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Original Article

Association of Pituitary Hormones and Anthropometric Parameters in Obese Infertile Women

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ABSTRACT

Introduction: World Health Organization (WHO) has acknowledged infertility as a public health problem because it challenges medical, economic and psychosocial aspects of society. Obesity has a definite impact on ovulatory function that can result in menstrual abnormalities, recurrent miscarriage and infertility. The objective of this study was to compare hormone and anthropometric parameters between primary and secondary obese infertile women and to appraise any association between these two indices in primary and secondary obese infertile females.

Material and Method: This cross sectional study was carried out from January 2020 to December 2020 in infertility clinic of Bahawal Victoria Hospital. Out of 135 obese females, 90 were included in this study and secondary infertility was found in 57 of females while 33 had primary infertility. Serum FSH, LH, LH/FSH and prolactin were measured on day 3rd of menstrual cycle and BMI, waist and hip circumferences and Waist to hip ratio was calculated in both groups.

Results: Serum prolactin and LH/FSH ratio was statistically raised in obese secondary infertile group. In both groups, serum FSH and central obesity indices comprising of waist circumference and waist hip ratio exhibited significant positive association. In primary infertility, serum FSH demonstrated positive association with BMI and hip circumference while in secondary infertile women, prolactin level and BMI manifested positive association.

Conclusion: There was a link between hormonal derangement and obesity indices that can lead to infertility. Hence weight reduction should be considered important part of infertility treatment.

Key words: Obesity indices, Primary infertility, Secondary infertility, hormonal imbalances

Introduction

World Health Organization (WHO) has acknowledged infertility as a public health problem because it challenges medical, economic and psychosocial aspects of society. Social stigma associated with it brings unbearable stress for family and adversely affects the human behavior [1, 2]. It is calculated that 60-80 million couples are affected by this problem worldwide and it is estimated that every 4th couple might suffer from infertility in developing countries [3].

Although Pakistan is one of thickly populated countries of the world with growth rate of 2%. The analysis of recent data shows that prevalence of infertility is about 21.9% in which primary infertility is seen in 3.5% and 18.4% belongs to secondary infertility group [4].

The female reproductive function is under the intricate and complex control of gonadotropins (FSH, LH), gonadotropin releasing hormones GnRH and ovarian hormones. Previous studies have concluded that BMI influences the hypothalamo–pituitary– gonadal hormonal balance and fertility treatments showed poor outcome in obese infertile women [5, 6]. Pituitary hormones not only manifested major contributory role in normal growth and development of female reproductive system but also regulates the ovarian and menstrual cycle in reproductive age group. Many of reproductive disorders are caused by disturbance in the pulsatile frequency and secretion of gonadotrophin releasing hormone that influences

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normal secretory pattern and amount of luteinizing hormone (LH) and follicular stimulating hormone (FSH) [7]. The level of FSH strongly predict fertility outcome as higher levels seen in on 3rd day of reproductive cycles were associated with poor outcome of fertility treatment. Similarly pulsatile secretion of GnRH is influenced by prolactin hormone and hyperprolactinemia can lead to prolonged luteal phase resulting in menstrual problems of oligomenorrhea and amenorrhea in younger women [8]. The maturation and function of female reproductive system is dependent on distribution of adipose tissue and severity of obesity. Body mass index and waist to hip ratio (WHR) are major indicators used to determine obesity. Obesity has a definite impact on ovulatory function that can result in menstrual abnormalities, recurrent miscarriage and infertility [9]. The objective of this study was to compare hormone and anthropometric parameters between primary and secondary obese infertile women and to appraise any association between these two indices in primary and secondary infertile females.

Material & Method

This cross sectional study was carried out from January 2020 to December 2020 in infertility clinic of Bahawal Victoria Hospital. The clinical examination of study group was performed and their medical records were reviewed for any history of tuberculosis, hepatitis B or C'', benign ad malignant tumors and any hormonal profile finding suggestive of postmenopausal status. The study participants were divided into primary and secondary infertility groups. In primary infertility groups those females were enrolled that "have never conceived for a period of 1 year despite exposure to the risk of pregnancy" while secondary infertile participants were those "who despite cohabitation and exposure to the risk of pregnancy fail to conceive following a previous pregnancy (in the absence of contraception, breastfeeding or postpartum amenorrhea) for 1 year". The anthropometric measurements were done by one person to rule out any inter-individual variation. Height and weight of participants were measured and BMI was calculated and those with BMI more than 29.9 kg/m2 were included in the study. Waist and hip circumferences were measured and waist to hip ratio was calculated by dividing the waist circumference to gluteal circumference. A WHR of > 0.70 was considered as an indicator of central obesity.

