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ORIGINAL ARTICLE

Association of Body Mass Index with Orexin- A Levels in Reproductive Age Group Women

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ABSTRACT

Background and Aim: Orexin-A are hypothalamic neuropeptides contributing to regularization of neuroendocrine homeostasis, feeding behavior and sleep-wakefulness rhythm. Blood pressure, sympathetic activation, blood glucose level, and metabolic status is controlled by neuropeptide. The present study aimed to evaluate the association of body mass index with Orexin-A levels in reproductive age group women.

Methodology: This cross-sectional study was carried out on 120 healthy reproductive age group women at the Department of Physiology, Lady Reading Hospital, Peshawar from November 2020 to April 2021. Prior to study conduction, ethical approval was taken from the institute ethical committee. Informed written consent was obtained from each individual. All the healthy women of reproductive age group with age range from 18 years to 40 years were enrolled. Women with obstetrical problems and had pregnancy were excluded from the study. A pro-designed proforma was used for taking medical history and complications of each participant. All the participants underwent standardized questionnaire based interview regarding medical history, menstrual history, and obstetrical history. Anthropometric parameters of each participant was measured. Orexin-A/hypocretin-enzyme immunoassay kit was utilized for the measurement of fasting serum orexin levels. For data analysis and descriptive statistics, SPSS version 25 was used.

Results: Of the total 120 reproductive age group women, about 66 (53%) were in age group 18 to 25 years followed by 25 (20.8%) between 26 and 30 years, 17 (14.2%) in 31 to 35 years, and 12 (10%) in 35 to 40 years. Based on different age group women, the mean serum orexin-A levels ranged from 47.26±16.48 pgm/ml for women aged above 35 years to 51.31±13.89 pgm/ml for 26 to 30 years. However, no significant association were revealed in both group with statistically significant of P=0.781. A positive correlation was found between women BMI with serum orexin levels r=0.172, p=0.05 and weight of the women with orexin serum levels r=-.179, p=0.41.

Conclusion: The current study concluded that mean orexin-A levels was significantly associated with BMI. But no statistical significant association between women age and mean serum orexin level has been reported.

Keywords: Body mass index, Orexin-A levels, Reproductive age group women.

INTRODUCTION

The physiological mechanism that control reproduction are reciprocally associated with those that control energy balance and both the mechanisms improve the success of reproduction under changing metabolic conditions. The metabolic status of organism is connected to the brain cells through fuel detectors known as metabolic fuel detectors. These detectors are of different types present at both central such as orexin, neuropeptide Y etc. and peripheral insulin, leptin etc. [1, 2]. Orexin-A are hypothalamic neuropeptides contributing to regularization of neuroendocrine homeostasis, feeding behavior, and sleep-wakefulness rhythm. Blood pressure, sympathetic activation, blood glucose level, and metabolic status is controlled by neuropeptide [3]. De Lecea et al [4] first introduced the Orexin or hypocertin in 1998. The body's neuroendocrine homeostasis, feeding behavior, and sleep wakefulness are controlled by hypothalamic neuropeptides referred to Orexin A and B. During feeding and waking, alertness is promoted by Orexin. Brain is projected by hypothalamus Orexin neurons [5]. The peripheral structures contains the orexin receptor in thyroid, kidneys, vagal nerves, placenta, adrenals, and testes. Besides, it is present in pancreatic plexus, stomach endocrine cells, islets acini, and small intestines [6-8]. The barrier of blood brain infused by orexin-A not orexin B [9].

Orexin-A play a significant role as a hormone due to direct secretion of peptides into circulating blood [10]. The orexin-A peripheral levels in reproductive age women help in establishing a new functional vision. Obesity is a public health issue that affects millions people socially, medically, and economically worldwide [11]. The increasing BMI from ≥30 kg.m2 has adverse effects on women's health and causing increase risk of developing different diseases such as diabetes, cancer, and cardiovascular diseases [12]. A recent study conducted in a US reported that about 75% American has been transmuted from normal to overweight in 2020 [13]. The incidence of obesity increased almost doubled in European countries over the last two decades. Perez-Leighton et al [14] conducted a longitudinal study on reproductive age women and found that transition of older women from normal to overweight and obesity is less likely compared to younger women. Women's hormone play a significant role in appetite regulation. Additionally, the regularization of energy intake is significantly controlled by orexin neurons and metabolic complications might occurs due to energy homeostasis imbalance [15]. As per Mengesha et al study [16] on non-pregnant women reported that reproductive age women are more susceptible to obesity compared to men. The study of orexin action in humans has provided and continues to provide many new insights into human physiology as well as the development of novel scientific approaches. Therefore, the present study aimed to assess the association of body mass index with Orexin-A levels in reproductive age group women.

