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Association Between Body Mass Index and Infertility Among Women: An Age-Matched Case-Control Study

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Abstract: Ample literature exists which time and over has established the association between overweight/ underweight and fertility problems. Further in this context, it should be noted that there are very few studies in the Indian context regarding the effect of body mass index (BMI) on infertility in women. To evaluate the association of BMI with infertility among women in Tamil Nadu, India. An age-matched hospital-based case-control study was conducted including 204 women attending a tertiary care hospital in the Chengalpattu district of Tamil Nadu. Of these, 102 women who had a clinical diagnosis of infertility were selected as cases. Hospital controls were defined as women who did not have a clinical diagnosis of infertility and were selected after matching for age and years of marriage (± 2 years). BMI was calculated from the height and weight measurements taken during the time of recruitment to the study. Basic socio-demographic data were also collected from all the study participants. Among cases, 17.6% were underweight, 25.5% were overweight and 5.9% were obese. Whereas, among controls, 7.8% were underweight, 47.1% were overweight and 11.8% were obese. Among the cases, 68% had primary infertility and 32% had secondary infertility. Overweight and obese women had 2.82 odds (95% CI, 1.48 – 5.38) and 3.06 odds (95% CI, 1.05 – 8.93) respectively of having infertility when compared to women who fell within the normal BMI range. Both overweight and obesity were observed to be significantly associated with infertility. The focus should be given to the prevention and control of both as an effective means of reducing the risk of infertility and other associated disorders.

Keywords: Infertility, BMI, Case-control, Overweight, Obesity

1. Introduction

Infertility, by definition, is "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse".(Ibitoye *et al.,* 2023) Infertility is considered a major public health issue which not only affects the couple's life but also the utilization of health care services and socio-economic aspects of life. (Kundu *et al.,* 2023) It interferes with one of the most fundamental and highly valued human activities and thus presents a significant life challenge.(Ibitoye *et al.,* 2023; Kredentser, 1986) According to the 2020 Ernst and Young report, 27.5 million couples, who are keenly trying to conceive, are shaken by infertility in India.(Bhardwaj, 2023; Ganguly & Unisa, 2010)

Infertility can be classified into two groups namely, primary, and secondary infertility. (Waheed *et al.,* 2019) Siega-Riz AM, *et al*, in 2005 analyzed 53 demographic health surveys and reported that the observed global prevalence of primary and secondary infertility was 0.6% to 3.4% and 8.7% to 32.6% respectively.(Siega-Riz et al., 2006) The report went on to state that the observed national prevalence of primary and secondary infertility was 2.7% and 24.6% respectively in India. In a study by Borumandnia *et al*. using data from the Global Burden of Disease database spanning 1993 to 2017 across 195 countries, the longitudinal trends of primary and secondary infertility prevalence rates (PSIPR) per 100,000 were examined. The study revealed that globally, primary and secondary infertility rates were higher among women than men. Notably, in high-income countries, primary infertility rates

decreased by 9.3% for men and 11.6% for women, while regions like South Asia saw significant increases in primary infertility among women (40.9%) and Middle Eastern/North African men (19.0%). Secondary infertility declined among women in Central Asia, Central Europe, Eastern Europe, and high-income countries (-16.9% and -11.7%, respectively), but showed alarming increases in the Middle East, North Africa, and South Asia (119.9% and 83.4% for women, and 48.4% for South Asian men). These findings underscore the need for region-specific interventions and further research in addressing infertility disparities.(Borumandnia *et al.,* 2022)

Both overweight and underweight have been significantly associated with reproductive dysfunctions, which may or may not expose the confounding influence of both biological and social factors on infertility. (Yang *et al.,* 2021) Underweight as well as overweight and obese are linked to an amplified risk of anovulatory infertility, proving to be a major public health concern with nearly one-fifth of reproductive dysfunctions being attributed to underweight or overweight. (Nelson & Bulun, 2001, Thoma *et al.,* 2021, Woodward & Mehta, 2019) A review of the existing literature showed that both overweight (BMI ≥ 25 kg/m2) and underweight (BMI ≤ 18.5 kg/m2) can contribute to fertility problems. (Rafael *et al.,* 2023; Rich-Edwards *et al.,* 2002) A study done by Jokela M et al reported that the probability of having children is significantly decreased in obese and underweight adolescent girls when compared to women who had a BMI within the prescribed normal range.(Jokela *et al.,* 2007)

