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Review Article

Review on Mental health illness in patient with hyper androgenic anovulation

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ABSTRACT

Hyper androgenic anovulation (HA) is also called as polycystic ovary syndrome (PCOS). It concerned with the monthly cycle abnormalities, hyperandrogenism and obesity. The functioning of HA remains unclear, but basic imperfections in the hypothalamus pituitary axis, insulin secretion and action of ovarian function. The clinical symptoms highlighted by the HA patient was obesity, acne, hirsutism, infertility and irregular menstrual cycle. Above 50% of patients develop diabetes, heart attack, dyslipidemia, blood pressure, anxiety, depression, endometrial cancer and sleep apnea after HA was diagnosed. It affects the patient's quality of life and resulted in emotional disorder and psychological problems. The physical health, mental health and social health of HA patient were totally affected. So the study concluded that the patients with PCOS are more prone to depression and anxiety which affects the quality of life. Weight loss and dietary management have been improved the ovulation and insulin sensitivity in PCOS patient**.** So early clinical intervention in PCOS patient and psychological supports will improve the patient mental health and quality of life.

Keywords: Anxiety, Depression, Hyperandrogenism, Infertility, Obesity

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INTRODUCTION

Hyperandrogenic anovulation (HA) is also called as Polycystic ovary syndrome (PCOS). It is a most familiar heterogenous endocrine disorder amongst the women of reproductive age [1]. It is also recognized as hyper androgenic anovulation that concerned with their cycle abnormalities, hyperandrogenism and obesity. The symptoms include amenorrhea, oligomenorrhea, anovulation, infertility, hirsutism, acne and small cyst over one or both ovaries [2]. The hyperandrogenism is considered as the clinical hallmark for HA. Due to inhibition of follicles formation of micro cyst in the ovaries, absence of ovulation and change in menstural cycle and approximately 60% of patients were reported [3]. Women's having HA showed higher incidence for cancer of endometrium, cardiac disease, dyslipidemia, and type-2 diabetes mellitus. The variation of phenotype will occur and totally liable on genotype, life stage, ethnicity and environmental factors comprising body weight and lifestyle. All the features of HA was significantly exacerbates by obesity induced insulin resistance [4]. About 60-80% of women having HA was reported to have insulin resistance and 95% were reported with obesity [5]. The study showed that 5-10% of women concerning the age group of 18-44 were reported with HA. Beyond 50% of patients develop diabetes, heart attack, dyslipidemia, blood pressure, anxiety, depression, endometrial cancer, and sleep apnea after HA was diagnosed [6]. Increased rates of miscarriage, gestational diabetes, pre-eclampsia, and premature delivery were reported in pregnant patient with HA. It affects the patients quality of life and resulted in emotional disorders and psychological problems [7]. The most common psychiatric disorder that reported in HA patient were anxiety and depression. Other than anxiety and depression many women were reported with eating disorder, somatization and aggression when compared with the normal healthy women. The prevalence of HA is increasing gradually in world wide.

The recent adolescent HA prevalence data showed that 15-20% in European population, 2.2% in china, 6% in Mexico, 6.3% in Spain. In addition, 26% of Indian adolescent women reported with HA [8]. The occurrence of psychiatric comorbidity in HA patient was 50% in Japan, 52.7% in Kashmir. The approximate occurrence of psychiatric illness in depressive disorder 33%, anxiety disorder 13.6%, panic attack 15.45%, obsessive compulsive disorder 6.36%, suicidality 8%, eating disorder 6.8% and bipolar disorder 2.72% [9,10]. The aim of this review is to study the mental health illness and quality of life effects in patient with hyper androgenic anovulation. The research articles between the year of 2006-2018 was searched and collected from PubMed, Google scholar, embase were used.

Pathophysiology: The functioning of HA remains unclear, but basic imperfections in the hypothalamus pituitary axis, insulin secretion and action of ovarian function.

