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## INVITED COMMENTARY

Sperm Quality

### The impact of male overweight on semen quality and outcome of assisted reproduction

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The impact of obesity on male reproductive health remains a contested topic as evidence is inconclusive and inconsistent.<sup>1,2</sup> Even more debatable is the effect of male obesity in assisted reproduction. In the manuscript, “the impact of male overweight on semen quality and outcome of assisted reproduction” published in *Asian Journal of Andrology*, Thomsen *et al.*<sup>3</sup> investigated the effect of male obesity on fertilization outcomes in intrauterine insemination, *in vitro* fertilization (IVF) and intracytoplasmic sperm injection (ICSI) programs further contributes to the increasing body of evidence in this field.

Thomsen *et al.*<sup>3</sup> showed no significant impact of male obesity (body mass index (BMI) >30) on various semen parameters, IVF rates, number of good quality embryos and implantation or pregnancy outcomes in a set of 74 males, when compared to 268 overweight (BMI = 25–29.9) and 259 normal weight (BMI = 20–24.9) patients attending assisted reproductive technology (ART) programs. It is well-established that male obesity negatively affects the endocrine system resulting in hypogonadism and increased estrogen.<sup>4</sup> In many cases, various metabolic changes directly or indirectly negatively influence male reproduction pathways, including hyperinsulinemia, hyperleptinemia, oxidative stress and low-grade systemic inflammation (Leisegang *et al.* unpublished). These changes and their potential impact on spermatogenesis and sperm function may provide some insight into inconsistent results published regarding obesity and male fertility and stimulate investigation of metabolic parameters that may better predict pregnancy outcomes than BMI alone. In the discussion, the authors reported that the lack of altered semen parameters is not affected by an altered endocrine profile. However, there is no evidence of follicle-stimulating hormone or testosterone concentrations in males reported in this paper. Therefore, it is difficult to assume that these patients had significant differences in the endocrine profile.

Yet, such investigations are important as the impact of paternal obesity on reproductive outcomes is under-investigated when compared to female obesity, particularly in ART. With high financial and emotional investment in the ART process by couples, it is important to identify factors that may decrease successful pregnancy and live birth rates in order to adequately advise patients. Based on these results, and supported by the literature, male weight should not be considered as a potential confounder in the outcome of ART. Nevertheless, there is evidence that male obesity negatively influences IVF outcomes as

discussed by Thomsen *et al.*<sup>3</sup> These discrepancies are possibly due to the multifactorial nature of fertilization or the sperm selection process and need to be addressed in larger, controlled multi-center studies.

Age is well-associated with the decline in testosterone levels, and to a lesser degree paternal fertility potential. In this study, men were relatively young (mean  $32.8 \pm 5.1$  years), thus reflecting normal reproductive age. However, it is plausible that in younger males obesity may have a less dramatic negative impact on endocrine and fertility parameters than in older men. This may partly explain some of the inconsistent results in the literature cited by Thomsen *et al.*<sup>3</sup> Indeed, the mean male age in Keltz *et al.*<sup>5</sup> was  $37.2 \pm 8.5$  (BMI < 25) and  $38.4 \pm 7.5$  years (BMI > 25). Thomsen *et al.*<sup>3</sup> discuss that others reported no negative effect of increased BMI on ICSI outcome. However, although not reported as a predictor for fertilization, implantation, pregnancy or miscarriage, a high BMI negatively impacted on ICSI success.<sup>6</sup> The entire cohort in this study ( $n = 250$ ) had a mean age of  $38.4 \pm 9.3$  years.<sup>6</sup> Considering that the subjects in the Thomsen study were significantly ( $P = 0.0001$ ) younger than in other studies, it is plausible that obesity may impact more on male reproductive health with increasing age.

Many of the cited studies appear to suggest a less dramatic impact on ART outcome for ICSI than in IVF. Although no study has looked at this specifically, many of them seem to suggest ICSI superior in paternal obesity. This too requires detailed investigation, which may also suggest novel mechanisms for obesity-related fertility problems. However, the key question arising is why are these studies continuously inconsistent? The answer could lie in an age-related impact of obesity, different degrees of underlying metabolic changes or other potential confounders.

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