METHODOLOGY

This cross-sectional study was carried out on 120 healthy reproductive age group women at the Department of Physiology, Lady Reading Hospital, Peshawar from November 2020 to April 2021. Prior to study conduction, ethical approval was taken from the institute ethical committee. Informed written consent was obtained from each individual. All the healthy women of reproductive age group with age range from 18 years to 40 years were enrolled. Women with obstetrical problems and had pregnancy were excluded from the study. A pro-designed proforma was used for taking medical history and complications of each participant. All the participants underwent standardized questionnaire based interview regarding medical history, menstrual history, and obstetrical history. Orexin-A/hypocretin-enzyme immunoassay kit was utilized for the measurement of fasting serum orexin levels.

Anthropometric parameters of each participant was measured. A standard technique was used for measuring

anthropometric parameters at different position such as relaxed, face directed, and standing upright toward the examiner. Rigid staiometer was used for the measurement of height with barefoot. Calibrated balance was used for weight measurement at a scale set within 100 g without heavy clothes. BMI was determined for each participant by dividing weight over height in m2 (kg/m2). Centrifuge was set at 3000 rpm for serum separation. Blood sample were collected early in the morning on 10th day of their cycle to avoid cycle variations. SPSS version 25 was used for data analysis. Continuous data were described as frequency, percentage, and mean and standard deviation. Student's t-test was used for two mean values. Orexin-A correlation with continuous variables was calculated by Pearson's correlation with 5% level of significance.

RESULTS

Of the total 120 reproductive age group women, about 66 (53%) were in age group 18 to 25 years followed by 25 (20.8%) between 26 and 30 years, 17 (14.2%) in 31 to 35 years, and 12 (10%) in 35 to 40 years. Based on different age group women, the mean serum orexin-A levels ranged from 47.26±16.48 pgm/ml for women aged above 35 years to 51.31±13.89 pgm/ml for 26 to 30 years. However, no significant association were revealed in both group with statistically significant of P=0.781. A positive correlation was found between women BMI with serum orexin levels r=0.172, p=0.05 and weight of the women with orexin serum levels r=-.179, p=0.41. Figure-1 depicts the age-wise distribution of all the participants. Association of age-wise distribution with serum orexin levels is represented in Table-I. Figure-2 demonstrate the BMI based distribution of the participant. Table-II shows the association of serum orexin levels with BMI.

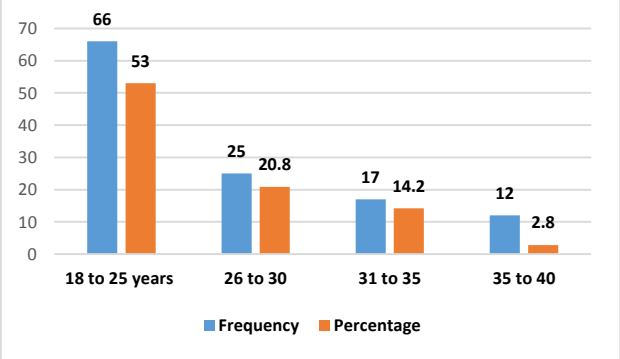

Figure-1: Age-wise distribution (n=120)

Table-1: Association of age-wise distribution with serum orexin levels

Age groups in years	Serum orexin-A levels in pgm/ml
18-25	50.69±12.92
26-30	51.31±13.89
31-35	50.12±11.93
35-40	47.26±16.48

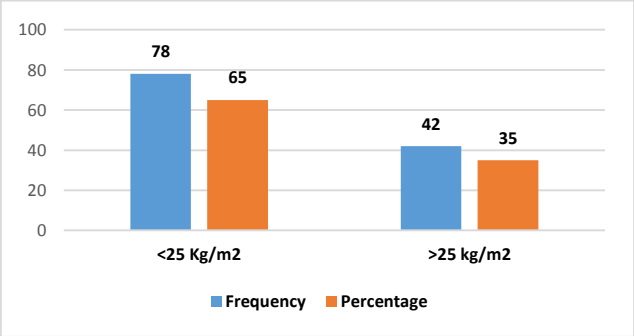

Figure-2: BMI based distribution of the participant (n=120)

Table-2: Association of serum orexin levels with BMI

BMI in Kg/m2	Serum Orexin-A levels
<25	49.13±13.24
>25	54.19±14.75

DISCUSSION

The main findings of the current study was a significant association between body mass index and serum orexin levels. There was no association between age of the women and serum orexin levels. It has been observed that serum orexin level increases with overweight and obesity among reproductive age group women. About 120 women of reproductive age between 18 and 40 years were investigated and found that there was decreasing trend in the levels of orexin serum with increasing age regardless of serum orexin levels were independent of age. A previous study by Williams et al [17] seen that with increasing age, there was absolute gain in weight and BMI and prevalence of major weight gain was higher in women of age between 25 years to 34 years. Similar to our findings, Gupta et al [18] investigated premenopausal women and found no significant association of increasing age with levels of serum orexin. Another study carried out on obese children reported no association between age and serum orexin levels [19].

