

Prevalence and Causes of Infertility in Overweight and Obese Women in a Tertiary Care Hospital Setup in Mangalore - A Retrospective Secondary Data Analysis

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ABSTRACT

BACKGROUND

Obesity has become an epidemic worldwide. Several mechanisms are involved in the relationship of fertility and obesity, including metabolic and reproductive functions. In light of the fact that most of the causes of infertility are treatable, there is a need to document the diagnostic findings in overweight and obese infertile women. The causes of infertility prevalent in a particular region can be provided by hospital-based studies. So, the present study is designed to find out the common causes of infertility in overweight & obese women and to gain knowledge regarding the prevalence of primary and secondary infertility among these infertile women.

METHODS

The data of 115 infertile women (18 to 45 years) were collected from hospitals under Kasturba Medical College (KMC), Mangalore retrospectively. Data of history of previous conception, body mass index (BMI), type of infertility, duration of infertility, age and the causes of infertility were collected. The prevalence of each cause was evaluated.

RESULTS

Among 115 infertile women, 92 (80 %) were pre-obese and 23 (20 %) were obese (P = .001). Primary infertility was most common in pre obese women and secondary infertility in obese women which was statistically significant (P < .05). Ovulatory dysfunction was the most common cause in obese infertile women (P = .004), whereas in pre obese women, it was uterine and adnexal causes.

CONCLUSIONS

Comparatively, maintaining a healthy lifestyle can avoid fertility problems in pre obese women, because the effect of BMI on hypothalamic-pituitary-gonadal (HPG) axis is higher in obese women in whom ovulatory disorders were the leading cause. The significance of weight reduction before pregnancy should be informed to overweight and obese patients and should be aided to lose weight. Treatment of anaemia itself may resolve the infertility issues and should be taken as a first line treatment in all cases.

KEYWORDS

Female Infertility, Adipose Tissue, Obesity, Infertility Causes, Ovulatory Dysfunction

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BACKGROUND

There is great concern at the high prevalence of and the increasing trend to obesity worldwide. The increase in obesity worldwide is attributable to a combination of reduced exercise, changing dietary composition and increased energy intake. Gynaecologists and reproductive scientists have encountered the reproductive consequences of a society increasing in weight as a higher frequency of women diagnosed with disorders of menstruation, infertility, diabetes mellitus in pregnancy and other significant sequelae. Previous studies assessing trends in obesity found that its prevalence has increased in both adults and children of all ages, indiscriminate use of geographical locality, ethnicity or socioeconomic status.¹ Obesity is associated with many adverse maternal and fetal effects prenatally, but it also exerts a negative influence on female fertility.

In low-income countries, obesity is generally more prevalent among middle-aged adults from wealthy and urban environments (especially women).² Globally, a total of 609 million adults were estimated to be obese in 2015. The prevalence of obesity was generally higher in women than in men in all age groups. The rates of obesity increased with age from 20 years old onwards. Kelly et al. estimated that 57.8 % of the world population will be overweight or obese by the year 2030 if the current trends continue.³ The rise in the prevalence of obesity was greatest between 1992 and 2002, and was always greater in women than in men throughout this period; sex differences in obesity remained remarkably constant over time.¹ Generally, the prevalence of obesity is higher in women than men in all sociodemographic levels.⁴

Infertility is a critical medical condition affecting many couples. Infertility is worldwide problem affecting people of all communities, though the cause and magnitude may vary with geographical location and socioeconomic status. It is estimated that globally 60 - 80 million couples suffer from infertility every year, of which between 15 - 20 million are in India alone.⁵ Infertility seems to be a multidimensional health issue which occurs not only due to health problems, but it may also be a result of ovulation problems, tubal blockage, age-related factors, uterine problems, hormone imbalance and the choices imposed by the modern lifestyle, like the higher average age of people who get married and stress.⁵

Obesity is a pressing health issue and a common problem with reproductive aged women. Abnormal and excessive fat accumulation are seen in obese individuals which influence their health. Obesity is also associated with anovulation, menstrual disorders, infertility, difficulties in assisted reproduction, miscarriage, and adverse pregnancy outcomes.

With an escalating figure of overweight and obesity worldwide, the findings of this study should therefore be of general and administrative interest throughout India and similar countries. In light of the fact that most of the causes of infertility are treatable, there is a need to document the diagnostic findings in overweight and obese infertile women. The causes of infertility prevalent in a particular region can be provided by hospital-based studies. We focused on the

information mainly from a tertiary care hospital attended by most of the infertile couples from that region.

The present study is designed to find out the common etiological causes of female infertility with respect to overweight & obesity and to gain knowledge regarding the prevalence of primary and secondary infertility among these infertile women.

