

An Impact of Essential Fatty Acids on Reproduction- Can it be Passed on Over Generations-A Short Communication

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We had reviewed how obesity has reached epidemic proportions [1,2]. In the last century obesity has surfaced as the biggest global health problem in view of both, the changes in environment along with changes in society where positive energy balance and thus weight gain has resulted, main changes being consumption of high-calorie foods/high-fat foods, associated with inadequate physical activity, moving towards sedentary lifestyle. [3]. As a result obesity prevalence practically doubled since 1980 all over the world, with world health organization (WHO) showing greater than 39% of adults greater than/equal to 18 year were overweight of which 13% were obese [4]. Additionally, a minimum of 41 million children below 5 years were overweight or obese. Importantly severe obesity, a body mass index (BMI) greater than 35 kg/m² is becoming a part of this global epidemic, and that has severe bad effects on health, with increase in BMI implying increased mortality risk just like low BMI does [5]. However, now overweight or obese have become bigger killers in contrast to malnourished or underweight [4]. As per WHO overweight and obesity are the causative factors for 44% of type 2 diabetes mellitus (T2DM), resulting in 23% of ischemic heart disease patients and roughly 7 - 41% of some cancers [5] involving practically all systems.

As far as gynaecology is concerned obesity correlates with enhanced polycystic ovary syndrome (PCOS) as well as metabolic syndrome (MetS), Endometrial cancer as well as breast cancer, along with enhanced perinatal complications and congenital defects in offspring [6]. Women having overweight as well as obesity present with infertility rate [7]. Poorer outcomes have been documented in *in vitro* fertilization (IVF) cycles in obese women who are obese when done in either autologous or donor oocyte cycles [8,9]. That obesity might cause detrimental effect on oocytes as well as endometrium has been suggested [8-12]. Obese women need gonadotrophin doses as well as have abortion rate [13]. Certain research pointed that there are impaired IVF results though unanimous results are not there [14]. Further rates of fetal macrosomia as well as other perinatal complications have been seen in off-springs of these women [14]. Recently Barker hypothesis has invited attention [15,16, reviewed by us regarding DoHAD hypothesis]. Undernutrition during pregnancy, as well as impaired fetal growth are correlated with an exaggerated risk of hypertension, cardiovascular disease (CVD), as well as type2 diabetes mellitus (T2DM) [15-17]. Children of mothers who are obese have a likelihood of obesity, T2DM as well as CVD as adults [18].

Lipids have key role in manipulation of physical properties as well as giving the cell enough nutrients [19]. Fatty acids are important essential sources of energy from food meant for energy for humans as well as are important structural parts of cells. Omega fatty acids or n-3 fatty acids, are not synthesized in adequate amounts in body and hence need to be taken via dietary resources, thus known as essential fatty acids. Usually n-3 fatty acids have been demonstrated to help in ailments like psychiatric disease, heart disease, metabolic syndrome (MetS), ADHD, fetal brain formation, autoimmune disease as well as cancer [20-22].

Earlier Matorras., *et al.* [3] evaluated the fatty acids in general, as well as PUFA's specifically, composition of human oocytes and observed that the n-6: n-3 ratio was 7.7 [23]. Since n-6: n-3 ratio is tightly linked to a healthy diet. It gets impaired in a lot of obese as well as overweight humans they posited that the FA composition of oocytes of women who are obese as well as overweight might be changed.

But role of n-3 fatty acids in human oocytes is not clear. Recently Matorras., *et al.* [24] tried to evaluate the fatty acids concentration in human oocytes probably for the 1st time. Since obesity has an effect on all walks of life including assistive reproductive technology (ART) it becomes an important topic with us in the midst of obesity epidemic in world.

Matorras., *et al.* [24] examined 250 women undergoing *in vitro* fertilization (IVF) and grouping them as per body mass index (BMI) and analysed their oocyte fatty acids amounts. Oocytes from metaphase I, metaphase II as well as germinal vesicle stage utilizing capillary gas chromatography. An overall 922 oocytes were analysed in batches of 9 groups. They observed that women that had obesity showed amount of saturated fatty acids as well as poly unsaturated n-3 fatty acids (PUFA) across all studied stages of oocyte formation, and overweight women had n-3 fatty acids in metaphase II oocytes. Knowing that n-3 fatty acids are a must for embryo formation, besides from neurologic point of view but also at cell signalling level, this could explain the bad results in obese women having *in vitro* fertilization (IVF). Further it is intriguing to know that n-3 fatty acid docosahexaenoic acid (DHA) was maximum in obese patients whereas eicosapentaenoic acid (EPA) was lowest. Matorras., *et al.* [24], observed that obesity was not definitely correlated with the amount of fatty acid as one anticipates with an unhealthy western diet choice. Hence it is of utmost importance to examine diet choices as well as their effect on oocyte fatty acid composition and not only BMI as a surrogate.

It is of interest that Barker's hypothesis was brought in by them in their discussion. Animal model studies have revealed recently that obesity induced via high fat diet (HFD) influenced skeletal muscle's as well as cardiometabolic health across multiple generations [25]. Evidence exists that the in utero environment induces a response in the fetus, that can cause increased susceptibility to disease later in life. This concept is described as the 'Developmental origins of health and disease (DOHaD). Fetuses which are developing can adapt to unsuitable in utero environment by undergoing structural, physiological and hormonal changes that are of benefit for short term survival, but it affects future health that can be transmitted through generations [17]. At present, it is not in our knowledge what is the exact importance of fatty acids in reproduction. Could obesity with specifically dietary content of fatty acids also influence oocyte quality across generations? Is it possible that epigenetic changes that influence reproduction would be caused by these diet changes in multiple generations and can we prespecify these alterations? Essential queries for future lie in these that needs more evaluation. Knowing that lipids, especially PUFA are essential as far as embryo as well as fetal formation is concerned this study has great importance. They have emphasized now that that the effect of fatty acids begins from the oocyte stage and further.

More important thing to bother is about role of fatty acids in oocyte as well as embryo cryopreservation [26]. Though the mode is not clear. High lipid amounts makes cryopreservation difficult in both oocyte as well as embryo is a known fact and leads to cryo damage. The fatty acids amounts of human oocytes have been quantified successfully as well as profiled during this study. Though oocyte vitrification in humans is a refined as well as very successful, it is not clear if differential fatty acids concentration influences the success rate of oocyte as well as embryo cryopreservation and thus if dietary intake can influence vitrification as well as warming. If there is actually important part of diet in oocyte fatty acids content, what is the essential next step is to examine in animal models regarding how this translates to reproductive results as well as cryopreservation. Later it could get translated to human evaluation with regard to dietary fatty acid composition or ratio as well as its role in fertility.

Omega 3 fatty acids are believed to be essential fatty acids since they can't be manufactured in our bodies but can only be got from diet. They have a role in different structural as well as functional aspects of cell membrane. They have an essential part in cell-cell communication, nutrient import as well as export, gene control etc. A well balanced diet having these essential fatty acids is important and this study points that essential fatty acids might even effect the oocyte quality. The role of essential fatty acids especially the effect of dietary composition of n-3 fatty acids in infertility are still to be studied [27].

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