The variation in metabolic state changes the orexin levels while orexin detected in the blood circulation. Lateral and dorsal hypothalamus contains orexin neurons [20]. However, in peripheral circulation of plasma orexin sources has not been clarified. Hypothalamus containing orexin neurons are activated by nervous system that alerts in fasting response. Orexin levels has strong correlation with obesity and raised BMI [21]. The present study report that women of reproductive age with BMI greater than 25 kg/m2 had higher levels of orexin serum. Additionally, overeating cause obesity and energy homeostasis is significantly influenced by orexin serum as an appetite-inducing neuropeptide [22]. The hypothalamus, a critical component in the regulation of energy homeostasis, constantly monitors signals indicating energy status and initiates appropriate behavioural and metabolic responses. It regulates glucose utilization in insulin-sensitive organs like skeletal muscle as well as overall energy metabolism.

Heinonen et al. [23] studied obese Indian women and found that obese women had significantly lower orexin serum levels compared to that control group women. Similarly, studies conducted by Matsumura et al [24] reported a negative correlation between BMI and plasma orexin-A levels. The suitable explanation for the above study's findings could be due to metabolic syndrome women were chosen as participants subjects. Also, central obesity caused by waist circumference and waist-hip ratio factors that affects orexin serum levels. Gupta et al [18] similarly done comparative study on premenopausal women and reported inverse correlation between orexin levels and waist circumference.

Previous few studies found varying orexin-A levels in blood of various age groups. Arihara et al [25] calculated the concentration of orexin levels in basal plasma was 1.94 ± 0.24 pmol/l (6.9 ± 0.9 pg/ml) in healthy women. The range of orexin-A levels in plasma measured by RIA from 1 pg/ml to 100 pg/ml. Tomasik et al [26] studied different age children and found higher levels of orexin from 175 pg/ml to 847 pg/ml. in the current study conducted on varying age reproductive women measured serum orexin levels varied from 47.26±16.48 pgm/ml for women aged above 35 years to 51.31±13.89 pgm/ml for 26 to 30 years. Long-term deleterious effects on healthy women could be imposed based on transition from normal to overweight or obese fertile women which in turn will effect pregnancy outcomes adversely in case women get pregnant [27]. The current study result resemble the findings of three different studies conducted by Sakurai et al., [28], Barreiro et al.[29], and Heinonen et al.[30] who reported a positive association between serum orexin levels and BMI. The levels of serum orexin was measured by ELISA.

CONCLUSION

The current study concluded that mean orexin-A levels was significantly associated with BMI. But no statistical significant association between women age and mean serum orexin level has been reported.

