The Journal of the Association of Physicians of Tamil Nadu,
Vol. 3, Issue 1, English Quarterly, January – March 2024

Body Weight and Reproduction

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Introduction:

The role of lifestyle factors, particularly excess weight gain in the genesis of metabolic diseases has been studied extensively. The results of these studies have always been consistent. If there is a dispute, the primary reason behind this is that statistics always involves a group of people and there will be some outliers. We fail to understand that the hormonal milieu and their activity varies from individual to individual. The reproductive hormones are extremely sensitive to changes in weight. It is a well-known fact that the onset of puberty is earlier in overweight and obese girls.[1] Obesity may also lead to central precocious puberty in girls.[2] Obesity often leads to delayed puberty in boys. Likewise, significant weight changes can also affect the reproductive function in both men and women. Subfertility may ensue in couples where considerable weight gain has led to sexual dysfunction in men and irregular or absent menstruation in women.

Body weight and reproduction in women:

Significant weight gain results in oligo/anovulation by inducing various hormonal changes (Fig 1). Women present with irregular or absent menstruation or subfertility. Spontaneous ovulation and resumption of regular menstruation have been noted with lifestyle modification and weight reduction alone.[3] Similarly, significant weight loss as in anorexia nervosa leads to hypothalamic amenorrhea.[4]

Body weight and reproduction in men:

Sexual dysfunction is commonly seen in overweight and obese men. Erectile dysfunction is seen in 30-50% of men with obesity.[5] Most of the studies have not shown an association between obesity and semen parameters like sperm concentration or motility.[6,7]

The Body mass index:

The body mass index (BMI) is currently considered the most accurate (available) anthropometric measure of an individual's ideal body weight. It is calculated by the formula, BMI = kg/m^2 (kg is a person's weight in kilograms and m^2 is height in meters squared). According to the BMI, an individual can be classified in one of these categories:

Underweight	-	<18.5 kg/m^2
Normal	-	18.5-24.9 kg/ m^2
Overweight	-	25-29.9 kg/ m^2
Obese	-	≥30 kg/ m^2

According to the Revised Consensus Statement for diagnosis of Obesity in Asian Indians, the cut-off for Indian women is even lesser. A BMI of 23.0-24.0 kg/ m^2 and ≥25 kg/m^2 is considered overweight and obesity, respectively given higher obstetric risks in women belonging to these categories.[8]

Polycystic ovary syndrome (PCOS) was always linked to either overweight or obesity in earlier literature.[9] In our practice, we noticed that women presented to the fertility clinic with

oligo/anovulation and PCOS irrespective of their BMI. They were almost equally distributed in the categories of normal BMI and overweight, whereas the number of women with obesity was comparatively lesser. While trying to explore the reason behind this pattern of distribution not corresponding to BMI, we found that almost all of these women had a history of significant weight gain after adolescence.[10] Similar findings of increased incidence of Diabetes mellitus and heart disease even in Indians with normal BMI have been noted.[11] This proves that BMI is not a very good indicator of good health or a predictor of disease, at least in Indian men and women. Moreso, this also conveys that there has to be a common factor involved in the pathogenesis of PCOS and other metabolic diseases in lean individuals and individuals with a higher BMI. Excess weight gain is probably the factor. All weight gain in adult life, except during pregnancy or bodybuilding is abnormal and may have metabolic and reproductive consequences.

Why is it so? What could be the reason behind this?

As we had mentioned in the previous section, significant weight gain during any part of an individual's lifetime can result in various hormonal changes. Although Insulin resistance (IR) has been implicated in the pathogenesis of PCOS and other metabolic diseases like DM, the exact mechanism has not been identified yet.[12] Tools for assessing IR are no longer considered clinically relevant due to their non-standardization and inability to correlate with clinical outcomes.[13] The practice of testing women with PCOS for higher serum insulin levels and IR has also been withdrawn from routine clinical practice due to the inconsistent results obtained.[14] From the available evidence, it could be discerned that the common factor behind these metabolic or hormonal derangements may not be insulin resistance after all.[12] 'Insulin' can still be considered as the primary instigator of these changes, where relative hyperinsulinemia due to excessive intake of carbohydrates could result in lower circulating sex-hormone binding globulin levels and thereby increased serum free testosterone levels resulting in hyperandrogenism and the other changes associated with PCOS. (Fig 1)

Revisiting Barker's hypothesis:

