Overweight and obese men are more prone to infertility-Myth or Fact?

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ABSTRACT

To investigate the association of sub-fertility/ infertility with increased BMI in overweight and obese men and in control group in Karnataka, South India. In this pilot study 20 overweight and obese men, aged 25-45, and 10 normal-weighed men with proven fertility were included. Both groups were married. All cases and controls were evaluated for different semen parameters according to World Health Organization (WHO) standards. Statistical analysis was performed using the SPSS software, version 16.0. P-values less than 0.05 were considered statistically significant. Different infertile conditions are evident among overweight and obese individuals recruited for this study. Variations in the semen parameter are significant in obese men compared to controls but sperm function test does not show statistical significant values in overweight and obese men when compared with control group. In case of oligoasthenospermic subjects pH shows a significant increase ($p=0.002$) compared to controls. Also the levels of Fructose show a significant decline in both azoospermic ($p<0.001$) and oligoasthenosermic ($p=0.002$) groups when compared to control group. With reference to the data obtained from this pilot study we found that increased BMI in men affects the semen quality which ultimately results in decreased fertility rate in men.

Key words: Obesity; BMI; Erectile Dysfunction; Male Infertility

INTRODUCTION

The prevalence of overweight (BMI > 25) and obesity (BMI > 30) is on the increase, especially in industrialised countries [1]. Obesity is a well recognized risk factor for female infertility [2]; however, its relation with decreased sperm count has not been documented in men so far [3, 4]. It is believed that with the increasing prevalence of sedentary life styles and dietary changes, obesity is emerging as an important cause of adverse health outcomes, including male infertility. Male factors alone constitute 25%–30% of all cases of infertility [5] and another 30% in combination with female factors. Known etiologies of male infertility include cryptorchidism, testicular torsion or trauma, varicocele, seminal tract infections, antisperm antibodies, hypogonadotropic hypogonadism, gonadal dysgenesis, and obstruction of the reproductive channels [6]. Obesity is a new addition to these known etiologies of male infertility. Thus, obesity is a chronic disease resulting in compromised physical and psychological well-being, and it may contribute to reduced fecundity as well. Though genetic link between obesity and infertility in women is quite well understood, such study has not yet been carried out in India to explain the discrepancies between obese fertile and infertile men. It is possible that other, less severe genetic mutations with less clinical effect or polymorphisms exist that might describe these discrepancies. This pilot study was carried out to find out evidences of association between overweight and obesity in men on fertility rates in Mysore population and the results will give us an insight for further molecular and genetic analysis.

MATERIALS AND METHODS

In our pilot study 20 overweight and obese (BMI>25 kg/m^2) men, aged 25-45, were recruited randomly from different obesity clinics of Mysore, India. To select these subjects, BMI was calculated using the measurement of height and weight. The control population includes 10 normal healthy donors without obesity (BMI<25kg/m^2) and with proven fertility. Both subject and control men were interviewed to

collect information about family history, medical history, presence or absence of consanguinity in the family, parental diseases, etc. After obtaining informed consent from both the subjects and controls, semen was collected and analyzed after liquefaction (within one hour of collection). Sperm parameters analyzed included semen volume, pH, liquefaction time, sperm count, total progressively motile sperm per ejaculate, sperm morphology, sperm vitality and sperm function tests such as acrosomal intactness test (AIT), [7], hypo osmotic swelling test (HOS) [8] and nuclear chromatin decondensation test (NCD) [7]. Then, semen was centrifuged at 1500 rpm for 10 minutes and plasma was separated and stored at -20^0 C for fructose analysis according to the World Health Organization criteria (1999). Fructose is a marker of seminal vesicle function; it could also be used to find out the obstruction of seminal vesicle. The SPSS software version 16.0 was used for data analysis. The Mann-Whitney test was performed for comparing the groups and P-values less than 0.05 were considered statistically significant.

