ORIGINAL ARTICLE

Gender and Stress Perception Based Differences in BMI, Hormonal Response and Appetite in Adult Pakistani Population

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ABSTRACT

Objective: To evaluate and compare the gender based variations in stress perception induced changes in leptin, cortisol and serotonin (5-HT) trends, appetite and Body Mass Index (BMI).

Study Design: An analytical comparative study.

Place and Duration of Study: Neurochemistry Laboratory, University of Karachi, from January to August 2013.

Methodology: Appetite, BMI and serum leptin, cortisol, and 5-HT were measured in 100 men and women of aged 30 - 60 years, working in teaching institutes of Karachi, to evaluate gender based, stress perception induced variations. The samples were identified by stratified random technique. The chemical variables were estimated through ELISA. Results were analysed using one-way ANOVA and multivariate general linear model using SPSS version 17.

Results: Mean stress perception, BMI and serum leptin levels were significantly more in women ($p < 0.05$). Serum cortisol and 5-HT were found significantly reduced in women ($p < 0.05$). BMI, serum cortisol and leptin were found to be increased with increasing level of stress perception ($p < 0.05$). VAS for hunger and desire to eat as the measure of appetite was significantly higher in men ($p < 0.05$).

Conclusion: Stress perception attenuates the positive effect of cortisol and negative effects of leptin and 5-HT on appetite through changes in their circulatory levels. Women perceive more stress and exhibit significantly attenuated changes in hormonal levels and appetite which may be the contributing factor towards obesity. Increased BMI in women despite decreased appetite merits more studies.

Key Words: *Stress perception. Obesity. Gender. Appetite. Leptin. Cortisol. 5-HT.*

INTRODUCTION

Gender based differences in Body Mass Index (BMI) and leptin have been reported earlier.[1] Peripherally, leptin affects several hormonal processes which are attenuated by stress perception.[2]

Stress attenuates appetite ranging from anorexia to bulimia nervosa. During a stressful event, stimulated HPA- axis leads to increased amounts of cortisols that favours the utilization of glucose and alleviate appetite. Increased stress-induced central serotonin (5-HT) levels during stress are also reported to affect the eating behaviour.[3] The expression of 5-HT receptors on adipocytes suggests its link with the adipose tissue metabolism and its homeostasis.[4]

Cortisol increases appetite while leptin and 5-HT are known anorectic agents.[5] It is also reported that the perception of stress, whether the social stressors or the work stress at job environment varies with gender, which also attenuates the hormonal response in coping with stress perception.[6]

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It was earlier reported that the perception of stress attenuates the circulatory levels of cortisol, leptin and 5-HT with varying biological responses.[2] The interaction of hormonal factors in both genders has to be further explored.

The present study was aimed at comparing the gender variations in stress perception induced changes in appetite, BMI and serum leptin, cortisol and 5-HT levels.

METHODOLOGY

It was a comparison-based analytical study conducted from January to August 2013. One hundred adult male and female subjects each of an age ranging from 30 - 60 years, working at teaching institutions were selected by stratified random technique for this comparative study. Pregnant women, subjects diagnosed with clinical depression and psychosis were excluded. An informed consent was obtained from all the subjects. Stress levels were monitored subjectively by a standardized questionnaire.[7] All participants submitted a written consent for the use of information contained in the questionnaire and for the donation of serum samples. The study procedures were approved by the Ethical Committee for Advanced Research of University of Karachi.

Stress perception was calculated by evaluating social psychological and physiological stressors. The subjects were asked to respond each statement as never (1),

rarely (2), sometimes (3), often (4) and always (5). The response number was added for one sample and stress level calculated as none/minimal (level 0, score range 52 - 58), mild (level 1, score range 59 - 65), moderate (level 2, score range 66 - 76), and severe (level 3, score range 80 - 86). Social stressors encompassed the aspects of satisfaction, social life, comfort, environment, behaviour with other people during stress and the effect of change in the social surroundings. Psychological stressors addressed the effect of workload on physical and mental well-being, sound sleep at night, difficulty to control emotions and if there was any particular behaviour during excess workload/stress. Physiological stress encompassed the various physiological experiences during stress like quality of work at the start of the day, self-control, perspiration breakout, tiredness at work, dryness of mouth and throat and yawning and dozing out at work.

Subjective appetite was measured using Visual Analogue Scale (VAS) method using 100 mm lines. The questions asked related to hunger (over the last month in general how hungry you have been feeling?) and desire to eat (over the last month in general how strong your desire to eat been?). The questions were weighted with the extremes at each end (0 = not at all and 100 = extremely).[8] The VAS were administered in a single session and designed to reflect retrospective ratings of motivation to eat rather than the state of time. Body mass index of all the subjects was calculated by dividing weight in kilograms with height taken in meter squares.