Dr David Barker's hypothesis on Fetal Origin of Adult Diseases (FOAD) claimed that the compromised nutritional state during early in-utero development had a profound impact on the risk for the development of diseases like coronary artery disease, hypertension, obesity, and insulin resistance later in adult life.[15] This was also earlier implicated to IR, whereas scientists have re-looked into this concept and believe that the actual reason behind this is the rapid 'catch-up' growth that happens after birth and during growth. An individual's weight is decided in utero depending on their genetic makeup and the nutrition they are provided with. The various systems in the body acclimatize to this and the memory is maintained. *The human body does not have a BMI chart or a calculator*. It was tuned to function for a particular weight and it falters when it is exposed to nutrition which is exponentially more than what that individual's body was actually made for and requires. This results in PCOS in women and sexual dysfunction in men, to begin with, and later leads to all the other metabolic diseases.[16]

Weight gain – Carbohydrates and activity:

The article focuses on the primary aetiology behind hormonal-cum-metabolic disorders affecting fertility, as treating the cause

provides better results and prevents long-term health complications in these conditions.

நோய்நாடி நோய்முதல் நாடி அதுதணிக்கும்
வாய்நாடி வாய்ப்பச் செயல்.

The above verses are from Thirukkural, a classic Tamil language text written by Thiru Tiruvalluvar in 300 BCE. This Kural emphasizes that it is crucial to identify the cause of a disease and treat the cause. In PCOS or erectile dysfunction due to weight gain, lifestyle particularly diet modification is the foremost and the only effective available treatment without side effects.

Although ovulation induction provides good results in women with anovulatory cycles, literature evidence suggests that these women are still at a higher risk for miscarriage, gestational hypertension, gestational diabetes and neonatal complications.[17] The rationale behind this is that the underlying cause, which is weight gain was not addressed or rectified.

Carbohydrates form the major source of energy required for the functioning of all systems. Yet, the consumption of excessive carbohydrates or the addition of more refined carbohydrates to the diet has been shown to have health implications. Comparatively, whole grain intake was found to be a better alternative in reducing the risk of metabolic diseases.[18] In the South Indian population, the glycemic load and glycemic index of the ingested food also seemed to play a role in the risk of developing Type 2 diabetes mellitus (Type 2 DM).[19] Considering PCOS as the predecessor for Type 2 DM, consuming food containing high calories or a high glycemic index can be considered the major risk factor for the development of PCOS, too. Even though wheat was considered as a substitution for rice a few years ago, recent studies have shown that the glycemic index with both diet patterns is not different.[20] The surging epidemic of diabetes and other lifestyle diseases in India is primarily due to the excessive intake of ultra-processed food rich in added sugars.[21] Unfortunately, health drinks, beverages, chips and biscuits have become part of the regular diet in most households in India.[22] The above-mentioned items contribute to the 'empty calories' ingested without much nutritional value and they also prevent intake of well-balanced nutritious food.

Therefore, the first-line management of lifestyle disorders affecting reproductive function is similar to that suggested by physicians for metabolic diseases. A diet comprising of lesser refined carbohydrates and more complex carbohydrates has been shown to reduce the postprandial rise in serum glucose and thereby insulin secretion in response to dietary load. Foods with high fibre content and low glycemic index promote early satiety and reduce hunger. Vegetables contain high quantities of fibre, minerals, vitamins and antioxidants. Non-starchy vegetables are low in calories and carbohydrates. Over the centuries, eating habits have changed-with more refined food. Modern processing also leads to the loss of essential nutrients in the diet. It is important to ensure adequate intake of fibre, especially soluble (as in vegetables and fruits). Some studies also insist that the quality of a plant-based diet plays an important role in improving markers associated with adiposity.[23]

Physical activity and exercise are also vital to achieve the desired outcome.[24] Physical activity not only improved body dimensions and modulated hormone levels in women with PCOS, but it also improved their psychological wellness.[25] The risk of developing cardiovascular disease in

