

**Androgens in polycystic ovarian syndrome (PCOS) – beyond testosterone**

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PCOS (Reproductive Metabolic Syndrome) is the most common endocrine disorder in women of reproductive age group (5-15%). One of the major criteria for diagnosis is clinical or biochemical (Total testosterone >55ng/dl or free testosterone . 9pg/ml) hyperandrogenism. There has always been a disparity between FG score and testosterone (T) levels in PCOS women. Around half of those with mild hirsutism and small proportion of those with moderate-severe hirsutism are not associated with biochemical hyperandrogenism. The circulating levels of testosterone vary according to the diurnal rhythm, phase of menstrual cycle, SHBG, time of day and reproductive maturity. The commercially available immunoassays are not standardized for female range (20-60ng/dl) on which to base an assay. The gold standard is LC-MS but it is costly and time consuming hence limited to research purposes. Some studies showed calculated free testosterone and free androgen index as better screening tool for hyperandrogenemia than total testosterone.

Functional adrenal hyperandrogenism is also pathogenic feature of PCOS and testosterone precursor androstenedione (A4) shown to be a more sensitive marker of PCOS-related androgen excess and, in combination with T, predictive of metabolic risk. It has also been shown that androstenedione – free testosterone ratio have a favourable metabolic profile. DHEA-S is mainly used to rule out adrenal cause for hyperandrogenism rather than as a marker for PCOS.

The recent focus has been on 11-oxygenated C-19 steroids in PCOS.

11OHA4 is a major product of adrenal steroidogenesis and its

downstream conversion to 11-ketotestosterone (11KT) and

11-keto-5 $\alpha$ -dihydrotestosterone which can bind and activate

the androgen receptor with affinities and potencies similar to that

of T and 5 $\alpha$ -dihydrotestosterone, respectively. 11-KT has been shown

to be 3-fold higher than T in PCOS.

The latest focus in diagnosing PCOS is on urinary steroid metabolome. Out of the 40 metabolites tested androstenediol is the best single metabolite for classifying PCOS while in a combination of steroids a ratio comprising androstenediol, estriol, 20 $\beta$ DH cortisone and cortisol were the markers.

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