BMI is one of the most significant anthropometric measures which describes weight to height and objectively describes the nutrition status of an individual. (WHO, 2021; Risch *et al.,* 2023) It is believed that to achieve optimal health existence, an individual's BMI range should be between 21 and 23 kg/m2. However, the 18.5-24.9 range is considered normal according to the World Health Organization, which by default classifies anything below the lower limit as underweight and above the higher limit as overweight. In 2016, the prevalence of overweight (BMI = 15.0 to 29.9 kg/m2) was observed to be 39% in both men and women. However, the obesity (more than 30 kg/m2) prevalence was slightly higher among women when compared to men with 15% and 11% respectively. In India, the proportion of overweight and obese individuals has been increasing at an alarming rate. According to the National Family Health Survey, India (NFHSI), the prevalence of overweight was 8.4 and obesity was 2.2 in 1998, this has increased to 15.5 and 5.1 respectively by 2015. Luhar *et al*. employed a multi-state life table approach to project the prevalence of overweight and obesity in Indians aged 20 to 69 years by age, gender, and urban or rural residence up to 2040. Their study utilized data from national surveys and health studies to estimate initial overweight rates. The findings indicate a significant increase in overweight and obesity among Indian adults over the three decades from 2010 to 2040, with the most substantial rises occurring in older age groups and rural areas. By 2040, it is anticipated that 30.5% of men and 27.4% of women will be overweight, while 9.5% of men and 13.9% of women will be obese. (Luhar *et al.,* 2020; NFHSI, 2009)

The objective of this research study was to investigate and assess the potential relationship between Body Mass Index (BMI) and infertility in the female population residing in Tamil Nadu, India.

2. Methodology

The study employed a hospital-based age-matched case-control design and was conducted in the Department of Reproductive Medicine at a tertiary care centre in Chengalpattu. Convenience sampling, a non-probability sampling method, was utilized to select participants based on their availability and accessibility within the hospital setting. The sample size was determined based on the findings of a previous study by Kumar D *et al.*,(Kumar, 2007) which reported a 15% prevalence of infertility. Assuming a 95% confidence level with a 10% allowable error, the minimum required total sample size was calculated to be N = 204. This approach aimed to ensure an adequate representation of participants for reliable statistical analysis in the study.

The cases consisted of 102 newly diagnosed infertility patients, who were consecutive cases from both outpatient and hospital admissions in the Departments of Reproductive Medicine at a Tertiary care centre in Chengalpattu District of Tamil Nadu. These individuals were considered as the cases for the study. For the control group, age and years of marriage were matched (±2 years) to avoid confounding factors. Healthy women who were not diagnosed with infertility were selected as controls. These control participants were recruited from among the women accompanying patients in the same Tertiary care centre in Chengalpattu District of Tamil Nadu. The study was conducted over 16 months, specifically from October 2018 to January 2020, during which data collection and analysis took place.

Data collection involved the use of a pre-tested, validated, semi-structured questionnaire that included socio-demographic information, physical measures, and weight measurements. Body mass index (BMI) was calculated based on the World Health Organization classification. The BMI classification considered a range of 18.5-24.9 as normal, 25.0-29.9 as overweight, above 30 as obese, and below 18.5 as underweight. This allowed for the assessment of participants' weight status and its potential association with the variables under investigation Outcome variables in this study included BMI category and fertility status (WHO, 2021).