RESULTS

In the present study, 10 cases (50%) were found to be overweight with Body Mass Index (BMI) between 25 to 29.9 and 10 cases (50%) were obese (BMI > 30). BMI calculation was done based on WHO growth charts and cutoff points. Among 20 cases of overweight and obese individuals, we identified different infertile conditions wherein 6 cases (30%) with azoospermia, which means no sperm in semen, 5 cases (25%) with oligoasthenozoospermia [both sperm count and motility found to be less than normal values], 3 cases (15%) with asthenozoospermia, 2 cases (10%) with oligozoospermia and one (5%) case with unejaculatory condition and the remaining 3 cases were normal with reference to count and motility (Figure 4). Basic semen analysis and sperm function tests showed that among 8 cases the vitality rate were found to be less than 75%, pH value in 15 cases were above normal value (7.2-8) and less semen volume (<2 ml) were found in 12 subjects (Tables 1- 4). The results of performed parameters for different condition were depicted in the separate tables wherein 7 cases had less value than normal for AIT, 5 cases with less HOS test value, and 3 cases with decreased NCD value when compared to normal reference. We also found a significant decrease in fructose value in Azoospermic ($P < 0.001$) and oligoasthenospermic ($P=0.002$) groups but further study is needed to ensure the reverse correlation between fructose level and increased BMI. Positive and negative results for different sperm function tests are shown in Figures 1-3. The distribution of different infertility conditions in overweight and obese men attended in our study is represented in Figure 4.

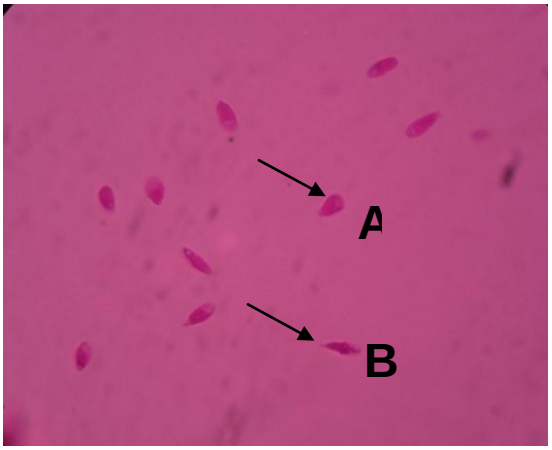

Figure 1. Nuclear chromatin decondensation test in normal and obese individual with infertile condition. Letter **A** shows positive response with enlarged sperm head and **B** indicates negative response with condensed sperm head

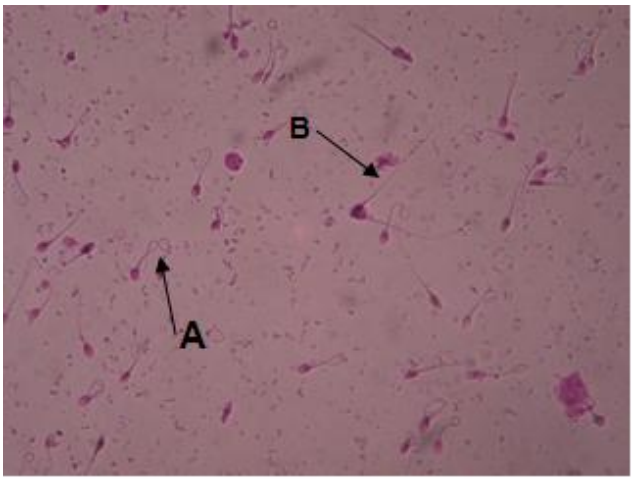

Figure 2. Hypo-osmatic swelling test in normal and obese individual with infertile condition. Letter **A** shows positive response with tail coiling and **B** indicates negative response without coiling in the tail

