Importance of studying infertility from a life course perspective

Childhood obesity, independent of adult body weight, is increasingly recognized as an important determinant of chronic disease later in life (1, 2). Yet, very few studies have attempted to study the link between early childhood adiposity and reproductive function in adulthood. While obesity in reproductive aged women is well established as a major risk factor for infertility, it is unclear the extent to which excess body weight earlier in life has on fertility. Since childhood and adolescence are the time periods when the hypothalamic pituitary ovarian axis is developing, body fatness during this critical window could, in theory, have a persistent impact on reproductive function.

Better understanding this link between early life exposures and fertility requires taking a life course approach to examine how factors, such as body weight, experienced throughout a woman's life act independently, cumulatively, and interactively to influence health. However, the logistical challenges of conducting a study to address this type of question are numerous and perhaps one of the leading reasons for this gap. In this issue of *Fertility and Sterility*, He and colleagues (3) utilized data from a unique cohort of Australian children where anthropometrics were measured between 7 to 15 years of age and then quite amazingly, almost 20 years later, many of the children were able to be traced and re-contacted to assess their reproductive health. The authors' main findings were that childhood obesity between 7 to 11 years, but not between 12 to 15 years, was associated with increased risk of female infertility. These results suggest that the prepubertal time window may be a sensitive period where the effects of excess body weight are pronounced and have lasting consequences on fertility.

It is important to note, that this was not a longitudinal cohort where childhood body weight was measured twice-both in early and mid-childhood. The two groups of girls being contrasted (e.g. <12 and 12-15 years of age) were two separate groups of children which somewhat limits the ability to make inference as the vast majority of obese children at ages <12 years were probably also obese between 12-15 years (although this wasn't measured in the study). What this likely indicates is that while excess body fat is an important determinant of female fertility throughout life, the earlier the onset of obesity, the potentially greater the lasting effects. This was also noted in the Bogolusa Heart Study which found that kids who were ever obese before 12 years of age were significantly more likely to report the inability to become pregnant and any fertility difficulties (4). This effect, however, was diminished among children who were ever obese before 18 years of age. So, is prepubertal obesity a specific exposure window with lasting effects on fertility or is it the longer persistence of excess body fat throughout a women's life that is the main culprit?

Unfortunately, due to the high propensity of body weight to track over time, this is a hard question to tease out. For example, in this Australian cohort, of the 70 girls who were overweight or obese between 7 to 11 years-old, only 20% ended up at a normal body mass index in adulthood. Reassuringly though, the effects of prepubertal obesity on infertility appeared to be driven by the subgroup of obese girls who stayed persistently obese into adulthood. The obese girls who became normal weight in adulthood in fact had a non-statistically significant lower risk of infertility. These results, while preliminary (and based on small numbers), indicate that excess adiposity in early life does not have to have irreversible effects on fertility. And if a woman can break from her weight trajectory, the consequences on fertility may be avoidable. This is a more convenient public health message as it presents an opportunity to intervene and avoid the negative implications of early life obesity.

Above and beyond this paper's specific findings, this work also highlights the need for and importance of studies that take a life course approach to investigating determinants of fertility and reproductive health. Adult men and women are more than just their current exposures and thus solely focusing on their contemporary behaviors likely misses a bigger part of the picture as this paper nicely illustrates. Researchers should be encouraged to take inspiration from the study design utilized by He and colleagues (3), which leveraged and expanded on information collected 25 years ago to investigate a relevant public health question today. Given the rise in childhood obesity, and its co-exposures such as poorer diet quality and increased screen time, the impact of excess adiposity in early life on reproductive health outcomes is likely still under realized. By implementing life course studies of reproductive health, we can hopefully strengthen our ability to make timely interventions that can benefit current and future generations of men and women.

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