Insulin sensitivity and secretion: The primary role of insulin is to regulate the ovarian function and the ovaries were over response to insulin that leads to excess making of androgen and resulted in follicular immaturation and anovulation [4]. It can be also explained genetically by, increased secretion of androgen due to the release of luteinizing hormone and insulin. Due to increased level of luteinizing hormone produce more androgen in young girls and women who having HA. The main reason for HA include obesity, nutrition or eating disorders and insulin resistance [11,12].

Androgen secretion: Hirsutism is the coarse hair that seems in male pattern and differentiated from hypertrichosis (increase in hair follicles). Most usual reason of hirsutims was mainly due to partying androgen level and the changeover of testosterone to dihydrotestosterone at pilosebaceous unit. Based on racial factors the pilosebaceous unit may vary and also distribution of hair follicles and responsiveness of androgen also vary [13,14].

Obesity, fat distribution and adipose tissue function and morphology: Obesity and other adipose tissue related factors play a vital role in HA. Obesity will exacerbate the preexistent clinical, hormonal, metabolic features in HA women. Due to presence of increased level of androgen there will be a buildup of abdominal fat in women associated accompanying with lower levels of partying sex hormone binding globulin(SHBG). So weight loss in obese patient with HA through diet, exercise and lifestyle management will reduce the circulating androgen and increase SHBG level, reduction in ovarian volume and follicle count, improve insulin sensitivity and also menstrual cycle [15,16] .

Increased sympathetic nerve activity: HA related characteristics such as hyperandrogenism, inhibition of insulin reuptake, obesity, hypertension, obstructive sleep apnea and depression lead to improved symphathetic nerve activity. Due to increased level of insulin and obesity stimulate the symphathetic nervous system thereby increase the glucose breakdown in hypothalamic neurons [11].

Diagnostic tools for polycystic ovary syndrome [17]:

NICHD/NIH Criteria (1990)

- Hyperandrogenism
- Oligo-ovulation/anovulation
- Exclusion of other related disorders

ESHRE/ASRM Rotterdam Criteria (2003)

- Hyperandrogenism
- Oligo-ovulation/anovulation
- Polycystic ovaries

Androgen Excess Society (AES) Criteria (2006)

- Hyperandrogenism
- Oligo-ovulation/anovulation
- Polycystic ovaries
- Exclusion of other related disorders

Mental health illness: Now a days, the women's quality of life were solely determined by the society through the conception and external appearance. But the women with HA stayed primarily presented with infertility, obesity, irregular menstrual cycle. Due to their self-esteem and self-image, the worth of life was totally disturbed and that may lead to mental health illness [18]. Many studies were conducted to find out the connection between the psychiatric illness and polycystic ovary syndrome. Several studies disclosed that depression and anxiety were highly reported in HA patient. Other than depression and anxiety, bipolar disorder, sleep disorder, eating disorder was also reported. Some studies showed psychological status were appearing to be normal in patient with endocrine disorder. Many scales were available to find out the association between the HA and psychiatric illness. The hospital anxiety and depression scale was used repeatedly to find out the relationship [19] .

Depression: Corresponding to the neurology, the depression occurs due to imbalance of neurotransmitter particularly increased level of cortisol and decreased serotonin level in the central nervous system due to reduced 5-HT transporter at the nerve endings. Studies revealed that almost 28% to 64% of HA patient was reported with depression [20]. But however the connection between HA and depression were unknown due to lack of evidence. Through the knowledge assessment of HA patient the causes for depression was enlighted. The studies revealed that patient who have increased weight and change in physical appearance as acne, hirsutism, and loss of feminine which increases the negative perception towards them. Due to unpraised insulin resistance may increase the risk for depression as highlighted by the study. Hyperandrogenism was reported highly in patient with HA. Certain androgen hormone like testosterone didn't showed any relationship to depression but group of androgen hormone called dihydroepiandrosterone (DHEA) may buildup the risk for both depression and anxiety [21,22]. These false perceptions alter the physical and mental status which cause social withdrawn and culminate them into depression. The study showed amongst the infertility HA patients also showed moderate depression status and high depression status in obesity HA patient and anxiety were exist prominently in obese patient. Based on Rosenberg scale the patient with hirsutism and obesity showed a psychosocial disturbance [23].