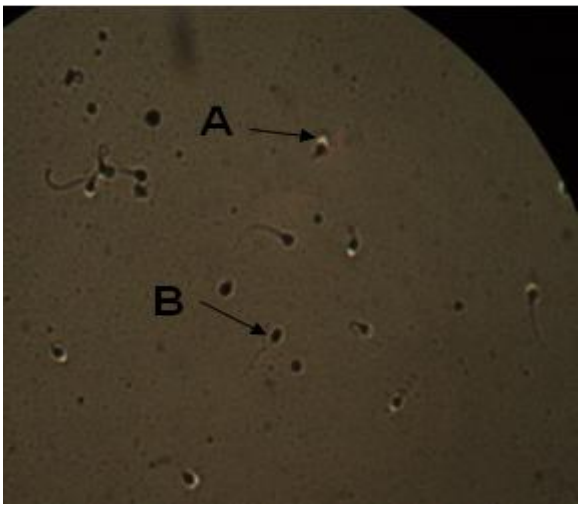

Figure 3. Acrosomal intactness test in normal and obese individual with infertile condition. Letter **A** shows positive response hallows formation around sperm head the and **B** indicates without hallow formation negative response without coiling in the tail around sperm head.

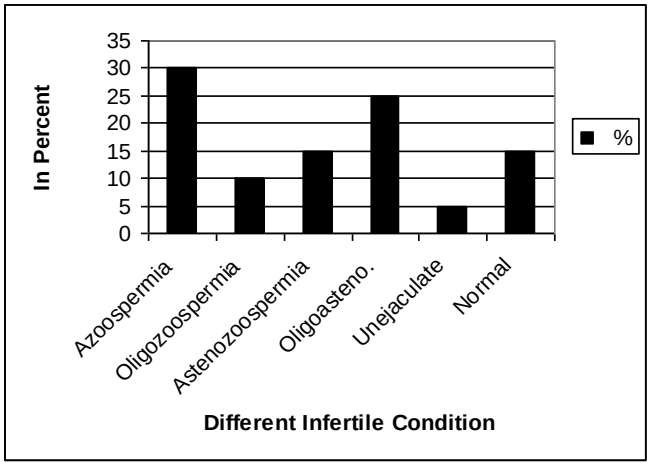

Figure 4. Distribution of different infertility condition in obese men attended in this study from Mysore, Karnataka, India.

Table 1. Routine semen analysis and Sperm function and biochemical tests among Azoospermic condition [BMI > 25 kg/m^2] compared with control group [BMI < 25 kg/m^2].

Parameters	***Azoospermic N=6***	***Control N=10***	***P-Value***
BMI	28.1±2.1	22.5±1.3	<0.001
Volume	1.5±1.2	3.0±0.9	0.022
Count	0	60.9±25	<0.001
Motility	0	63.0±7.5	<0.001
Vitality	0	79.9±6.7	<0.001
pH	8.1±0.4	7.8±0.2	0.051
NCD	0	71.1±10.4	<0.001
HOS	0	73.1±7.6	<0.001
AIT	0	65.6±14.5	<0.001
Fructose	7.9 ±7.6	28.4±3.3	<0.001

BMI: Body mass index
NCD: Nuclear Chromatin Decondensation test.
HOS: Hypo-Osmotic Swelling.
AIT: Acrosome intactness test

Table 2. Routine semen analysis and Sperm function and biochemical tests among Oligoasthenospermic condition (BMI > 25 kg/m^2) compared with control group (BMI < 25 kg/m^2).

Parameter	***Oligoasthenospermic N=5***	***Control N=10***	***P-Value***
BMI	30.2±1.8	22.5±1.3	0.002
Volume	1.5±0.7	3.0±0.9	0.012
Count	14.5±4.1	60.9±25	0.002
Motility	33.4±7.9	63.0±7.5	0.002
Vitality	52.0±21.6	79.9±6.7	0.017
pH	8.3±0.1	7.8±0.2	0.002
NCD	78.4±10.1	71.1±10.7	0.188
HOS	65.0±28.2	73.1±7.6	0.902
AIT	25.6±34.5	65.6±14.5	0.084
Fructose	2.3±0.7	28.4±3.3	0.002

Table 3.Routine semen analysis and Sperm function and biochemical tests among Asthenospermic condition (BMI>25kg/m^2) compared with control group (BMI<25 kg/m^2).