METHODS

This is a cross-sectional study that was carried out at hospitals attached to Kasturba Medical College (Lady Goshan hospital, KMC Attavar hospital), Mangalore. The file numbers were collected from the out-patient department (OPD) of OBG (Obstetrics and Gynaecology) Department and only cases of infertility were taken for the study. The data for this study was collected from hospitals under Kasturba Medical College (KMC), Mangalore. The study population included 115 infertile women (failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse) with overweight and obesity who came for infertility work up in the age group of 18 to 45 years. The duration of the study was 1 year and 1 month from November 2017 to December 2018.

The Asian criteria of classification of BMI were used in this study to categorize pre obese (BMI of 23.0 – 27.5) and obese women (BMI of > 27.5).⁶ Data were collected from standardized history sheets at the medical records department (MRD) after taking permission. The following parameters were obtained for the study: History of previous conception, body mass index, type of infertility, duration of infertility, age and the causes of infertility.

The entire sample population was divided into primary and secondary infertility based on world health organization (WHO) infertility definitions and terminologies⁷ and the results were analyzed. The causes of female infertility were grouped into ovulatory dysfunctions (which includes polycystic ovarian syndrome (PCOS) and hyperprolactinemia), uterine and adnexal causes (includes salpingitis, tubal occlusion, tubal dysfunctions, uterine fibroids, endometrial polyps, intrauterine synechiae, uterine malformations, endometriosis) and systemic causes (includes hypothyroidism, hyperthyroidism and anaemia).

Women with primary infertility, secondary infertility and infertile women with hypothyroidism, hyperthyroidism and anaemia within the age group of 18 – 45 years attending the above hospitals were included in the study. Pre obese infertile women (BMI of 23.0 – 27.5) and obese infertile women (BMI of > 27.5) were included in the study. Couples who had not lived together for at least 12 months, couples with male factor infertility were excluded. Infertile women classified as under underweight (BMI of < 18.5) and normal weight (BMI of 18.5 – 22.9) were excluded in the study. Infertile women > 45 years of age were also excluded.

Statistical Analysis

Data analysis were done using SPSS (statistical package for social sciences) version 17.0. To compare the proportion

between two groups in each diagnostic category chi - square test was used. A value of $P < 0.05$ was considered statistically significant. Appropriate description and inferential statistics were used for data analysis and presented in the form of tables, graphs and figures.

Definitions

Primary Infertility

When a woman is unable to ever bear a child, either due to the inability to become pregnant or the inability to carry a pregnancy to a live birth she would be classified as having primary infertility.⁷

Secondary Infertility

When a woman is unable to bear a child, either due to the inability to become pregnant or the inability to carry a pregnancy to a live birth following either a previous pregnancy or a previous ability to carry a pregnancy to a live birth, she would be classified as having secondary infertility.⁷

Ethical Considerations

Time bound research ethics committee approval to conduct the study was obtained.

RESULTS

Among the study population, the prevalence of primary infertility was 63.48 % and secondary infertility was 36.52 %. (Figure 1). Among 115 infertile women, 92 were pre-obese & 23 were obese. Mean BMI ranged between 26.9 and 31.9 in pre obese and obese groups. Mean age was almost similar in pre obese and obese groups. On an average, the duration of infertility was between 2 – 3 years. (Table 1). Primary infertility was more prevalent in pre-obese women [65 (70.65 %)] whereas in obese women, secondary infertility [15 (65.22 %)] was prevalent (Table 2).

Ovulatory dysfunctions were found to be higher in obese infertile women [14 (60.87 %)] and uterine adnexal causes in pre obese women [37 (40.21 %)]. Systemic causes which includes hypothyroidism, hyperthyroidism and anaemia is highest in overweight infertile women. (Table 3).

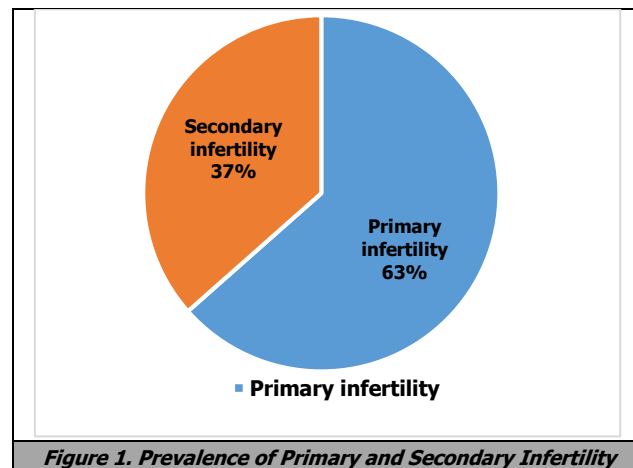


Figure 1. Prevalence of Primary and Secondary Infertility

DISCUSSION

Exploration of the relationship between reproductive functions and obesity are still being continued. However, the mechanism of how obesity affects the reproductive system is complex and multifactorial. The insulin resistance and leptin levels are increased and hyperandrogenaemia occurs in obese women. Similarly, anovulation, changes in adipokine levels and the HPG axis, and steroidogenesis in obese women affects the reproductive system.⁸ Obesity may impair reproductive functions by affecting both the ovaries and endometrium.⁹ The HPG axis deteriorates because of changes in hormonal and some substrate levels. The levels of luteinizing hormone (LH), androstenedione, estrone, insulin, triglycerides, and very low density lipo-protein are increased and high-density lipoprotein levels are decreased in obese women. Because of these changes, the HPG axis deteriorates.¹⁰

