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Ghrelin levels in hypertensive obese and normotensive obese subjects.

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ABSTRACT… Objective: The purpose was to determine the ghrelin level, its effect and relationship with blood pressure levels in obese subjects. **Study Design:** Comparative Cross Sectional study. **Settings:** General OPD of Madinah Teaching Hospital (MTH) and District Head Quarter hospital Faisalabad (DHQ**)**. **Period:** 2019 to 2020. **Material & Methods:** Blood samples were collected from hypertensive and compared with the normotensive obese (BMI >30). Ghrelin level was measured by Enzyme-linked immunosorbent assay (ELISA). Statistical analysis was done on Statistical Package for the Social Science (SPSS) 20 software. Mean ±SD has been given for quantitative variables. Independent sample t test was used for comparisons. Significance has been chosen as $p \leq 0.05$. **Results:** Total 114 obese patients were selected for this study, of which 57 were hypertensive and 57 were normotensive. Minimum age was 30 years and maximum age was 60 years with mean age 39.35 ± 10.08 years. Mean age of hypertensive obese was 43.42 ± 10.46 years and mean age of normotensive was 35.28 ± 7.87 years. Statistically significant difference of mean fasting ghrelin levels between hypertensive obese and normotensive obese was noted with p value 0.013. **Conclusion:** Obese persons with elevated circulating concentration of ghrelin may be susceptible to the progression of increasing blood pressure.

Key words: Ghrelin, Hypertensive, Obesity.

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INTRODUCTION

Ghrelin is an orexigenic, amide hormone. It is released by the abdomen, pancreas and from P/D1 cells, located in upper part of stomach.[1] The cells that secrete ghrelin are also called epsilon cells. Ghrelin was discovered by scientist, Kojima.[1] It is produced once abdomen is empty and inhibited once abdomen is stretched. It is a potent appetite stimulant. This hormone exerts its effects on GIT motility, bone formation, vessel wall and insulin.[1] Previous studies shows that its levels are low in obesity and also in hypertension, however ghrelin has important vascular and metabolic effects.[2,3] It increases the gastric secretion and gut motility as well. Ghrelinergic cells are located in stomach, jejunum, lungs, is lets of Langerhen's, adrenal cortex, placenta, kidney and brain.[4] It is a peptide hormone that is composed of 28 organic compounds and exists in two forms. The primary one is des-acyl hormone and the other one is n-octanoyl-modified hormone.[5,6,7] Ghrelin-O-acyl transferase (GOAT) is an enzyme which modifies the 3serine by n-octanoic acid to increase ghrelin activity.[8,1] This enzyme was discovered by Yang 2008[8] and is present in GIT and testis. Its optimum temp is 37-50 °C and pH between 7-8.[9] Growth hormone receptors for ghrelin is called growth hormone secretogogous receptor 1. Its mRNA is present in ventromedial nuclei, (VMN) arcuate nuclei (ARC) of hypothalamus and in hippocampus.[10] It is a 366 amino acids forming heterotrimeric G protein-coupled receptor (GPCR). Its structure consists of seven transmembrane domains (TMI-V11).[10] Ghrelin receptor (GHSR1) is involved in usual effect of ghrelin, including growth hormone release, aid in hunger, glucose and lipid metabolism, increase motility and secretion of GIT, and protection of nervous and cardiovascular cells. It also plays

role in cell signaling mechanism.[11] Obesity is a common disease in our population and has adverse effects on health. Subjects having BMI ≥ 30 kg/m^2 considered to be obese. Unnecessary food intake, not having physical activity and genetic susceptibility are contributing factors for obesity. Obesity causes various types of diseases, especially Type 2 diabetes, heart diseases, and different types of cancers and osteoarthritis.[12] Obesity has become an important public –health challenge worldwide. Similarly, hypertension is the main cause for cardiovascular disease morbidity and mortality. According to American association 140mmHg is systolic and 90mmHg is diastolic. There are general risk factors for hypertension including age, sex, size, race, life style and obesity. Some risk factors are specific for causing hypertension such as tumor, kidney failure, diabetes, hyperthyroidism, menopause, pregnancy and Cushing syndrome.[13,14]

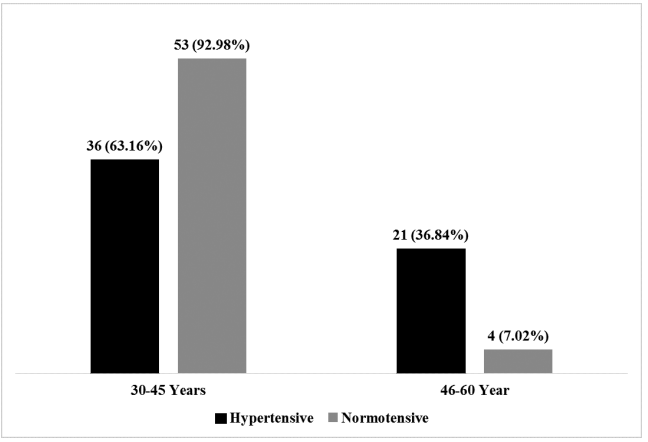
MATERIAL & METHODS

It was a comparative cross sectional study, conducted on 114 subjects (both males and females), divided into two groups, 57 obese hypertensive 57 obese normotensive. The study was done after approval by ethical committee. Sample size was calculated through this formula. $N=s^2 (t_1+t_2)^2/d^2$

Sample was collected using convenient sampling technique.

