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Polycystic Ovarian Syndrome – Multiple Choice Answers for Vol. 37

1. a) T b) F c) F d) T e) T

There is growing evidence to demonstrate the strong association among PCOS, NAFLD and NASH. Most of the endocrine and metabolic characteristics of women with PCOS, including elevated androgen levels, insulin resistance, dyslipidemia, and elevated low-grade inflammation levels are considered to contribute to the presence and progression of NAFLD. Due to their common characteristics, including obesity, insulin resistance, and metabolic syndrome, women with liver biopsy or ultrasound-proved NAFLD were not surprisingly found to have higher prevalence of PCOS. It has been reported that modest weight loss and exercise can improve the NASH in women with PCOS by liver biopsy documentation. It has also been reported that intrahepatic fat is more closely related to the metabolic complications of obesity than visceral fat that might be represented by waist circumference or waist-to-hip ratio - central obesity. Furthermore, lots of studies showed that the prevalence of NAFLD is increased in young women with PCOS, independent of coexisting metabolic features and obesity. Such findings might suggest a more close relationship between NAFLD and PCOS rather than sharing risk factors of obesity and metabolic syndrome. Liver enzymes such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are cytosolic enzymes and are thought to be specific markers of liver damage. However, ALT levels can be normal in patients with NAFLD. Previous studies demonstrated that amongst a total of 48/88 (55%) women with PCOS who had NAFLD proven by ultrasonography, only 7 (15%) had elevated aminotransferase levels. Therefore, elevated ALT levels in women with PCOS may represent a higher severity of liver cell injury. Not only aminotransferase levels, but also some innovative markers as the caspase 3-cleaved fragment of cytokeratin 18, have been found to also represent the progressive hepatocyte injury in women with PCOS.

2. a) T b) T c) T d) T e) F

Women with PCOS were reported to have a higher prevalence of NAFLD and NASH diagnosed by liver biopsy, magnetic resonance spectroscopy, computed tomography and abdominal ultrasonography.

3. a) F b) F c) F d) T e) T

Statins are effective in reducing chronic inflammation, lipid profiles and biochemical hyperandrogenemia in women with PCOS. Meta-analysis revealed that statins might improve serum liver enzymes (aminotransferase levels) as well as ultrasound findings in NAFLD and NASH. However, there were no available studies regarding the beneficial effects of statins on the histological changes, liver-related morbidity or mortality of patients with NAFLD. Women with PCOS are characterized by having either elevated ovarian or adrenal androgen levels including decreased SHBG levels, increased

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testosterone and/or DHEAS levels. Testosterone levels, which mainly come from ovarian origin, highly associate with the presence of a higher prevalence of obesity, metabolic syndrome, dyslipidemia and NAFLD in women with PCOS. On the contrary, DHEAS/DHEA, which mainly comes from adrenal glands, has been reported to have opposing effects from testosterone regarding obesity, insulin resistance and metabolic syndrome in women with PCOS. DHEAS levels are inversely associated with the presence of NAFLD and NASH. Flutamide, a non-steroidal anti-androgen, is commonly used in the treatment of acne and hirsutism. Though two prospective studies of 190 and 230 hyperandrogenic girls or young women, respectively, who took a low dose of flutamide for range of period for 3-54 months in one study, and 10 years in another study revealed no cases of hepatotoxicity, there was still a case series study reporting severe hepatotoxicity after treatments in the same population. Though OCP has been reported to have an adverse impact on lipid profiles and being metabolized in the liver, might potentially increase the severity of NAFLD, according to a population-based study, current OCP usage was associated with a reduced risk of NAFLD. The protective effect of OCP usage on NAFLD might be secondary to the effect of androgen reduction, but was attenuated after adjusting for the confounding effect of adiposity. Spironolactone, another common anti-androgen used to treat acne and hirsutism in women with PCOS, was recently found to exhibit favourable effects on serum insulin and insulin resistance in patients with NAFLD.

4. a) T b) F c) F d) T e) T

Options a), d), and e) are true as the criteria to diagnose PCOS based on the available guidelines/consensus statements such as the NIH 1990 criteria, Rotterdam criteria 2003 and AES-PCOS 2006 include the presence of clinical/biochemical evidence of androgen excess such as hirsutism and raised levels of testosterone including polycystic ovarian morphology on transvaginal ultrasonography such as $>$ 12 follicles measuring 2 – 9 mm and/or ovarian volume $>$ 10 cm^3. Options b) and c) are false as these factors are not part of the diagnostic criteria for PCOS. They form part of the criteria to diagnose metabolic syndrome which include elevated blood pressure, dyslipidaemia and raised glucose levels.

5. a) T b) T c) T d) F e) T

The diagnostic criteria for PCOS in accordance to the 1993 Japanese Society for Obstetrics and Gynecology requires the presence of all the following three criteria: anovulation, the presence of polycystic ovarian morphology, and high serum LH levels. Measurement of luteinizing hormone (LH) was chosen instead of hyperandrogenism. Serum testosterone level is used only as a "referential factor". The Japanese criteria can impact on the number of women diagnosed with PCOS in the Japanese population. Additionally, other studies in other ethnicities utilised the NIH or Rotterdam criteria do not require any ultrasound evidence of polycystic ovarian morphology to make a diagnosis of PCOS. Current studies in Caucasian women show the prevalence of PCOS remains higher (up to 15%) when compared to East Asian women (up to 5.7%). Option (c) is true as evidenced by a large Chinese population study of $>$ 15, 000 women. The Rotterdam criteria is the broadest and most inclusive when compared to the NIH 1990 criteria or the AE-PCOS criteria. The wide range of reported prevalence of PCOS is likely due to differences such as subjective variation in clinical assessment of hirsutism, lack of reference standards for androgen assays, and inter-observer differences in the measurement of ovarian morphology.

6. a) T b) T c) F d) T e) F

Options (a) and (b) are true as the mFG score to diagnose hirsutism is $>$ 3 in Thai women based on the current studies, this is the lowest score for hirsutism amongst other ethnicities such as Chinese and Japanese women. In South Asians, women were reported to have a higher mean mFG score and in one particular study the mean score can be as high as 18. Option (c) is false as a study comparing Middle Eastern and Caucasian women with PCOS shows that Middle Eastern women are found to be more hirsute. NIH criteria 1990 and AES-PCOS 2006 criteria both indicated that clinical/biochemical evidence of hyperandrogenism is an essential requirement to diagnose PCOS.