ABSTRACT

Obesity is a medical condition in which excess body fat has accumulated to the extent that it may have an adverse effect on health, leading to reduced life expectancy and/or increased health problems. Worldwide obesity has increased more than three-fold since 1980. In 2008, more than 1.4 billion adults, 20 years and older, were overweight and obese. Of these, over 200 million men and nearly 300 million women were obese. In the USA, the incidence of obesity in adult males has increased from 11.7% in the year 1991, 17.9% in 1998, to 30.6% in 2004, emphasizing that the incidence of overweight and obesity is reaching epidemic levels. Overall, more than one in ten of the world’s adult population was obese. In 2010, more than 40 million children under five years were overweight. Overweight and obesity are once considered as high-income country problem, but now on the rise in low and middle-income countries, particularly in urban settings. Close to 35 million overweight children are living in developing countries and 8 million in developed countries.

Obesity has reached epidemic proportions in India in the 21st century, with morbid obesity affecting 5% of the country’s population. Urbanization and modernization has been associated with obesity. The incidence of obesity as a risk factor for normal life is increasing worldwide. Its impact on hypertension, cardiovascular diseases, osteoporosis, insulin resistance and diabetes mellitus, is well recognized. Previous studies have proved the association between female obesity and infertility and several linked genes have been worked out. However, a little is known about the effect of obesity on male reproductive system and infertility. Recently some clinical studies have reported diminished semen parameters like sperm count, motility and viability and changing in reproductive hormones in over
weight and obese men. Lack of such study in Asian countries and particularly in Indian population who are genetically more prone to obesity necessitates picking up this research to achieve robust findings in this regard.

In view of this, the present investigation was undertaken in the overweight and obese fertile and infertile men in Mysore, South India with objectives of analysis of pedigree, assessment of seminal Reactive Oxygen Species, analysis of the inflammatory pathway by measuring the seminal interleukin 6 (IL-6) level, analysis of seminal Protamine-1 (PRM1) and sequence variation analysis of the varied samples in three exons of the candidate gene in order to find single nucleotide polymorphism (SNP).

A total of 250 subjects including obese infertile, non-obese infertile and obese fertile subjects were considered in the present study from different Fertility Hospitals, gyms and obesity clinics in Mysore. The age of the participants ranged from 20 to 45 years. A total of 100 healthy control men (non obese with proven fertility) were also randomly selected as controls from different ethnic backgrounds and locations of Mysore, South India. This study was approved by the institutional Human Ethical Committee of University of Mysore. The written consent was obtained from the participants. The infertile cases then were analyzed and classified into different subgroups which includes Aspermia, Azoospermia, Oligozoospermia, Asthenozoospermia and combined conditions according to WHO Guidelines.

The findings are: (a) subfertility and infertility were common among overweight and obese participants and there was a significant association of family history of obesity in all the first and second degree relatives with obese infertile and obese fertile cases. (b) Parental and proband consanguinity was significantly
associated with infertility. (d) In obese males, high prevalence of obesity was more prominent in families with obesity. (e) Reactive oxygen species level in seminal plasma was significantly higher in males with higher BMI and the difference of mean value was significant between obese and non-obese infertile males. (f) Hyperactivation of inflammatory pathways in obese infertile subjects was significantly associated with increased seminal level of IL-6 and it was negatively correlated with spermiogram. (g) In obese fertile and non-obese infertile males the level of IL-6 was significantly higher than controls but lesser than obese infertile males. (h) Obese infertile and non-obese infertile subjects expressed significantly lower sperm PRM1 concentration than other study groups and the difference was significant among these two groups as well. (i) Data revealed neither association of variation in exon 24 with different conditions in our study nor sequence variation in exon 23 of JHDM2A gene in all study groups, but variations in form of SNP and insertion in exon 25 were observed in 11 cases.

The present research was taken up to gain new insight into how the male obesity might promote sub-fertility or infertility in our population. Findings obtained have mainly focused towards the understanding of the genetics of male obesity/infertility in general population and India in particular.