mainly bile salts and cholesterol that are needed for emulsifying dietary fat. The duodenum also secretes gastric inhibitory peptides. Gastric juice is mainly hydrochloric acid and protein digesting enzymes. With high gastric acidity (< pH 3), gastrin secretion declines, contributing to reduced or halted gastric secretion. Generally protein-rich foods also contain high amounts of purines and pyrimidines. Urea and uric acid are catabolic products of amino acid metabolism and purine metabolism respectively. Fasting also creates physiological stress [9]. Serum urea can be the result of catabolism of body proteins used as a source of energy or for gluconeogenesis [8].

The positive association between BMI and serum gastrin level in our study agrees with the findings of others [24,25]. Serum gastrin has been positively associated with BMI [24]. Significantly high serum gastrin levels have been noted among obese women compared with lean subjects [25].

A negative relationship between fasting serum gastrin (pg/mL) and percent of time or duration of high acidity in 24 hours has been previously reported (pH < 4, $r = -0.55$, $P < 0.01$) [10]. In a rabeprazole dose-related response study, decreased intra-gastric acidity (median 24-hour integrated acidity) and increased plasma

gastrin (median 24-hour integrated gastrin) were noted [11]. Baak et al. found a significant elevation of serum gastrin with the increased gastric pH [12]. Contrary to the some findings, Iraki et al. noted decreased gastric pH and increased plasma gastrin during Ramadan [1, 10–12]. In the Iraki report, gastrin level went up on day 10 of Ramadan and down on day 24 in comparison with levels before or after the Ramadan period. There was a significant difference between the mean gastrin levels of these 2 days of Ramadan [day 10 gastrin = 76.0 (SD 2.4) pg/mL, pH = 2.35 (SD 0.06); day 24 gastrin = 56.5 (SD 2.3) pg/mL, pH = 2.25 (SD 0.05)]. There seemed to be a positive association between the two variables. We, however, did not find a significant difference in serum gastrin levels with various days of fasting, which may be due to presence of sufficient dietary fibre in the diets of our study subjects.

Gastric emptying is an important aspect of avoiding high gastric acidity. Dietary fibre, especially insoluble fibre, plays an important role in gastric emptying and chyme movement in the digestive tract [16]. There is a need for further Ramadan studies on gastrin and gastric acid regulation on subjects with optimal dietary fibre and nutrient intake.

Based upon the findings of our study and a review of the literature, the diagrammatic representation of fasting serum gastrin to various serum variables may be described as follows:

$$\begin{aligned} &\downarrow \text{Cholesterol, } \uparrow \text{urea, } \uparrow \text{uric acid or } \uparrow \text{BMI} = \\ &\uparrow \text{Gastrin} = \uparrow \text{Gastric pH or } \downarrow \text{Acidity} \end{aligned}$$

Conclusion

The prediction equation generated by our study may be useful for the estimation of fasting serum gastrin levels and for the planning of an appropriate diet. The diet from all food groups which includes sufficient dietary fibre through intake of fresh fruit/s at the end of each meal or before sleep is suggested. An appropriate diet and medicine regime may help avoid high gastric acidity during Ramadan fasting and thus reduce gastrointestinal discomfort and the risk of gastric ulcer.

Studies need to be conducted at institutions with 24-hour gastric sample collection facilities to develop an equation between fasting serum gastrin levels and blood parameters among people with optimal nutrient and fibre intake and to develop a gastrin–gastric acidity equation.

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