Published in final edited form as:

Diabetes Obes Metab. 2007 July ; 9(4): 591–593. doi:10.1111/j.1463-1326.2006.00627.x.

Serum ghrelin levels are higher for men 40-49 years of age in the U.S. than Japan

Seiko Matsunaga-Irie, MD, PhD¹, Hirotsugu Ueshima, MD, PhD², Wahid Riad Zaky, MD¹, Takashi Kadowaki, MD, PhD², Rhobert W. Evans, PhD¹, Tomonori Okamura, MD, PhD², Tomoko Takamiya, MD, PhD¹, Yoshiyuki Kita, PhD², Lewis H. Kuller, MD, DrPH¹, and Akira Sekikawa, MD, PhD¹

¹the Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh USA

²the Department of Health Science, Shiga University of Medical Science, Otsu, Japan

Abstract

Background—Ghrelin, a 28-amino-acid gastric peptide hormone, has an appetite-stimulating effect and controls the energy balance. Serum ghrelin levels inversely correlate with body mass index. Recently, several papers reported the ethnic difference in the ghrelin levels. To our knowledge, however, no studies have compared the serum ghrelin levels between Caucasian in the United States (U.S.) and the Japanese in Japan.

Methods—We conducted a cross-sectional study of 189 men 40-49 years of age (91 Caucasian in the U.S. and 98 Japanese in Japan) to examine serum ghrelin levels and metabolic and other factors.

Results—Serum ghrelin levels correlated with waist circumferences and lipid profiles among Caucasian American and the Japanese. Serum ghrelin levels were significantly higher among Caucasian Americans than among the Japanese (904.5 (632.0, 1132.0) pg/mL, 508.0 (399.0, 1378.3) pg/mL (median and 95% confidence interval), respectively, $P < 0.01$), although Caucasian Americans were much more obese (BMI: 26.9 ± 3.3 kg/m² versus 23.3 ± 3.1 kg/m² respectively, $P < 0.01$). The ethnic difference remained after adjusting for metabolic factors, smoking status, and other factors ($P < 0.01$).

Conclusions—We have shown in our population-based study that serum ghrelin levels among men aged 40-49 are significantly higher in Caucasian Americans than in the Japanese in Japan. Reasons for the ethnic difference in the ghrelin levels are largely unknown and warrant further investigation.

Keywords

gut hormones; ghrelin; ethnic difference

Introduction

Ghrelin is a 28 amino acid peptide hormone, has an appetite-stimulating effect and controls the energy balance. The serum ghrelin level rises preprandial, falls postprandial and is lower in obese subjects than in non-obese subjects [1]. Recently, the ethnic differences in the ghrelin levels were reported, suggesting that genetic background could regulate ghrelin

metabolism [2,3]. Hence, we investigated the ethnic difference in serum ghrelin levels between Caucasian and Japanese men aged 40–49 years and also investigated the association of ghrelin with metabolic factors.

Materials and Methods

Study protocol has previously been described in detail [4]. Briefly, we examined 189 men aged 40–49 years; 98 Caucasian residents in Allegheny County, Pennsylvania, USA and 91 Japanese residents in Kusatsu City, Shiga, Japan. Informed consent was obtained from all participants. The study was approved by the Institutional Review Boards of University of Pittsburgh and Shiga University of Medical Science. Serum ghrelin and leptin levels were measured using a radioimmunoassay procedure (Linco Research, St Charles, MO, USA). Other variables were obtained as previously reported [4]. Values are expressed as means $\pm$ s.d. and compared using a t-test. Skewed continuous variables (leptin, ghrelin, triglycerides and C-reactive protein) were compared using the Mann–Whitney U test and expressed as median and interquartile range. Additionally, ghrelin was log transformed to obtain a normal distribution for multiple regression analysis. Dichotomous data were compared with the chi-squared statistics. The p value of <0.05 was considered as significant.

Results

Waist circumference, body mass index, insulin and insulin resistance index (HOMA-IR) were higher in the Caucasians than in the Japanese. In contrast, glucose, total cholesterol, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol were lower in the Caucasians than in the Japanese. Rates of smokers and drinkers were lower in the Caucasians than in the Japanese (table 1).

Unexpectedly, serum ghrelin levels were significantly higher in the Caucasians than in the Japanese. Serum leptin levels were also higher in the Caucasians than in the Japanese (table 1). Spearman correlation analyses showed that serum ghrelin negatively correlated with serum leptin and waist circumference among the Caucasians and the Japanese ($r = -0.24$ and -0.20 for Caucasians and $r = -0.21$ and -0.17 for Japanese).

A multiple regression analysis of all subjects showed that ethnicity and smoking status remained significant in predicting ghrelin levels after adjusting for other variables ($p < 0.01$). Among non-smokers, ghrelin levels remained significantly higher in the Caucasians than in the Japanese ($p < 0.0001$).

Discussion

This study shows that serum ghrelin levels among men aged 40–49 years are significantly higher in the Caucasians than in the Japanese and this ethnic difference remains after adjusting for metabolic factors. To our knowledge, this is the first report of the ethnic difference in ghrelin level between Caucasians and Japanese men.

We revealed that waist circumference and leptin negatively correlated with ghrelin levels for the Caucasians and the Japanese, which is consistent with previous reports [2,5,6], indicating that the biological functions of ghrelin are preserved both in the Caucasians and the Japanese.

The lower rate of cigarette smoking in the Caucasians cannot explain their higher levels of ghrelin compared to that in the Japanese since current smoking status should be positively associated with the ghrelin levels [5]. Actually, ghrelin levels were higher in the smokers than in the non-smokers for the Japanese.