Data analysis involved entering all collected data into a Microsoft Excel sheet and conducting the analysis using the IBM Statistical Package for Social Sciences (SPSS) software. Descriptive statistics were used to express the data in terms of frequency and percentage. Inferential statistics were performed using logistic regression to examine the relationships between variables. A p-value of less than 0.05 was considered statistically significant, indicating a strong level of confidence in the findings. Ethical consideration: All participants were informed regarding the purpose of the study, benefits, procedure, and confidentiality of the research study. Informed consent was obtained from all the study participants.

3. Results

A total of 204 women participated in this study. 53% of the participants were aged less than 35 years, while 47% had aged more than 35 years. Only 5.4% of the study participants were illiterate, while the rest 94.6% were literate. Almost half (52.5%) of the participants were employed, while the other half (47.5%) were unemployed. Most of the participants (61.8%) were married for 6 to 10 years, followed by less than or equal to 5 years (29.4%) and more than 10 years (8.8%).

Table 1. Socio-demographic characteristics of study participants

Socio-demographic variable	Cases n (%)	Control n (%)	Total n (%)
Age			
< 35 years	52 (48.1%)	56 (51.9%)	108 (53%)
≥ 35 years	50 (52.1%)	46 (47.9%)	96 (47%)
Education			
Illiterate	5 (45.5%)	6 (54.5%)	11 (5.4%)
Literate	97 (50.3%)	96 (49.7%)	193 (94.6%)
Occupation			
Unemployed / homemaker	40 (41.2%)	57 (58.8%)	97 (52.5%)
Employed	62 (57.9%)	45 (42.1%)	107 (47.5%)
Years of marriage			
0 – 5 years	34 (56.7%)	26 (43.3)	60 (29.4%)
6 – 10 years	62 (49.2%)	64 (50.8%)	126 (61.8%)
More than 10 years	6 (33.3%)	12 (66.7%)	18 (8.8%)
Socio-economic status (According to the modified BG Prasad classification)			
Upper class	4 (25%)	12 (75%)	16 (7.8%)
Upper-middle class	38 (70.4%)	16 (29.6%)	54 (26.5%)
Middle class	34 (50%)	34 (50%)	68 (33.3%)
Lower-middle class	24 (46.1%)	28 (53.9%)	52 (25.5%)
Lower class	2 (14.3%)	12 (85.7%)	14 (6.9%)

The socioeconomic status of the participants was classified according to the modified BG Prasad scale. Based on this, 33.3% of the participants belong to the middle class, 26.5% were from the upper-middle class, 25.5% were from the lower-middle class, 7.8% were from the upper class and 6.9% were from the lower class. [Table 1]