Out of 135 obese females between the age of 18-38 years 90 were included in this study who fulfilled the inclusion criteria. Secondary infertility was found in 57 of females while 33 had primary infertility and informed consent was taken from all study subjects. The standard venipuncture technique for blood sample collection was used and 5 ml of venous blood was drawn on 3rd day of menstrual cycle. The samples were centrifuged and serum FSH, LH, prolactin and testosterone were measured on Access 2 using chemiluminescence technique.

Statistical analysis was carried out using SPSS version 21.0. The normality of data was assessed by Kolmogrov–Smirnov test. The t test was applied comparison different hormones and anthropometric calculations between primary and secondary infertility groups. Pearson's correlation was performed for hormonal profile (FSH, LH and LH /FSH atio and prolactin) and anthropometric parameters (BMI, waist and hip circumferences and WHR). The p-value <0.05 was considered statistically significant.

Results

The obese females of both groups were compared for age variations and anthropometric estimation. Mean age of secondary infertile females were more as compared to other group and duration of infertility was prolonged in secondary infertility group (p = 0.001). Most participants were from middle socioeconomic class of urban areas. The two groups were compared for anthropometric measurements and calculation showed that hip and waist circumferences, waist to hip ratios and BMIs were statistically higher in females with secondary infertility (Table 1).

Table 1: Demographic and Anthropometric measurements between primary and secondary infertility

Parameters	Primary Infertility Mean±SEM	Secondary Infertility Mean±SEM	p – value
Age (years)	21.30±4.74	29.27±6.01	0.000
Duration of Infertility (years)	1.86±2.32	3.27±4.35	0.001
BMI (kg/m2)	25.69±3.84	28.13±2.73	0.004
Hip Circumference (cm)	99.89±6.06	104.03±7.88	0.000
Waist Circumference (cm)	85.13±7.06	89.89±9.79	0.002
Waist-Hip Ratio	0.84±0.36	0.88±0.86	0.012

Although levels of serum FSH were higher while low LH levels were observed in secondary infertility group but the difference were not statistically significant while calculated LH/FSH ratio and serum prolactin were found to be raised in secondary infertility group and statistically results were noted to be significant as noted in table 2. The serum testosterone levels of both groups showed no difference.

Table 2: Comparison of hormonal profile between primary and secondary infertility

Parameters	Primary infertility	Secondary infertility	p-value
FSH (IU/L)	8.74 ± 1.98	10.08 ± 2.01	0.09
LH (IU/L)	12.19 ± 1.56	9.84 ± 1.83	0.13
LH/FSH ratio	1.72 ± 0.17	0.95 ± 0.67	0.00
Prolactin(µg/L)	21.49 ± 2.33	24.39 ± 1.81	0.02

Correlation studies were performed on anthropometric parameters and hormonal profile of both study groups as shown in Table 3.

Table 3: Association between Anthropometric parameters and Pituitary Hormonal profile of both groups

	Primary infertile women				Secondary infertile women			
Parameters	FSH	LH	Prolactin	LH/FSH	FSH	LH	prolactin	LH/FSH
BMI (kg/m2)	R=0. 67 p = 0.005	R=-0.03 p=0.56	R=-0.22 p=0.75	R=-0.21 p=0.38	R=-0.17 p=0.37	R=0.031 p=0.59	R=0.56 p=0.003	R=0.04 p=0.63
Hip Circumference (cm)	R=0.51 p=0.02	R=-0.12 p=0.72	R=0.05 p=0.90	R=-0.29 p=0.15	R=0.04 p=0.82	R=0.109 p=0.32	R=0.54 p=0.021	R=0.11 p=0.43
Waist Circumference (cm)	R=0.62 p=0.000	R=-0.19 p=0.98	R=0.06 p=0.78	R=-0.13 p=0.26	R=0.62 p=0.043	R=-0.08 p=0.783	R=0.18 p=0.29	R=-0.21 p=0.51
Waist-Hip Ratio	R=0.58 p=0.002	R=0.07 p=0.63	R=0.12 p=0.97	R=-0.03 p=0.85	R=0.58 p=0.02	R=-0.19 p=0.24	R=-0.02 p=0.909	R=-0.24 p=0.65

The regression analysis was performed on different anthropometric indices and pituitary hormones. In both groups, serum FSH and central obesity indices comprising of waist circumference and waist hip ratio exhibited significant positive association. In primary infertility, serum FSH demonstrated positive association with obesity indicators of BMI and hip circumference. In secondary infertility group, prolactin level and BMI manifested positive association with each other that was quite significant statistically.