REFERENCES

1. Hao YY, Yuan HW, Fang PH, Zhang Y, Liao YX, Shen C, et al. Plasma orexin-A level associated with physical activity in obese people. Eat Weight Disord. 2016;19:69–77.
2. Digby JE, Chen J, Tang JY, Lehnert H, Matthews RN, Randeva HS. Orexin receptor expression in human adipose tissue: effects of orexin-A and orexin-B. J Endocrinol 2006;191:129–36.
3. Mishra S, Gupta V, Mishra S, Sachan R, Asthana A. Serum level of orexin-A, leptin, adiponectin and insulin in north Indian obese women. Diabetes Metab Syndr. 2017;11:1041-3.
4. de Lecea L, Kilduff TS, Peyron C, Gao X, Foye PE, Danielson PE, et al. Te hypocretins: hypothalamus-specific peptides with neuroexcitatory activity. Proc Natl Acad Sci U S A 1998;95:322-7
5. Jain S, Gupta V, Goel A, Gupta V. Orexin-A levels in reproductive age group women and its association with body mass index. Indian J Physiol Pharmacol 2022;66:70-4.
6. Khokhar KK, Kaur G, Sidhu S. Prevalence of obesity in working premenopausal and postmenopausal women of Jalandhar District, Punjab. J Hum Ecol 2010;29:57-62.
7. Sakurai T. Te neural circuit of orexin (hypocretin): Maintaining sleep and wakefulness. Nat Rev Neurosci 2007;8:171-81.
8. Barreiro ML, Pineda R, Gaytan F, Archanco M, Burrell MA, Castellano JM, et al. Pattern of orexin expression and direct biological actions of orexin-a in rat testis. Endocrinology 2005;146:5164-75.
9. Takahashi K, Arihara Z, Suzuki T, Sone M, Kikuchi K, Sasano H, et al. Expression of orexin-A and orexin receptors in the kidney and the presence of orexin-A-like immunoreactivity in human urine. Peptides 2006;27:871-7.
10. Adam JA, Menheere PP, van Dielen FM, Soeters PB, Buurman WA, Greve JW. Decreased plasma orexin-A levels in obese individuals. Int J Obes Relat Metab Disord 2002;26:274-6.
11. Kerman, I. A. (2008). Organization of brain somatomotor-sympathetic circuits. Exp. Brain Res. 187, 1–16. doi: 10.1007/s00221-008-1337-5
12. Messina G, Monda V, Moscatelli F. Role of orexin system in obesity. Biol Med. 2015;07:248–54.
13. Takahashi K, Arihara Z, Suzuki T, Sone M, Kikuchi K, Sasano H, et al. Expression of orexin-A and orexin receptors in the kidney and the presence of orexin-A-like immunoreactivity in human urine. Peptides 2006;27:871-7
14. Perez-Leighton CE, Billington CJ, Kotz CM. Orexin modulation of adipose tissue. Biochim Biophys Acta. 2014;1842:440–5.
15. Zink AN, Bunney PE, Holm AA, Billington CJ, Kotz CM. Neuromodulation of orexin neurons reduces diet-induced adiposity. Int J Obes (Lond) 2018;42:737–45.
16. Mengesha Kassie A, Beletew Abate B, Wudu Kassaw M. Education and prevalence of overweight and obesity among reproductive age group women in Ethiopia: Analysis of the 2016 Ethiopian demographic and health survey data. BMC Public Health. 2020;20:1189.
17. Williamson DF, Kahn HS, Remington PL, Anda RF. Te 10-year incidence of overweight and major weight gain in US adults. Arch Intern Med 1990;150:665-72.
18. Gupta V, Mishra S, Kumar S, Mishra S. Association of circulating orexin-a level with metabolic risk factors in north indian pre menopausal women. Indian J Physiol Pharmacol. 2015;59:422-7.
19. Chieffi S, Carotenuto M, Monda V, Valenzano A, Villano I, Precenzano F, et al. Orexin system: The key for a healthy life. Front Physiol. 2017;8:357–66.
20. Willie JT, Chemelli RM, Sinton CM, Yanagisawa M. To eat or to sleep? Orexin in the regulation of feeding and wakefulness. Annu Rev Neurosci 2001;24:429–58.
21. Kukkonen JP, Holmqvist T, Ammoun S, Akerman KE. Functions of the orexinergic/hypocretinergic system. Am J Physiol Cell Physiol 2002;283:C1567–91.
22. Adam JA, Menheere PP, van Dielen FM, Soeters PB, Buurman WA, Greve JW. Decreased plasma orexin-A levels in obese individuals. Int J Obes Relat Metab Disord 2002;26:274–6.
23. Heinonen MV, Purhonen AK, Ma¨kela¨ KA, Herzig KH. Functions of orexins in peripheral tissues. Acta Physiol (Oxf) 2008;192:471–85.
24. Matsumura T, Nakayama M, Satoh H, Naito A, Kamahara K, Sekizawa K. Plasma orexin-A levels and body composition in COPD. Chest 2003;123:1060-5.
25. Arihara Z, Takahashi K, Murakami O, Totsune K, Sone M, Satoh F, et al. Immunoreactive orexin-A in human plasma. Peptides 2001;22:139-42
26. Tomasik PJ, Spodaryk M, Sztefo K. Plasma concentrations of orexins in children. Ann Nutr Metab 2004;48:215-20
27. Modirrousta M, Mainville L, Jones B. Orexin and MCH neurons express c-Fos differently afer sleep deprivation vs. recovery and bear different adrenergic receptors. Eur J Neurosci 2005;21:2807-16.
28. Sakurai T. Te neural circuit of orexin (hypocretin): Maintaining sleep and wakefulness. Nat Rev Neurosci 2007;8:171-81.
29. Barreiro ML, Pineda R, Gaytan F, Archanco M, Burrell MA, Castellano JM, et al. Pattern of orexin expression and direct biological actions of orexin-a in rat testis. Endocrinology 2005;146:5164-75
30. Heinonen MV, Purhonen AK, Miettinen P, Pääkkönen M, Pirinen E, Alhava E, et al. Apelin, orexin-A and leptin plasma levels in morbid obesity and effect of gastric banding. Regul Pept 2005;130:7-13.