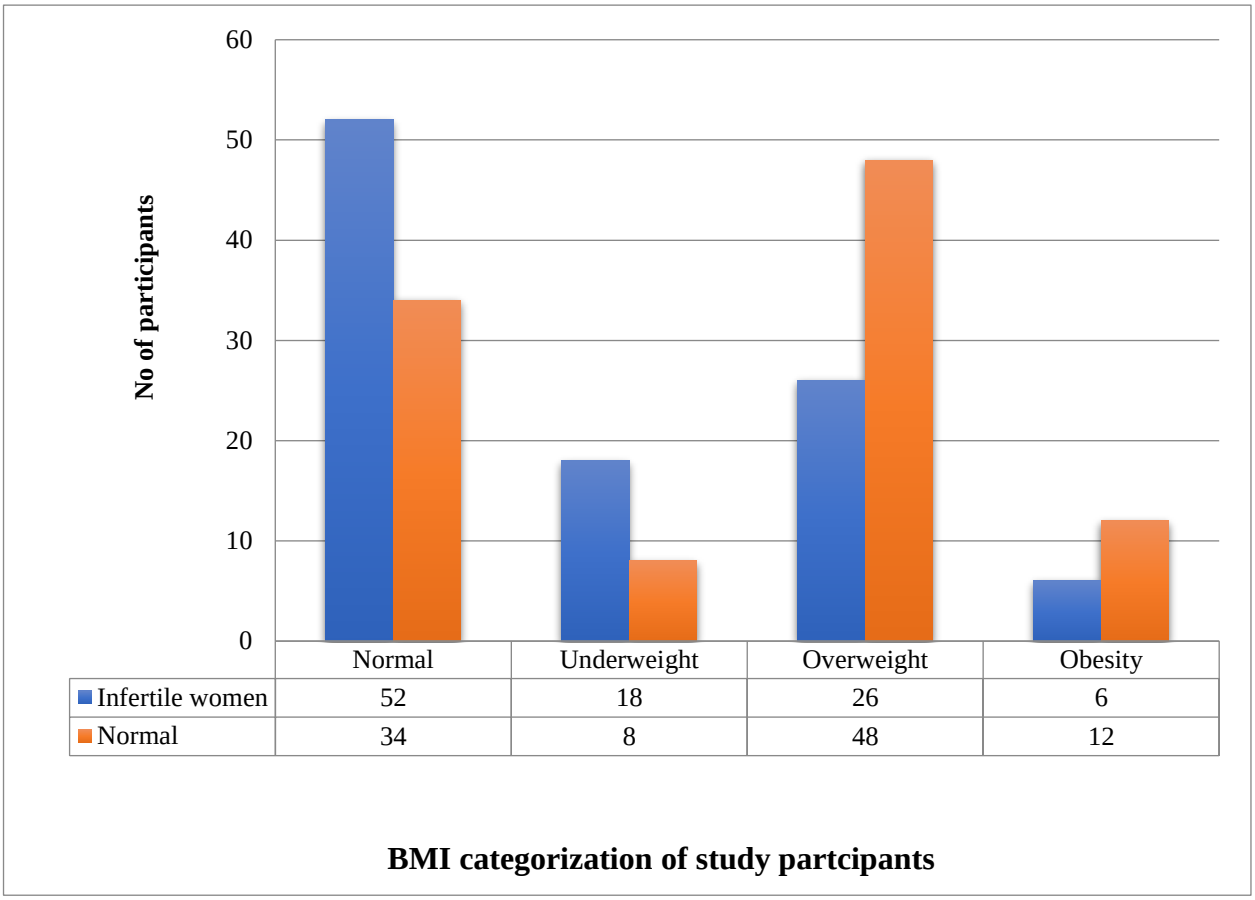

Figure 1. BMI categorization of the study participants

Table 2. Association Testing using Logistic regression

BMI category	Cases n (%)	Controls n (%)	Odds Ratio (OR)	Confidence Interval (CI)		p-value
				Upper limit	Lower limit	
BMI category and infertility status						
Underweight	52 (60.5%)	34 (39.5%)	0.680	0.266	1.737	**0.001***
Normal	18 (69.2%)	8 (30.8%)	1	Reference		
Overweight	26 (35.1%)	48 (64.9%)	**2.824**	**1.483**	**5.376**	
Obesity	6 (33.3%)	12 (66.7%)	**3.059**	**1.048**	**8.927**	
Socioeconomic status category and infertility status						
Upper / Upper-middle	28 (40%)	42 (60%)	2.308	0.961	4.589	0.058
Middle	34 (50%)	34 (50%)	1.538	0.775	3.053	
Lower / Lower middle	40 (60.6%)	26 (39.4%)	1	Reference		

Among the study participants, 50% had no infertility (control group), 34% had primary infertility and 16% had secondary infertility. Among infertile women, 68% had primary infertility and 32% had secondary infertility. Participants were classified according to WHO BMI categorization. Among cases, 51% were normal whereas, among controls, 47.1% were overweight [Figure 1].

In the review of the association between BMI category and infertility status, a significant association was found ($p < 0.05$). Overweight and obese women have 2.82 odds (95% CI, 1.48 – 5.38) and 3.06 odds (95% CI, 1.05 – 8.93) of having infertility when compared to women who have a BMI within the normal range.

