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Emerging Role of Obstructive Sleep Apnea and Body Mass Index on Semen Parameters of Infertile Men

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Abstract

The curiosity on possible association between Obstructive Sleep Apnea and infertility has gained considerable toehold over the recent years. Infertility, obesity and obstructive sleep apnea exhibit a vicious circle and, hence, their interrelationships are being explored incessantly. Our objective is to determine the influence of body mass index and Obstructive Sleep Apnea (OSA) on semen quality of infertile men. This cross-sectional study was conducted on 60 infertile male participants. Individuals were grouped based on their BMI. OSA screening was done with STOPBANG questionnaire, and risk stratification was done according to the scoring system. Semen analysis was done in accordance with WHO 2010 guidelines. Participants with normal BMI were 16 (26.7%) while 27 (45%) participants were overweight and 17 (28.3%) were obese. OSA risk stratification showed that 16.7% were at high risk for OSA, 40% were at moderate risk and 43.3% were at low risk. High OSA risk among infertile men was significantly associated with sperm concentration (p= 0.03) whereas elevated BMI had significant association with semen volume (p= 0.04). Certain seminal characteristics had a conceivable relation with both OSA risk and increased BMI. Hence, screening for OSA and maintaining an ideal body weight might improve the reproductive potential.

Keywords: Body Mass Index, Infertility, Obesity, Obstructive Sleep Apnea, Semen

1. Introduction

Obesity is a considerable health turmoil which the developing nations are confronting with its increasing prevalence and adverse sequelae due to multiple lifestyle factors. Further, a notable increase in non-communicable diseases has been witnessed among obese and overweight individuals[1]. Upon the many ramifications of obesity, the major area of concern today is reproductive capacity. And, more scholarly reports have documented those men with high Body Mass Index (BMI) to have poor sperm quality, reduced testosterone level and decreased fertility[2]. The chances of infertility increase by 10% for every 9kg increase in body weight[3].

The influence of obesity on male reproductive potential is mediated by assorted factors like oxidative stress, alteration in hypothalamo-pituitary–testicular axis, metabolic dysregulation, disruption of sperm

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DNA integrity and epigenetic changes. Also, obesity impairs the expression of kisspeptin mRNA resulting in hypothalamic hypogonadism. The levels of hormones involved in the regulation of spermatogenesis and Sertoli cell function were notably decreased in individuals with excessive weight. Further, it has been reported that the white adipose tissue, responsible for aromatization and secretion of leptin, is also increased in obese men. Leptin is another furtive signal linking metabolic signal to reproductive axis resulting in decreased testosterone production. In addition, the insulin resistance and increased levels of pro-inflammatory cytokines observed in obese individuals are associated with secondary hypogonadism. Metabolic syndrome, a disorder of energy storage and utilisation, has been reportedly associated with erectile dysfunction and hypogonadism[3].

Aberrant spermatogenesis arising from obesity is associated with downstream changes in key semen parameters, defective sperm capacitation and binding, and deleterious effects on sperm chromatin structure. Further, spermatogenic cell apoptosis is mediated by hyperlipidemia-induced stress on endoplasmic reticulum and dysregulation of Bcl-2 and Bax homeostasis. Moreover, recent investigations suggest that obesity induces molecular changes such as DNA methylation, protamination and histone acetylation in sperm that would adversely impact the development of offspring[4].

Obesity predisposes to upper airway obstruction during sleep by inducing anatomical alterations and results in partial or complete cessation of breathing called Obstructive Sleep Apnea (OSA). The most common mechanism underlying OSA is mechanical load caused by increased peri-pharyngeal fat deposition resulting in pharyngeal collapsibility. Furthermore, there is decrease in Functional Residual Capacity (FRC) which accentuates the pharyngeal collapsibility with consequent reduction in tracheal traction on the pharynx[5]. Snoring, excessive day time sleepiness and nocturnal hypoxemia are the key features of OSA. OSA is more common in men than women. The prevalence of OSA is also influenced by different environmental, social and ethnic backgrounds. In individuals with BMI greater than 28 kg/m^2, the risk of OSA increases by 8 to 12 times[6].

Undiagnosed OSA is a major health concern as it is associated with other comorbidities like type II diabetes mellitus, hypertension, coronary artery disease, stroke, and infertility. Though not well known, studies are instigating to demonstrate that sleep disorders contribute to infertility, hypogonadism and erectile dysfunction. Recently, a case control study conducted in Taiwan has proclaimed that OSA increases the risk of male infertility and the risk is associated with the OSA exposure time[7]. From the available literature we understand that obesity and OSA have a vicious role in the pathogenesis of male infertility. Hence, our study aims to determine the association of excess weight and OSA on various semen parameters.