Anxiety: Corresponding to American psychological association anxiety is an emotional condition characterized by tension, worried thoughts and physical changes like increased blood pressure. They usually have recurring intrusive thoughts or concerns. The 38.6% of HA patients was prevalent anxiety towards infertility and alopecia [23]. The pathological relationship concerning anxiety and HA was unclear. But scientifically, the researchers found that the increased testosterone interfered with the gene in amyglada (androgen receptor) and alteration in the receptor accountable for the estrogen as well as in the gene that regulates the serotonin and GABA [24]. The primary causes of anxiety in HA were highly due to infertility, loss of sexuality, acne, hirsutism and obesity. The German internet based survey showed anxiety was highly reported in patient with HA [25]. The female with HA might develop social phobia, panic attack, and specific phobia due to perception of people towards their masculine body features. One study navigated among the Oman population showed that 71% of people showed anxiety followed by depression and stress. When compared to depression only few studies were published to establish the relationship between anxiety and HA [26].

Obstructive sleep apnea: Obstructive sleep apnea is a condition where the walls of the throat relax and narrow during sleep and interrupted with the normal breathing pattern [27]. Estrogen and Progestrogens have a caring role adjacent to the development of sleep disorders in women. Depending upon the pregnancy status age, phases of the menstrual cycle, menopausal status, hormone replacement therapy the individual sleep status had been identified. Studies suggest that lower level of estradiol showed poor sleep quality with higher frequency then apnea [28]. The risk of sleep disorders depending upon the body weight of the individual. Presence of visceral body fats in women will show a superior amount to sleep disorder then with non-visceral fatty women[29]. This increase in visceral fat was due to sex steroid hormone especially due to androgen. Insulin resistance also found be a predictor for sleep disorder [30]. There is increasing sign for a relationship concerning HA

and sleep disturbances that is complicated and possibly bidirectional [31]. The literature signifying that HA were related with sleep disorder. The chronic presentation of HA may resulted in obstructive sleep apnea. The studies show up that persistent OSA in HA patient resulted in cardiovascular events. The reason behind the OSA was central obesity, hyperandrogenemia and insulin resistance, could be involved in the development of OSA in women with HA [26]. But however there is a lack of prevalence data for association between HA and OSA .

Eating disorder: Approximately 60% of women with HA were reported with eating disorder particularly bulimia nervosa and 26% were reported with binge eating. It is recommended that psychological distress accompanying with harmful signs of HA may dispose to disordered eating [32]. They had a habit of periodic eating disorder such as binge eating which might lead to obesity and change in the physical appearance can lead to depression. One study revealed that hirsutism, irregular mensuration and obesity may progress the eating disorder in HA patient. But however, association between HA and eating disorder was unknown [33].

Bipolar disorder: No study suggest that patient with HA will develop bipolar disorder. But the patient who have bipolar disorder with prolonged use of sodium valproate might resulted with irregular menstrual cycle, hyperandrogenemia and hormonal imbalance[34].

Quality of life in PCOS: Several studies had been conducted to find out the quality of life among HA patient. The quality was evaluated by using the standardized questionnaire related to health related quality of life (HRQOL) [35]. The physical health, mental health and social health of HA patient were totally affected. The clinical symptoms highlighted by the HA patients were obesity, acne, hirsutism, infertility and irregular menstrual cycle [36]. The women with HA showed poor quality of life when compared with normal women without HA. More studies were conducted to assess the quality of life in HA and psychiatric behavior. Majority of the studies enlighted that depression and anxiety were highly affect the quality of life in HA women than normal healthy women [37]. Due to their negative perception on physical appearance and overweight towards themselves and self-imagine resulted in depression. The social anxiety also affecting the life quality due to the societal thoughts due to their negative perception towards conception [38]. Women with poly cystic ovarian disease / symptoms are suffering from significant impaired quality of life as measured by HRQOL (SF 36), the impairment was found to be independent of their duration of illness. One study suggest that body mass index and hirsutism affect the quality of life.