Discussion

The obese females with primary and secondary infertility were compared and evaluated for the anthropometric indices (waist and hip circumferences, BMI and waist hip ratio) and various pituitary hormones (FSH, LH and prolactin levels) in this cross sectional study

The age of both partners is a contributory factor in deciding the fecundity of couple. The mean age (21.30±4.74 vs 29.27±6.01) and duration of infertility (1.86±2.32 vs3.27±4.35) of the women with secondary infertility was more as compared to those with primary infertility group. This finding was congruent with previous studies that fertility potential of female decreases with advancing age[10, 11].

The amount and distribution of adipose tissue plays an important role in the normal function of female reproductive system. Many reproductive disorders could be attributed due to abnormal secretory pattern of insulin, androgens and leptin in obese women. [12]The anthropometric parameters were higher in our secondary infertility group and they were statistically significant. Previous work supported that higher anthropometric measurements of secondary infertile are due to age related nutritional and life style modification and previous pregnancy associated fat accumulation in these areas [13]. But the results of Indian and Ghana studies were incompatible with this finding showing no difference between two groups [14, 15].

FSH is responsible for development and maturation of ovarian follicles and production of androgens that are aromatized to estrogen. LH regulates the ovulation, luteinisation and secretion of androstenedione from ovarian theca interna cells. The insufficient secretion and imbalance of these hormones are main causes of infertility and hormonal imbalances can be determined by blood tests of reproductive hormone levels. [16] Measurement of serum FSH, LH and prolactin are performed to determine ovulatory and menstrual abnormalities and to determine preconception hormonal status and to predict pregnancy outcome with different infertility treatment.

Serum FSH levels were higher while low LH levels were observed in secondary infertility group, though the difference was not proven statistically significant for both FSH and LH measurements but LH/FSH ratio between two groups were statistically significant as higher levels were noted in primary infertility group (1.72 ± 0.17 vs 0.95 ± 0.67)[11, 15].

The elevated level of FSH of secondary infertile females in early follicular phase is indicator of poor ovarian reserve and there will be less chances of successful ovulation induction [5]. Both groups showed positive correlation of FSH levels with waist circumference and WHR, indicators of central obesity [15]. The results are deviated from the finding of Ghanaian population that reported positive correlation of LH with obesity indicators of both groups [14].

The result of positive association of serum FSH and BMI were in align with work of Khan et al that exhibited similar findings in cases of secondary infertility[17].

The raised FSH levels seen in secondary infertility might be due to decreased negative feedback from inactive ovaries and also with advancing age there is increased weight gain resulting in more lipid accumulation around the waist giving android obesity. The finding of this study was in contrast to results of Italian infertile women where obesity was inversely related with LH and FSH levels [18].

Hyperprolactinemia is the most common endocrine abnormality that is responsible for about one-third of female infertility cases [19]. The prolactin levels were statistically significantly raised in secondary infertile female. The results of our study were in accordance with Nigerian study that showed that 72% of female with raised prolactin levels had secondary infertility [20]. Bangladeshi study produced contrary results stating that hyperprolactinemia was more prevalent among primary infertile women. [21]. It has been suggested that prolaction impairs the gonadotrophin hormone function by decreasing GnRH secretion resulting in decreased production of ovarian hormones. This impairs the cyclic rhythm of FSH and LH production resulting in decrease estrogen production that can result in infertility [18]. The work of current study revealed that serum prolactin had positive association with BMI and this was in accordance with Yilmaz et al that showed significant positive correlation between prolactin and two anthropometric measurements i,e BMI and body weight[22].

In our study, a statistically positive association was found between serum prolactin and BMI in secondary infertile women. This relationship was also observed in another study where basal and TRH stimulated prolactin level were compared between obese and control groups were measured and definitive association were exhibited between serum prolactin and obesity indicators [23].

However study conducted by Ernst et al failed to show any relationship between prolactin and various obesity indices [24].

The limitation of our study is that it was conducted on small group of obese infertile women due to financial constraints and large population based study should be conducted to support the findings of our results. Second our study lacked control group for comparison of anthropometric and hormone parameters.

Conclusion

The present study revealed that central and visceral obesity might contribute to infertility and our results showed positive correlation with various hormonal parameters. Hence weight reduction should be considered important part of infertility treatment. Hormonal imbalance can be managed successfully if appropriate measures are taken to control obesity. The beneficial effects of weight reduction can be seen in the form regular menstrual periods and chances to become pregnant through spontaneous conception by ovulatory cycle are also increased. Before commencing any medical or expensive surgical management of infertility, obese female should be encouraged to adopt healthy lifestyle and carry out weight reduction exercises.

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