2. Methodology

This crosssectional study was initiated, after obtaining clearance from the Institutional Ethics Committee (IHEC/05/12 Dec 2014/ Desp. No 444) and the study was conducted in accordance with the declaration of Helsinki among the infertile subjects attending the Department of Andrology and Reproductive medicine, Chettinad Hospital and Research Institute, a tertiary care hospital. Sample size of 120 was calculated based on OSA prevalence among Indian population and the attrition rate was found to be 19.2%. Inclusion criteria were history of infertility for at least 12 months duration despite regular unprotected intercourse in the age group of 25–40 years. Infertile men with craniofacial abnormalities, recent upper airway surgeries and upper airway cancers were excluded. Also, male participants with erectile dysfunction and infertility with extra-testicular causes were also excluded from the study. Infertile couples were evaluated by andrologists and gynaecologists with expertise in infertility. They also underwent physical examination, evaluation of endocrine functions, genetic assessment and other necessary investigations for infertility. Only those couples with male factor infertility (n=60) were included in the study.

Recording of subjects' case history and their routine clinical assessment, including semen analysis, were carried out as per the standard protocols of the Department of Andrology and Reproductive Medicine. Seminal fluid analysis was performed according to WHO 2010 criteria[8].

Infertile men, who consented and satisfied the criteria for participation, were explained in detail about the study in their regional language. Subjects were encouraged to fill in the OSA screening questionnaire –STOPBANG- in consultation with their bed partners. This questionnaire

has four subjective and four objective components namely snoring, tiredness, observed apneas, blood pressure, Body Mass Index (BMI), age, gender and neck circumference. Each component has a yes or no option, to categorize the risk. Positive responses to 0–2, 3–4, 5–8 were at low risk, intermediate risk and high risk, respectively. Basic anthropometric measurements like height, weight and vital signs were recorded.

3. Results

The association of BMI with semen parameters and OSA risk were analyzed. Statistical analysis was conducted using SPSS version 21 and *p* value less than 0.05 was considered statistically significant.

Patient demographics and seminal fluid characteristics by body mass index are shown in Table 1. Based on the revised consensus guidelines for India, subjects were grouped as normal (18.5–22.9 kg/m^2), overweight (23–24.9 kg/m^2) and obese (>25 kg/m^2). Of the total 60 participants, 16 (26.7%) had normal BMI, 27 (45%) were overweight and 17 (28.3%) were obese.

Subjects with primary infertility constituted 85% and those with secondary infertility formed 15%. Among the infertile male, 17 (28.3%) were at high risk for OSA, whereas 24 (40%) were at moderate risk and 19 (31.7%) were at low risk for OSA (Table 2).

Of the seminal parameters, semen volume had significant association with BMI (p=0.043), whereas sperm concentration positively correlated with OSA risk (p=0.003). There was a significant decrease (p<0.05) in the mean semen volume among patients with BMI>25 kg/m^2 (1.87) when compared with the patients of BMI<25 kg/m^2 (2.62) (Table 3).

Among high OSA risk individuals 54.5% had elevated BMI and there also existeda statistically significant difference between BMI and OSA risk (p=0.001) (Table 4).

Table 1. Seminal fluid characteristics based on body weight

Parameter	Normal weight n = 16	Overweight n = 27	Obese n = 17	*p* value
Age (years)	31.79±5.3	32.07±7.48	31.62±3.89	0.45
Durationof infertility (years)	4.46±2.96	4.94±3.67	3.76±2.71	0.63
Volume (ml)	2.84±1.03	2.62±1.04	1.87±0.77	0.043*
Sperm concentration (x 10^6 ml)	34.56±8.35	34.28±7.86	29.67±8.95	0.74
Progressive motility (%)	30.75±7.64	29.24±10.52	28.17±11.39	0.067
Total motility (%)	37.47±11.34	36.65±12.63	36.21±13.39	0.98
pH	7.32±0.74	7.34±0.61	7.26±1.12	0.21

Table 2. Frequency distribution of OSA risk based on STOP-BANG score

Risk	Frequency	Percent
Low	19	31.7
Intermediate	24	40.0
High	17	28.3

Table 3. Seminal fluid characteristics among different OSA risk groups.

Parameters	Low OSA risk n = 17	Intermediate OSA risk n = 24	High OSA risk n = 19	*p* value
Volume (ml)	2.37±0.54	1.84±0.72	1.87±0.65	0.53
Sperm concentration (x 10^6 ml)	35.21±6.84	32.16±5.44	29.05±3.24	0.003*
Progressive motility (%)	31.18±8.93	26.83±10.21	27.61±7.72	0.62
Total motility (%)	37.82±9.38	35.48±8.76	36.13±8.04	0.33
pH	7.31±5.73	7.29±4.61	7.28±5.26	0.29

Table 4. Association between OSA and BMI in the study population

Stop Bang	Mean BMI	Mean difference	P value	95% CI	
				Lower	Upper
Low risk	26.03±4.93	5.28	0.063	3.46	7.09
Intermediate risk	27.52±6.57	4.90	<0.001	2.92	5.45
High risk	28.65±6.28	5.36	<0.001	2.78	6.19

4. Discussion

Infertility is an acute global health concern, affecting around 60-80 million couples worldwide, of which 15 and 20 million (25%) couples comprise the Indian population. The magnitude of infertility is high in developing countries with one in every four couples being affected by infertility[9].