Treatment: Treatment goals should include modifying anovulation, preventing the action of androgens on target tissues, and decreasing insulin resistance [39,40].

Non pharmacological:

- Weight loss for obese patients with HA helps to decrease androgen, luteinizing hormone (LH), and insulin levels [41].
- Laparoscopic ovarian drilling is an surgical procedure were the multiple perforations are created in the ovarian surface and stroma [41].
- Psychological Treatment
    1. Motivational Interviewing (MI) is a counseling method that helps to solve indeterminate moods and uncertainties to determine the internal motivation they need to change their behavior. These strategies into the counselling sessions have been proven to enhance participant motivation in life style modification programs [42].
    2. Cognitive Behavioral Training and Primary and Secondary Control Enhancement Training involved in reductions in obesity and depression in adolescents with PCOS. They also showed decreased rates in functional comorbidities such as menstrual irregularity; high percent of fat mass, sleep-related breathing disorder; blood pressure and mid-region adiposity associated with HA [42].
    3. Techniques such as relaxation therapy and Cognitive Behavioural Therapy (CBT) to treat stress can be used to address the cortisol secretion abnormalities often present in HAwomen. It was observed that CBT intervention resulted in significant decreases in weight and depressive symptoms and significant improvements in menstrual regularity and sleep-related breathing [15,41].

Pharmacological:

Anovulation

Clomiphene: Used for inducing ovulation in HA is clomiphene citrate (Clomid, Sanofi), although the precise mechanism of action is unknown.

Dose: 50 mg/day for 5 days.

If ovulation occurs but no pregnancy results, 50 mg/day for 5 days is continued for the subsequent cycles. If there is absence of ovulation, the dose of 100 mg daily for 5 -30 days can be given [15,41-43].

Anti androgen

Spironolactone at a dose of 25 to 100 mg twice daily, is the most commonly used anti androgen because of its safety, availability, and low cost.. Due to its increased risk of teratogenicity, contraception is recommended [15,41].

Anti diabetic agents:

Antidiabetic drugs are used to improve fertilization and to reduce the insulin resistance. Metformin will show more efficacy when compared with other antidiabetic agent. The usual dose of metformin was 1500 – 2000mg/day in divided doses [42].

Oral contraceptives (OCs) like estrogen and progestin combinations are the primary OCs used in the treatment of hirsutism and acne associated with HA.

Medroxyprogesterone acetateata dose of5 to 10 mg/day for 10 to 14 days each month can be used to treat amenorrhea or dysfunctional uterine bleeding in women with HA [41,42].

Statins: In women with hyperthecosis statins can be prescribed to the reduce testosterone levels, bad cholesterol (LDL-C), triglycerides and total cholesterol [43].

Aromatase inhibitors: Aromatase inhibitors may be considered for patients with clomiphene resistance. Letrozole was an aromatase inhibitor was approved for polycystic ovary syndrome. The dose of letrozole was 2.5mg or 5 mg orally daily for 5 days [43,44].

CONCLUSION

Polycystic ovary syndrome is the most common endocrine disorder that occurs between the age group of 18-30. Obesity, hyperandrogenism, irregular mensuration, absence of mensuration shows more risk to polycystic ovary syndrome which results in infertility, acne and excess hair growth over face will affect the women's physically and mentally. Women who are having PCOS showed psychological disturbances like depression, anxiety, sleeping disorder and eating disorder. Most common reason behind the mental health illness was acne, infertility, loss of feminine and obesity which makes false perception towards them and leads to mental health illness. From this study we concluded that the patients with PCOS are more prone to depression and anxiety. Apart from that the patient with depression and anxiety showed poor quality of life. Weight loss and dietary management have been improved the ovulation and insulin sensitivity in PCOS patient**.** So early clinical intervention in PCOS patient and psychological supports will improve the patient mental health and quality of life.

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