Blood samples were collected from 57 hypertensive obese and 57 normotensive obese subject. Venous blood sample was collected from the obese women after twelve hours fasting. Three ml blood was placed into plastic tube contained 15 μl protease inhibitor (pefabloc) supplied by sigma-aldrichger many with catalog number (76307) for serum ghrelin assay. (Barhoomlaboratory, Rafah). The sample of the blood was left for some time without any anticoagulant that allows the blood to coagulate. Serum was attained by centrifugation at 3000rpm/10 minutes. One mL of serum with protease inhibitor was placed in plastic tube and 10 μl of 5 N Hcl were added and samples were stored at 20±5°C for serum ghrelin assay.

RESULTS



Mean ghrelin levels in hypertensive obese were (872.6ng/L ± 731.8) and a mean ghrelin level in normotensive obese was (602.7ng/L ± 541.8). Statistically significant difference of mean fasting ghrelin levels between hypertensive obese and normotensive obese was noted with p value 0.013. Table below showing relation of Fasting serum ghrelin levels with Systolic BP of the cases (n=114). The Pearson correlation test showed that the level of Fasting ghrelin increase with increasing systolic BP. This positive correlation was statistically significant between two variables.

Relation of Fasting ghrelin levels with diastolic BP

Table below showing relation of fasting ghrelin levels with diastolic BP of the cases (n=114). The Pearson correlation test showed that the level of Fasting ghrelin decreased with decreasing diastolic BP having positive correlation. This positive correlation between two variables was statistically insignificant.

Group	N	Mean	Std. Deviation	P-Value
Hypertensive obese	57	872.66	731.877	0.013
Normotensive obese	57	602.72	541.865	

Table-I

Systolic BP	Fasting Ghrelin Levels	
	Pearson correlation (r)	P-Value
	0.227	0.001

Table-II

Diastolic BP	Fasting ghrelin levels	
	Pearson correlation (r)	P-Value
	0.165	.08

Table-III

DISCUSSION

Obesity has become a most important community fitness predicament all over the world and at least one-third of Asians are obese. Fat accumulation encourages the extend of insulin resistance, glucose intolerance and type 2 diabetes mellitus.[1,3,7,8,9] The increasing incidence of obesity is a severe health apprehension. Obesity is well known to be connected with arteriosclerotic disease and hypertension, but the pathogenic systems related to increasing blood pressure and obesity are not completely known. Main functions of ghrelin and obestatin in obesity and metabolic syndrome were considered.[14,11,12] Detail research on ghrelin has proved that this peptide might have significant positive consequences on feeding, since exogenous ghrelin direction excites desire for food intake in both humans and rodents. Adding together, there is proof that ghrelin decreases energy disbursement, fat catabolism, and lipolysis, and endorse adipogenesis.[15] These discoveries show difference with the negative association between ghrelin levels and BMI. Ghrelin is a peptide hormone foremost produced from GIT, and desire of food intake boosts fat deposition in rodents. Though, numerous researches have explained that fat deposition is reducing ghrelin levels.[16] Ghrelin describe strong anti-inflammatory effects, reduction of proinflammatory cytokine generation and mononuclear binding of cell with in endothelial cells of vessels. Ghrelin has a protect function of endothelial and decreases hypertension. Decreased plasma ghrelin shown and association with conflict of insulin, increasing blood pressure and type 2 diabetes.[17,15]

As compare to prevalence of hypertension with our study, Pakistan has high prevalence of hypertension. The National health survey of Pakistan showed their figure those hypertension effects 18% of adults and 33% above 45 years old.

Mean ghrelin level in hypertensive obese was (872.6ng/L ± 731.8) and a mean ghrelin level in normotensive obese was (602.7ng/L ± 541.8). Statistically significant difference of mean fasting ghrelin levels between hypertensive obese and normotensive obese was noted with p value 0.013. Means serum fasting ghrelin levels were significantly high in hypertensive obese as compare to normotensive obese in our study similar to the results seen in other studies[18,12] in obese subjects with normal blood pressure, ghrelin levels were considerably low than in controls while with high blood pressure obese women had higher ghrelin level. Ghrelin levels lower regardless of the incidence of hypertension who had BMIs above 35 kg/m^2 in obese.[19] According to our study, underlying mechanism could be that physiological adjustment in obesity with positive energy stability as fasting serum ghrelin levels were increased in hypertensive obese subjects as compared to normotensive obese or it may be due to activation of sympathetic nervous system. One possibility is that NO (nitric oxide) might affect small vessels as compared to higher vascular resistance or it could be genetic makeup variability according to region. This study done in Pakistan and previous were done in Europe except few which was done in china.

CONCLUSION

Obese persons with elevated circulating concentration of ghrelin may be susceptible to the progression of increasing blood pressure. More work should be done in subcontinent region as it

has not been done in past.

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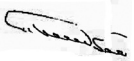
3	Muhammad Saeed	Proof reading.	
4	Sana Akram	Discussion writing.	
5	Sara Mahmood	Result compiling.