The higher ghrelin levels among the Caucasians may be explained by genetic and environmental factors. Postprandial ghrelin was elevated in Black women than in White women [3], and basal serum ghrelin was elevated in Caucasians than in Pima Indians [2], suggesting that genetic background could affect ghrelin metabolism. Environmental factors such as *Helicobacter pylori* infection may explain the ghrelin difference since the subjects with *H. pylori* infection showed lower serum ghrelin levels than those without the infection. Higher prevalence of *H. pylori* infection in the Japanese might explain their lower levels of ghrelin [6].

There are several strengths and limitations in this study. The strengths include the fact that this is the first study exploring the ghrelin levels in randomly selected samples of subjects at the population level in Japan and that the subjects are limited to 40–49 years of age. The limitations are (i) small sample size, (ii) the limited gender, (iii) the one-time measurement of fasting ghrelin levels and (iv) the measurement of total ghrelin levels instead of active (acylated) ghrelin levels. It is, however, known that gender does not affect ghrelin level, that a single measurement before breakfast serves as a surrogate for overall ghrelin levels and that total ghrelin levels are associated with active ghrelin levels [1,7,8].

In conclusion, we have shown that serum ghrelin levels among Caucasian men are significantly higher than among Japanese men aged 40–49 years. Since ghrelin regulates the appetite and the energy balance, revealing the ethnic difference of ghrelin might make it possible to find the key to the pathological process of obesity and type 2 diabetes.

Acknowledgments

This research is supported by AHA(0160512U), NIHR01(HL068200) and JMECSST ((A): 1337016).

References

1. Cummings DE, Purnell JQ, Frayo RS, Schmidova K, Wisse BE, Weigle DS. A preprandial rise in plasma ghrelin levels suggests a role in meal initiation in humans. *Diabetes*. 2001; 50:1714–1719. [PubMed: 11473029]
2. Tschoop M, Weyer C, Tataranni PA, Devanarayan V, Ravussin E, Heiman ML. Circulating ghrelin levels are decreased in human obesity. *Diabetes*. 2001; 50:707–709. [PubMed: 11289032]
3. Brownley KA, Light KC, Grewen KM, Bragdon EE, Hinderliter AL, West SG. Postprandial ghrelin is elevated in black compared with white women. *J Clin Endocrinol Metab*. 2004; 89:4457–4463. [PubMed: 15356047]
4. Sekikawa A, Ueshima H, Zaky WR, et al. Much lower prevalence of coronary calcium detected by electronbeam computed tomography among men aged 40–49 in Japan than in the US, despite a less favorable profile of major risk factors. *Int J Epidemiol*. 2005; 34:173–179. [PubMed: 15563587]
5. Fagerberg B, Hultén LM, Hulthe J. Plasma ghrelin, body fat, insulin resistance, and smoking in clinically healthy men: the atherosclerosis and insulin resistance study. *Metabolism*. 2003; 52:1460–1463. [PubMed: 14624407]
6. Isomoto H, Ueno H, Nishi Y, Wen CY, Nakazato M, Kohno S. Impact of *Helicobacter pylori* infection on ghrelin and various neuroendocrine hormones in plasma. *World J Gastroenterol*. 2005; 11:1644–1648. [PubMed: 15786542]
7. Marzullo P, Verti B, Savia G, et al. The relationship between active ghrelin levels and human obesity involves alterations in resting energy expenditure. *J Clin Endocrinol Metab*. 2004; 89:936–939. [PubMed: 14764817]
8. Purnell JQ, Weigle DS, Breen P, Cummings DE. Ghrelin levels correlate with insulin levels, insulin resistance, and high-density lipoprotein cholesterol, but not with gender, menopausal status, or cortisol levels in humans. *J Clin Endocrinol Metab*. 2003; 88:5747–5752. [PubMed: 14671163]

Table 1
Characteristics of study subjects

	Whites(n=98)	Japanese (n=91)	P value
leptin	10.2 (7.5, 15.6)	4.0 (2.6, 5.7)	<0.01*
ghrelin(pg/mL)	904.5 (632.0, 1132.0)	508.0 (399.0, 1378.3)	0.01*
age(years)	44.6±2.9	44.8±2.9	0.62
waist circumference (cm)	96.2±9.8	85.0±8.5	<0.01
BMI (kg/m ²)	26.9±3.3	23.3±3.1	<0.01
systolic blood pressure (mmHg)	113.8±9.5	122.8±14.4	<0.01
diastolic blood pressure (mmHg)	78.4±5.9	78.5±10.5	0.90
total cholesterol(mmol/L)	5.00±0.80	5.68±0.98	<0.01
triglycerides(mmol/L)	1.31 (0.89, 1.88)	1.48 (1.01, 2.05)	0.18*
HDL-C(mmol/L)	1.19±0.30	1.42±0.38	<0.01
LDL-C(mmol/L)	3.12±0.77	3.48±1.02	0.06
glucose(mmol/L)	5.29±0.51	5.74±0.49	<0.01
insulin(pmol/L)	85.3±45.2	56.3±25.7	<0.01
HOMA-R	2.93±1.67	2.10±1.07	<0.01
C reactive protein	0.84 (0.44, 2.09)	0.45 (0.22, 0.87)	<0.01*
Fibrinogen (g/L)	2.38±0.64	2.35±0.63	0.72
smoker (%)	15%	48%	<0.01
alcohol (%)	16%	45%	<0.01