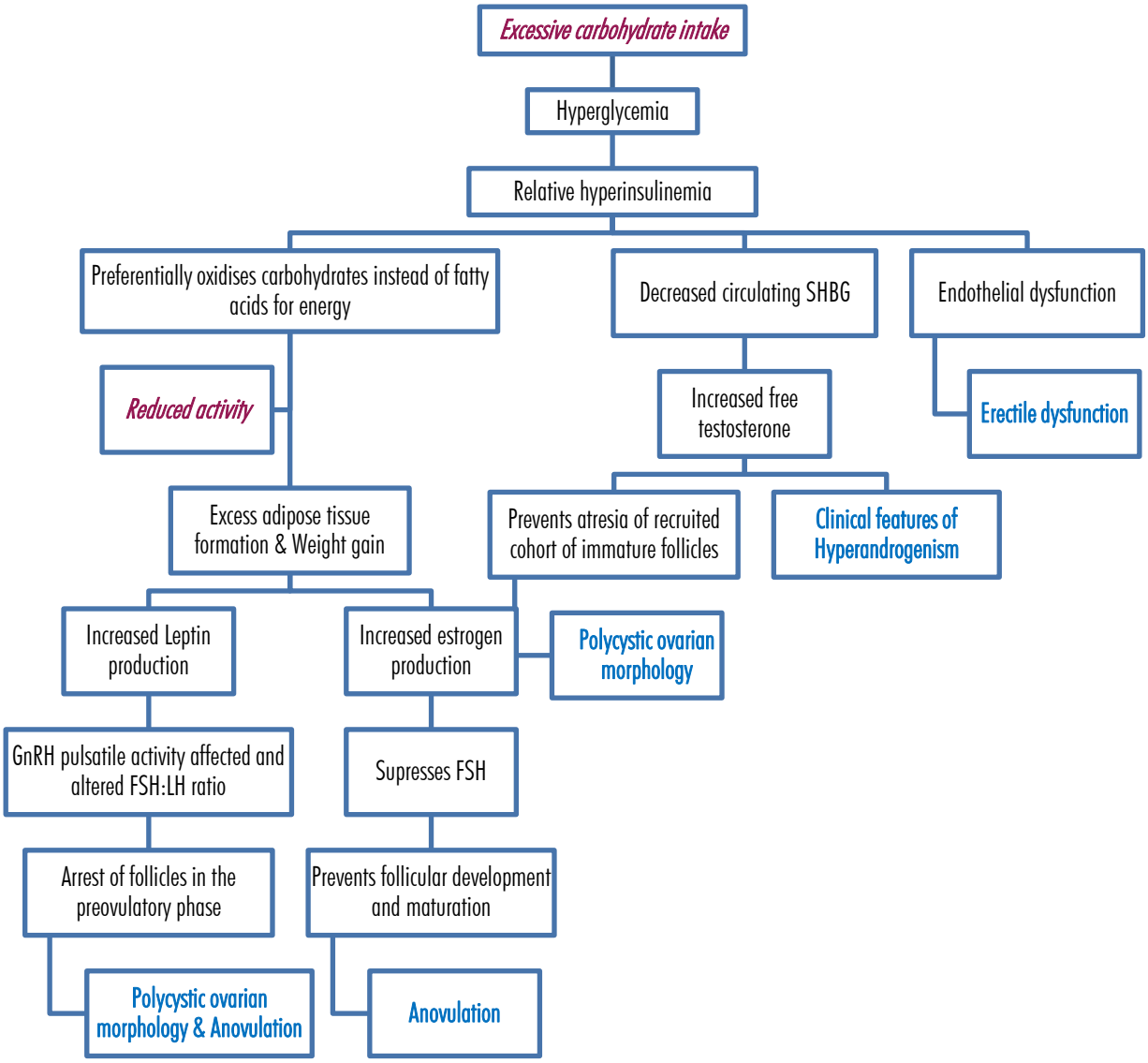

Fig 1: Pathogenesis of PCOS and Erectile dysfunction due to excessive refined carbohydrate intake, reduced activity and excessive weight gain

women with PCOS was less in those who followed regular intensive aerobic exercises.[26] This beneficial effect is due to the fall in adiposity and thereby rectification of the hormonal imbalance associated with it.

Lifestyle modification in the form of reducing refined carbohydrate intake and increasing physical activity improves the chance of spontaneous ovulation and thereby pregnancy rates in women with PCOS and anovulatory cycles.[3,27] Similarly in men, sexual function improves with lifestyle modification.[28,29]

Conclusion:

Non-communicable diseases are the leading cause of death in Tamil Nadu and many parts of the country.[30] Similarly, the incidence of PCOS is high in Indian women with it being the commonest cause of infertility. Although there

may be a genetic predisposition to these conditions, the development of disease as such is triggered by excess carbohydrate intake or reduced physical activity. Therefore, the major focus in the management of all these metabolic diseases should be lifestyle modification. This requires persistent efforts from the physician and the patient. PCOS in women and sexual dysfunction in men can be considered as the 'wake-up call' to prevent further development of other lifestyle disorders like diabetes, hypertension, cardiovascular disease or cerebrovascular disease.

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