In this study, on an average, the duration of infertility was between 2 – 3 years. The major factor for timing routine exploration and starting the treatment depends upon the duration of infertility, or time to conception. The assumption is that, the probability of conception is less if the duration of infertility is long and therefore investigations are started after 1 year of infertility. On the other hand, one of the indications to use assisted reproductive technology (ART), even without routine investigation of the female infertility is a prolonged duration of infertility. As seen in our study, couples with less than 3 years duration of infertility have a 1.8-fold higher probability of conceiving than those with longer duration. The probability of live birth is also 1.5-fold higher if the female partner is younger than 30 years and has had a previous pregnancy (secondary infertility).¹¹

The mean age ranged between 24 - 33 years in our study, which was almost similar in both pre obese and obese groups. Advanced age is a risk factor for female infertility, pregnancy loss, fetal anomalies, stillbirth, and obstetric

Characteristics	Body Mass Index (kg/m ²)	
	23.0 – 27.5 (n = 92)	> 27.5 (n = 23)
BMI, mean (SD)	26.9 (1.1)	31.9 (1.3)
Age (years), Mean (SD)	28.5 ± 5	28.2 ± 4.2
Infertility duration (years), median (IQR)	3 (2 - 5)	2 (2 - 6)

Table 1. Distribution of Study Population by Body Mass Index in Relation to Their Characteristics

SD – Standard Deviation; IQR – Interquartile range

Type of Infertility	Pre Obese (n = 92)	Obese (n = 23)	P Value
Primary infertility, n (%)	65 (56.52)	8 (6.96)	.001 ^a
Secondary infertility, n (%)	27 (23.48)	15 (13.04)	.001 ^a

Table 2. Distribution of Study Population by Type of Infertility

^achi-square test

Causes	Body Mass Index (kg/m ²)		P Value
	23.0 – 27.5 (n = 92)	> 27.5 (n = 23)	
Ovulatory dysfunctions, n (%)	27 (29.34)	14 (60.87)	.004 ^a
Uterine and adnexal factors, n (%)	37 (40.21)	7 (30.43)	.38 ^a
Systemic factors, n (%)	28 (30.43)	2 (8.69)	.033 ^a

Table 3. Distribution of Causes of Infertility According to Pre-Obese and Obese Women

^aChi - square test

complications. Women are delaying childbearing to pursue educational and career goals in greater numbers than ever before. So, the risks of advanced maternal age should be informed to the women and policy measures should be provided by a public health approach for women which will be convenient to start their family life at the right age without sacrificing personal career goals.

According to this study, primary infertility is more prevalent when compared to secondary infertility. Low prevalence of secondary infertility may be because the couples with secondary infertility tend to get less social support than couples who have primary infertility. However, it is eminent that most of these estimations use diverse infertility definitions and deal with varying duration of the study, which made the results incomparable. Thus, our results enlarge the inadequate data on infertility prevalence among South Indian population.

In our study, ovulatory dysfunctions which include polycystic ovarian syndrome and hyperprolactinemia were the leading cause in obese infertile women. This finding is supported by a study which included women from infertility clinics which says that the risk of ovulatory infertility is highest in obese women.¹² In obese women, gonadotropin secretion is affected because of the increased peripheral aromatization of androgens to oestrogens. The insulin resistance and hyperinsulinemia in obese women leads to hyperandrogenaemia. The sex hormone-binding globulin (SHBG), growth hormone (GH), and insulin-like growth factor binding proteins (IGFBP) are decreased and leptin levels are increased. Thus, the neuro-regulation of the hypothalamic-pituitary-gonadal axis deteriorates.¹⁰ These alterations may explain impaired ovulatory function and so reproductive health.