After all aseptic measures, 5 ml of venous blood was drawn from antecubital vein after answering the questionnaire for perceived stress. Blood was allowed to clot at 4°C and serum was separated and stored at -70°C until estimations of 5-HT, leptin and cortisol by ELISA.[9-11]

All data was expressed as mean ± SEM. Statistical analyses were performed by one-way ANOVA to analyze the gender differences in physical, chemical and behavioural parameters. Multivariate general linear model (two-way ANOVA) was adopted to evaluate the effect of stress perception in men and women regarding these parameters.

RESULTS

Figure 1 depicts the result of one-way ANOVA on physical, chemical and behavioural parameters on both genders. Multivariate general linear model was applied to analyze the data keeping gender and stress perception grades (0 - 3) as fixed factors that influenced physical (BMI), chemical (serum cortisol, 5-HT and leptin) and behavioural (VAS for hunger and desire to eat) parameters.

The Table I shows means ± SEM calculated at 95% confidence intervals of these variables.

Average ages of men and women included in the study were 38.38 ± 1.02 and 41.49 ± 0.9 years respectively. The proportions of men participants with no/minimal, mild, moderate and severe stress were 23.71%, 26.80%, 23.71% and 25.77% respectively. The stress perception among women participants were 3.06%, 20.20%, 56.57% and 17.17% for no/minimal, mild, moderate and severe stress respectively. Out of 97 men, only 3 reported severe stress perception and 6 out of 99 women perceived no/minimal stress.

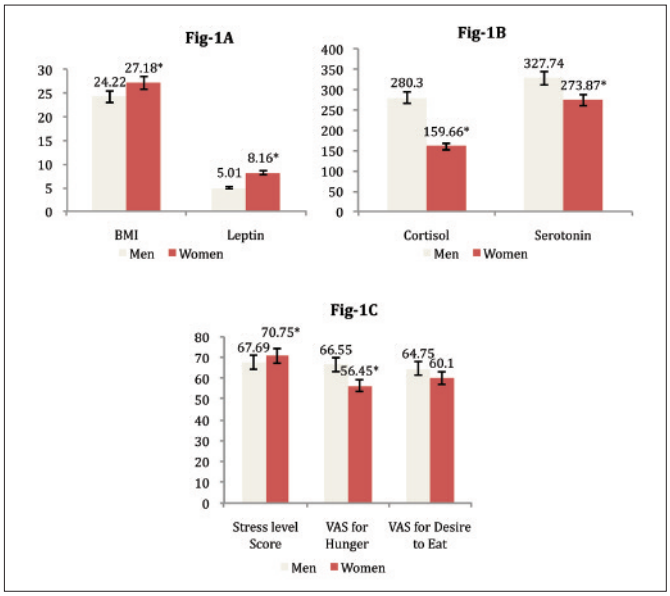

Figure 1: Comparison of gender based differences in **(A)** BMI and serum leptin levels, **(B)** Circulating cortisol and 5HT levels and **(C)** Stress level score and Visual Analogue Scale for hunger and desire to eat. Significant difference is considered at * $p < 0.05$.

Table I: Physical, chemical and behavioural variables in both genders having various stress level scores.

Variables	Stress levels							
	Men				Women			
	0	1	2	3	0	1	2	3
BMI (kg/m^2)	24.82 ± 0.72	23.30 ± 0.67	25.33 ± 0.72	23.63 ± 0.69	22.33 ± 1.40	26.56 ¥ ± 0.77	27.32 * ¥ ± 0.46	29.20 * ¥ ± 0.83
Stress level scores	54.65 ± 1.12	62.34 ± 1.05	69.56 ± 1.12	83.52 ± 1.08	58.66 ± 2.20	63.75 ± 1.20	71.92 ± 0.72	79.41 ± 1.31
Cortisol (ng/ml)	167.22 ± 17.13	261.75 ¥ ± 16.11	305.88 ¥ ± 17.13	380.07 ¥ ± 16.43	82.70 * ± 33.55	107.32 * ¥ ± 18.36	171.18 * ¥ ± 10.98	210.47 * ¥ ± 19.93
5HT (ng/ml)	480.84 ± 26.57	337.82 ¥ ± 24.99	290.63 ¥ ± 26.57	210.55 ¥ ± 25.49	544.66 ± 52.03	282.83 ¥ ± 28.49	266.94 ¥ ± 17.03	190.57 ¥ ± 30.91
Leptin (ng/ml)	2.45 ± 0.47	3.90 ± 0.45	5.11 ¥ ± 0.47	8.43 ¥ ± 0.46	5.11 * ± 0.93	7.07 * ± 0.51	8.11 * ¥ ± 0.31	10.70 * ¥ ± 0.55
VAS for hunger	52.52 ± 2.58	62.00 ± 2.43	71.69 ¥ ± 2.59	79.48 ¥ ± 2.48	32.00 * ± 5.06	50.15 * ¥ ± 2.77	57.87 * ¥ ± 1.66	67.71 * ¥ ± 3.01
VAS for desire to eat	38.30 ± 3.06	58.96 ¥ ± 2.87	75.13 ¥ ± 3.06	85.48 ¥ ± 2.93	31.33 ± 5.99	52.20 ¥ ± 3.28	61.94 ¥ ± 1.96	73.47 ¥ ± 3.56