Obesity is one of the key factors ascribed to the cause of infertility with its prevalence increasing over the recent decades. Over the past 5–10 years, studies have demonstrated that high BMI (>25 kg/m^2) negatively impacts the quality of both oocytes and sperm. In our study, BMI correlated with various semen parameters like volume, sperm concentration, pH and motility. These results were congruent with a study done by Chavarro *et al.*, who reported a significant reduction in semen volume among males with increasing BMI[10]. Further, a systematic review and meta-analytical study confirmed the sperm quality decreases with increasing BMI suggesting obesity as a pernicious factor of male infertility[11]. Another study evaluating the effect of weight loss on semen parameters, established a causal inverse relationship between BMI and semen quality[12]. However, some studies established no association between semen parameters and BMI. In a study by Alahmar *et al.*, no significant difference was observed in semen volume among infertile men of different BMI groups[13].

Our present study, though reports a low sperm concentration in the obese group, no statistical significance was observed among obese and normal weight individuals. For the past 15 years, several studies have reported a median sperm concentration of 41-55 x 106/mLamong the general population signifying a sub-optimal semen quality[14]. The findings of our study are consistent with a systematic review of a meta-analysis performed by MacDonald *et al.,* who reported no association between BMI and sperm concentration[15]. There are other studies substantiating similar findings with reduction of semen quality, if any, in high BMI individuals is not statistically significant[16,17]. On the other hand, some studies reported a significant decline in sperm concentration with increasing BMI[10]. In the present study, though the percentage of normal and abnormal

sperm morphologies was comparable among the three BMI groups, their association is weak. Studies are inconsistent with the effect of BMI on semen parameters including the sperm motility and concentration. Our results supplement the finding of a large cohort study which reported no significant relationship between BMI and sperm motility[18]. Further, there are studies which demonstrated significant association of BMI with only sperm morphology and oligozoospermia and not with other semen parameters[19,20]. Men with increased BMI had lower levels of testosterone and increased amount of estradiol[21]. Besides, it was also reported that the probability of reduction in semen quality is three times higher in obese men when compared to normal and overweight individuals[22].

Our study also categorised the risk of OSA among infertile population using the STOPBANG questionnaire and reported 28.8% were at high risk followed by 40.7% and 30.5% individuals at moderate and low risk for OSA, respectively. OSA has a worldwide distribution with the highest prevalence of 16.5% in the United States followed by 13.7% in India[23]. The distribution of OSA also varies with age and gender of the individual. In a cross-sectional study done by Pattanaik*et al.,*it was observed that OSA prevalence was highest in the age group of 50-59 and males are affected to a greater extent (14.8%) than females (12.9%)24. Moreover, the sensitivity of the STOPBANG questionnaire to find moderate to severe OSA was reported to be 89% and 93%, respectively. The STOPBANG questionnaire serves as a reliable indicator to predict OSA risk among the general population[25]. Obesity is a key factor in the development and evolution of OSA. In fact, it has been observed that OSA is twice more common among obese adults than normal weight individuals[26].

In our study, out of the 18 individuals at high risk for OSA, 15 were obese. Further, it was also observed that 27.02% of obese men were at low risk for OSA followed by 40.54% and 32.43% at intermediate and high risk for OSA, respectively. These results were comparable with a study done by Chung *et al.*, which reported 47% moderate to severe OSA and 27% severe OSA among obese individuals[27]. But the study employed overnight polysomnography to confirm the presence of OSA. Moreover it is postulated that odds of developing moderate to severe OSA is about six times for every 10% increase in BMI[28].

The association of OSA with male infertility has been elucidated by several studies and it has been proposed that oxidative stress, systemic inflammation, insulin resistance and aberrant reproductive hormone secretion are the plausible mechanisms. In our study, sperm concentration has a positive association with OSA risk whereas no significant association exists between other semen parameters and OSA. Though a relationship was established between OSA and sperm concentration in our study, the presence of OSA needs to be confirmed by overnight polysomnography. There is a dearth of comprehensive information to illuminate the role of OSA in male infertility.

As OSA has been stipulated to result in infertility, early recognition and intervention of OSA in infertile population might yield fruitful outcomes in treatment of in-vitro fertilization.

5. Limitations

A larger sample size could have a provided a greater clarity to the study. We need to investigate prospectively whether incorporation of OSA management into infertility treatment improves fertility outcome or not.

6. Conclusion

Infertility, a growing concern in recent years, is influenced by obesity and OSA. Both these factors disrupt semen quality particularly semen volume and concentration which could be attributed to disruption of hypothalamo-pituitary-testicular axis and other molecular changes. Hence, maintaining an ideal body weight along with early detection and treatment of OSA would improve the quality of semen and yield significant results in infertility management.

7. Declaration of Interest

The author(s) report no conflict of interest

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