The studies demonstrated that as the BMI increases, leptin levels increase both in blood and follicular fluid.¹³ Leptin stimulates HPG axis by signalling the hypothalamus to initiate the reproductive maturation. In a mouse model, after increasing the dietary fat intake in both male and female DBA / 2J strain mice, insulin resistance and glucose intolerance developed; however, only the female rats had a dietary-induced obesity and hyperleptinemia, thereby causing a 60 % decrease in the spontaneous pregnancy rate.¹⁴

Furthermore, obese women have higher levels of circulating free fatty acids, which damage non adipose cells by increasing reactive oxygen species (ROS) that, in turn, induce mitochondrial and ER stress resulting in apoptosis of multiple cell types including oocytes.¹⁵ This effect is related to the chronic low grade inflammatory state related to obesity which is proven by the increased circulating levels of C-reactive protein (CRP), as well as lactate and triglyceride concentrations in follicular fluid, and by the enhanced expression of pro-inflammatory (CXCL2) and oxidative stress related (DUSP) genes.¹⁶

Our study showed that there remained a greater percentage of women under overweight presented with uterine and adnexal factors. Infertility may be the result of anatomical defects or physiologic dysfunctions of the peritoneal cavity, including infection, adhesions, and adnexal masses. The conditions which affect the motility of the

fallopian tubes or produce blockage of the fimbriae with development of hydrosalpinx are pelvic inflammatory disease, peritoneal adhesions secondary to previous pelvic surgery, endometriosis, and ovarian cyst. Large myomas, pelvic masses, or blockage of the cul-de-sac hampers the accumulation of peritoneal fluid and interferes with the normal oocyte pickup mechanism. Peri-ovarian adhesions that encapsulate the ovary interfere with the normal oocyte release at ovulation, becoming a mechanical factor for infertility.¹⁷ The causes of infertility in women with endometriosis may range from anatomical distortions due to adhesions and fibrosis to endocrine abnormalities and immunological disturbances. Though these mechanisms have been proposed, none of them has been recognized to clarify the relation with infertility.

Thyroid dysfunction adversely interferes with the outcome of pregnancy, disturbs many organs as well as the female gonads and diminishes the probability of pregnancy. In our study, overall 29.4 % of women had thyroid disorders. In a hospital based cross sectional study done at Chennai, it was shown that 91.4 % of hypothyroid infertile women were obese and the association was strongly significant.¹⁸ Numerous studies have highlighted that thyroid functions have effects over female infertility by both direct and indirect ways. Obesity is generally regarded by patients as being secondary to thyroid dysfunction. Recent view shows that changes in thyroid-stimulating hormone (TSH) could well be secondary to obesity. Recent data have also disclosed a relation between obesity and thyroid autoimmunity with the adipocyte hormone leptin appearing to be the key factor linking these two conditions.

The link between obesity and the risk of autoimmune thyroid dysfunction (AITD), which is the main cause of hypothyroidism in adults, is a gray area. The prevalence of AITD in obesity has been reported to be 12.4 % in children and between 10 % and 60 % in adults.¹⁹ Marzullo et al. addressed the intriguing hypothesis of a link between obesity, leptin, autoimmunity, and hypothyroidism. This study suggested that obesity is a risk factor for thyroid autoimmunity, thus establishing a link between the main cause of acquired thyroid failure and obesity.²⁰ This investigation as well as other studies supports a role for autoimmune subclinical hypothyroidism in the pathogenesis of obesity.²¹

In economically deprived communities of developing countries dietary deficiency anaemia can be still a cause of infertility. The high incidence of anaemia amongst the deprived populations of developing world makes it a common cause of infertility. When likened to women with adequate iron stores, women who do not have enough amounts of iron, experience anovulation and possibly poor egg health. This finding shows a clear connection between female infertility and reduced iron intake, which shows the importance of intake of iron through food and as supplements for women trying to conceive. In the present study, 9.8 % of infertile women overall had anaemia. A study reported that, the risk of ovulatory infertility was significantly less in females who got the iron supplements than in women who did not consume iron supplements.²²

Any efforts to treat infertility or to even start preliminary investigations should be deferred until anaemia is treated. Treatment of anaemia itself may resolve the infertility issues and should be taken as a first line treatment in all cases. It is tough to express the number of couples having difficulty in conceiving because few couples might be against medical help. Increase in the incidence of infertility can also be attributed to exposure to environmental pollutants and chronic stress. Although the reasons for infertility are plentiful, and differ among the world regions, the nutritional factors, epidemic infections and lifestyle could be the major determinants in most latitudes.

CONCLUSIONS

Comparatively, maintaining a healthy lifestyle can avoid fertility problems in pre obese women, because the effect of BMI on HPG axis is higher in obese women in whom ovulatory disorders were the leading cause. Increase in chances of conception is possible by identifying and controlling chronic diseases such as hyperthyroidism and hypothyroidism. The need for health care should relate to the cultural realities of specific locations where infertility is a pervasive and serious concern it should be addressed through health care programs. The significance of weight reduction before pregnancy should be informed to overweight and obese patients and should be aided to lose weight. A positive relationship also exists between pre-conception body mass index and the time needed to fall pregnant in women who are overweight and obese.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

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