*Result is shown as mean ± SEM calculated at 95% confidence intervals. * = $p < 0.05$ compared to the values in men of same variable at same stress level. ¥ = $p < 0.05$ compared to the values of variables at no/minimal stress level in the same gender.*

Two-way ANOVA showed significant difference in BMI among men and women ($F = 25.55$; $p < 0.001$). The stress scores per stress level were observed to be higher in women but these were not significant ($F = 0.82$; $p=0.366$). A significant difference was observed in serum levels of cortisol ($F = 127.99$; $p < 0.001$) and leptin ($F = 64.81$; $p < 0.001$) among men and women. The circulating levels of 5-HT were not affected within genders ($F = 1.19$; $p = 0.277$). Gender influenced significantly on the behavioural patterns of appetite measured by VAS for hunger ($F = 50.68$; $p < 0.001$) and desire to eat ($F = 21.74$; $p < 0.001$).

The difference in the BMI of various stress groups was not found significant ($F = 1.79$; $p = 0.151$) as observed by two-way ANOVA. A significant difference was found among the four levels of stress perception in the circulating levels of cortisol ($F = 33.69$; $p < 0.001$), leptin ($F = 41.78$; $p < 0.001$) and 5-HT ($F = 29.38$; $p < 0.001$). The behavioural parameters for assessment of appetite were also significantly affected by stress perception. VAS for hunger ($F = 35.04$; $p < 0.001$) and VAS for desire to eat ($F = 60.75$; $p < 0.001$).

The combined effect of gender and stress perception as observed by general linear model was found significant on BMI ($F = 6.23$; $p < 0.001$) and stress level scores ($F = 3.85$; $p < 0.05$). Chemical [cortisol ($F = 1.28$; $p = 0.281$), 5-HT ($F = 0.97$; $p = 0.407$) and leptin ($F = 0.33$; $p = 0.805$)] and behavioural [VAS for hunger ($F = 0.64$; $p = 0.589$) and desire to eat ($F = 0.55$; $p = 0.645$)] parameters were not significantly affected by gender and stress perception.

DISCUSSION

The aetiology of obesity remains ambiguous despite decades of research. The spectrum of contributing factors of obesity ranges from physiological, behavioural and genetic predispositions. It also involves social and psychological elements affecting one's personality. Gender differences in eating behaviour and weight gain have also been reported.[12] The present study encompassed the gender based differences in serum cortisol, serotonin (5-HT), leptin and appetite in various levels of stress in adult Pakistani population. The target population was adults working men and women; working 8 hours/day, 5 days a week for more than 5 years. It was observed that BMI of women is significantly higher than men despite insignificant variation.

Many studies have shown that women have more BMI than men,[13] this may be attributed to the more adipose tissue mass and therefore, a higher level of obesity gene expressed by it. Obesity gene product leptin is expressed by adipose tissue. It regulates weight gain and energy expenditure acting through hypothalamic receptors. Receptors of leptin belong to cytokine family which polymerize upon stimulation and trigger the

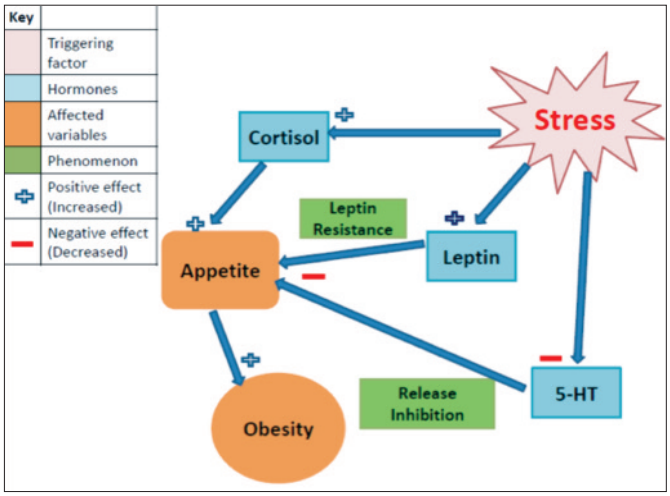

Figure 2: The possible hormonal interactions in circulation contributing in stress-induced obesity.