On the other side, Underweight women have a 32% lower chance of having infertility than normal women, but it was not significant (the confidence interval did not cross one). [Table 2]

In the review of the association between socioeconomic status and infertility status, a significant association was not found. Though they were not statistically significant, women in higher socio-economic classes had more risk of infertility than women from lower socio-economic classes.

Women from the upper or upper-middle class and middle class were found to have 2.3 odds (95% CI 0.96 – 4.59) and 1.54 odds (95% CI 0.78 – 3.05) of being infertile than women from the lower or lower-middle class.

4. Discussion

This study identified that, among cases, 51% were normal, 17.6% were underweight, 25.5% were overweight and 5.9% were obese. Whereas, among control, 33.3% were normal, 7.8% were underweight, 47.1% were overweight and 11.8% were obese. Further, an association was seen using logistic regression and found that overweight and obese individuals have a significantly higher risk than women with normal BMI.

A similar result was obtained from the study done by Dhandapani K *et al*, which was a cross-sectional study done among infertile women in Karnataka. They found that 43% were overweight, 42% had normal BMI, 8% had underweight and 7% had obesity. Among infertile women, 68% had primary infertility and 32% had secondary infertility. This was concurrent to the study done by Dhandapani K *et al,* which found that 67% had primary infertility and 33% had secondary infertility (Dhandapani *et al.,* 2016).

The present study reveals a non-linear relationship, indicating that, for BMI values below 19.5 kg/m², each unit increase in BMI reduces the risk of infertility by 33%, while above this threshold, a 3% increase in infertility risk is observed with each unit increase in BMI. Conversely, Zhu *et al.*'s study presents a linear relationship, showing that higher BMI is consistently linked to increased infertility risk, with an odds ratio of 1.03 (95% CI: 1.02–1.05) per 1% increase in BMI. Furthermore, Godstein et al.'s findings contribute to this discourse, reporting that obese women (BMI ≥ 27) exhibit a relative risk of ovulatory infertility of 3.1 (95% CI: 2.2-4.4) compared to those with lower BMI (20-24.9). Their study also identified modest effects in women with BMI values of 25-26.9 or less than 17, with relative risks of 1.2 (95% CI: 0.8-1.9) and 1.6 (95% CI: 0.7-3.9), respectively. Collectively, these findings underscore the intricate nature of the BMI-infertility relationship, urging further research to elucidate underlying mechanisms and guide tailored clinical interventions for women grappling with fertility challenges *(Grodstein et al., 1994; Zhu et al.,* 2022).

A study done by Fichman V *et al* found that overweight or obese women have a 7.5-fold increased risk of being infertile when compared to women within the normal BMI range. In our study, we found that overweight and obese women have a 2-4-fold increased risk of being infertile. Both studies have shown a significant association between BMI and infertility, but the odds were very high in the study by Fichman V *et al*, this could be because, studies were done in two different countries, hence the social and environmental factors were very different (Fichman *et al.,* 2020).

Limitations: While age and years of marriage were matched to address potential confounding, other factors such as smoking, alcohol consumption, and underlying pathologies were not taken into account. These unmeasured variables may have influenced the results. Additionally, the control group may have included individuals with infertility who were undiagnosed, potentially introducing bias to our findings. It is important to recognize these limitations when interpreting the study results and considering their generalizability.

5. Conclusion

This study highlights that deviations from normal BMI are associated with a higher risk of infertility. Overweight and obese women were found to have significantly increased odds of experiencing infertility compared to those with a normal BMI. These findings have important implications for women planning to conceive. Recommendations include recognizing and managing overweight and obesity as modifiable risk factors for infertility through interventions such as exercise, diet, lifestyle changes, and medical/surgical options. Health education programs should also be implemented to raise awareness about the BMI-infertility association among women of reproductive age. Implementing these recommendations can help mitigate the risk of infertility and improve reproductive health outcomes.

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Conflict of Interest

The authors have no conflicts of interest to declare. There is also no financial interest to report. The authors certify that the submission is original work and is not under review at any other publication.

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