.Parameters	***Asthenospermic N=3***	***Control N=10***
BMI	29.9±1.2	22.5±1.3
Volume	1.1±0.4	3.0±0.9
Count	40.6±7.6	60.9±25
Motility	30.3±12.8	63.0±7.5
Vitality	64.0±22.2	79.9±6.7
pH	8.1±0.1	7.8±0.2
NCD	77.3±5.5	71.1±10.4
HOS	70.6±16.1	73.1±7.6
AIT	40.0±21.7	65.6±14.5
Fructose	6.0±2.3	28.4±3.3

Table 4.Routine semen analysis and Sperm function and biochemical tests among Oligospermic condition (BMI>25kg/m^2) compared with control group (BMI<25 kg/m^2).

Parameter	***Oligospermic N=2***	***Control N=10***
BMI	30.7±0.3	22.5±1.3
Volume	2.0±0	3.0±0.9
Count	6.5±2.1	60.9±25
Motility	55.0±10.6	63.0±7.5
Vitality	72.5±10.6	79.9±6.7
pH	8.3±0	7.8±0.2
NCD	67.5±17.6	71.1±10.4
HOS	50.0±30	73.1±7.6
AIT	46.5±19.5	65.6±14.5
Fructose	3.2±2.4	28.4±3.3

DISCUSSION

The potential effects of increased BMI on male fertility have not been subjected to the same degree of scrutiny as female obesity. Recently some studies have been conducted on the relationship between overweight and obesity and semen parameters. Kort et al. (2007) showed significant negative relationship between high BMI and sperm motility in 528 Danish men [10]. In addition, men with BMI > 25 had fewer chromatin-intact normal-motile sperm cells per ejaculate [10]. Jensen et al. (2004) in accordance with other studies showed that overweight and obese men (BMI >25 kg/m^2) had significantly lower sperm concentrations than those of normal-weight men (BMI 20–25 kg/m^2) [3]. The prevalence of oligozoospermia was higher in overweight and obese men compared with normal-weight men. A substantial decrease in serum testosterone, sex hormone binding globulin and Inhibin B were also found with increasing BMI [3]. Reduction in total testosterone production in obese men can result in decreased intra-testicular testosterone levels, thereby affecting the function of the seminiferous epithelium and the synchrony of spermatogenesis [11]. Magnusdottir et al. (2005) found a statistically significant negative correlation between BMI and both sperm concentration and total sperm count [4]. A retrospective analysis of data from 390 men also suggested that high BMI was associated with reduced sperm concentration and motility [12].

In the present study, our data suggest that men with overweight and obesity are very prone to sub-fertility or infertility. Based on these available data we have found that the rate of infertility increased with BMI. Excess weight has been related directly or indirectly to biologic changes that could increase the risk of infertility. In this study, we found a significant decrease in semen volume, sperm count, sperm motility and sperm function tests in overweight and obese men that could be concluded that the increased BMI correlated negatively with above mentioned semen parameters. The prevalence of oligospermia and oligoasthenospermia was high in our study. The possible reasons for variation in spermatogenesis in obese men could be due to fat deposition in supra-pubic area and thighs which alters the hormone profiles particularly sex hormones which can impair the expression of genes involving in spermatogenesis pathways leading to impaired semen parameters [decreased total sperm count, concentration and motility; increased DNA fragmentation index]

[13,14] and also increase in scrotal temperature that can lead to erectile dysfunction [15,16]. Although the results suggest negative correlation between BMI and sperm parameters, this study needs further support by increasing the case numbers and further DNA analysis to confirm that overweight and obesity lead to sub-fertility/infertility in men.

Our study had limitations in its sample number. But data obtained from this study accords with previous studies which have shown overweight and obesity in men alters the semen parameters resulting in diminished fertility.

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