desired effect in the cell. The cytokine receptor family also shows resistance phenomenon resulting in decrease response despite higher than normal circulating amount of the hormone.[14] The present study also documented that serum leptin levels are significantly higher in women compared to men. Therefore, it is suggested that the higher normal levels of leptin observed in women than men contribute to early development of leptin resistance and hence a significant higher BMI than men. Moreover, female sex hormones are also reported to be associated with the development of obesity and *vice versa*.[15] It was further noted that although the overall mean BMI was significantly higher in women, group of women with no/minimal stress perception had lesser BMI than men while it increased with the severity of stress perception. Significantly, higher BMI with mild to severe stress perception (Table I) and a homogeneous increases in serum leptin levels with the severity of stress perception (Table I) suggests that early development of leptin resistance may be the mechanism of obesity in women.

Acute response to stress is reflected by the stimulated activity of HPA axis with increased circulating cortisol and catecholamine. The present results revealed significantly reduced cortisol levels in women compared to men ($p < 0.001$), despite increased stress perception (Figure 2 and Table I). Circulating levels of cortisol and 5-HT were found significantly raised in men compared to women (Figure 2, $p < 0.001$). Contrarily, men and women representing individual groups did not exhibit significantly different circulating 5-HT levels (Table I). An increased 5-HT was noted with a gradual decreasing pattern of 5-HT with the severity of stress. This suggests the integrated effect of cortisol and leptin on its synthesis. It may be due to adaptation to stress. It can also be the false positive response that women can think they are in stress, while their body is not showing a stress reaction. Many have reported that pre-

menopausal women have slightly lesser cortisol levels than age-matched men[16], whereas men show a little higher response to stressors compared to women in the same psycho-social environment.[17] Therefore, it may be suggested that the increases in circulating cortisol found in men are due to the gender difference and are normal for that particular person. This may also be explained that the decreases found in circulating levels of cortisol in women are increased for them. Hence, it may be suggested that their HPA axis also shows the signs of stress along with its perceptions.

Obesity gene, leptin, has gained a repute of an anti-depressant agent as well.[18] The scope of this study also included the interaction of leptin with the stress hormones resulting in altered eating behaviour due to job stress. Job stress relates to the day-to-day unnoticed stressors ranging from office work load to the off and on ringing of cell phone.[19] The continuous exposure to unidentified stressors triggers the HPA axis which in turn stimulates obesity gene expression.[20] The protein leptin thus expressed in adipose tissue decreases the cortisol levels by inhibiting its release from adrenal cortex.[21] Leptin also attenuates the eating behaviour and energy expenditure to keep the body weight constant by acting through the hypothalamic receptors. Therefore, it is suggested the weight gain due to stress involves the development of early leptin resistance. It also may lead to depression characterized by low hippocampal 5-HT.[22] 5-HT has been known to be a neurotransmitter associated with sleep and mood disorders. It also decreases appetite through 5-HT4 receptors.[23] It has also been documented in human depression.[24] Marazziti *et al*. have reported stress induced increases in cortisol which in turn stimulates the tryptophan pyrolase activity in liver shunting the tryptophan metabolism from 5-HT to kynurenine.[25] This is also reflected in decreased peripheral 5-HT levels. The authors have documented that stress leads to decreases in levels of circulating 5-HT.[2] The present study also confirmed that peripheral 5-HT decreases with the perception of stress. Women with higher perception of stress also have significantly low levels of circulating 5-HT which also contributes to our understanding of stressors leading to depression and attenuated eating behaviour resulting in higher than normal BMI observed in women.

The reduction of appetite by 5-HT is known since long. It has central function acting through 5-HT4 receptors. Presence of 5-HT receptors on adipose tissue shows a link with leptin secretion.[9] The significant differences in appetite measured through VAS for hunger and desire to eat of men and women ($p < 0.001$, Table I, Figure 1C) again relates to the elevated levels of cortisol and leptin and reduced serum 5-HT with severity of stress perception.

Glucocorticoids serve as appetite stimulants while leptin and 5-HT are known as anorectic agents. Leptin acts both centrally and peripherally, while 5-HT suppresses appetite through central actions. Present study documents that stress induced increases in cortisol directly increase appetite while increases in leptin also enhance appetite through leptin resistance. The novel findings of stress-induced decreases in circulating 5-HT also increase appetite through release inhibition. All these factors contribute in development of stress-induced obesity.

CONCLUSION

Stress perception attenuates the positive effect of cortisol and negative effects of leptin and 5-HT on appetite through changes in their circulatory levels. Women perceive more stress and exhibit significantly attenuated changes in hormonal levels and appetite which may be the contributing factor towards obesity (Figure 2).

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