Quality of Life and Sexual Health

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Lara Tiranini, Giulia Stincardini, Alessandra Righi,
Laura Cucinella, Manuela Piccinino, Roberta Rossini,
and Rossella E. Nappi

8.1 Quality of Life

According to the World Health Organization (WHO), quality of life (QoL) is the "individual perception of human beings of their position in life in the context of the culture and value systems in which they live and in relation to their goals." In this setting, health-related quality of life (HRQoL) is a multidimensional concept that examines the impact of a specific disease or its treatment on physical, mental, emotional, and social aspects and provides information on the benefits of medical therapies from the patient's perspective.

Polycystic ovarian syndrome (PCOS) is a major cause of psychological morbidity. Several systematic reviews have shown that PCOS has an overall negative impact on HRQoL [1–3]. It is not clear which aspects of PCOS have the strongest influence on HRQoL in affected women. Different traditions, religions, cultural-gender identity, and ethnicity are likely to influence the impact of PCOS on HRQoL in various societies. In a study by Benetti-Pinto et al. [4], Brazilian PCOS patients had worse self-perception regarding their general health with a negative correlation between weight and the physical domain. PCOS occurring in South Asian women adversely affected psychological well-being, especially due to the presence of hirsutism rather than obesity [5]; however, their HRQoL resulted not poorer than Caucasian women with PCOS [6]. In Iranian women, hirsutism has the strongest

L. Tiranini · G. Stincardini · A. Righi · L. Cucinella · R. E. Nappi (✉)
Research Center for Reproductive Medicine, Gynecological Endocrinology and Menopause,
IRCCS San Matteo Foundation, Pavia, Italy

Department of Clinical, Surgical, Diagnostic and Pediatric Sciences, University of Pavia,
Pavia, Italy

M. Piccinino · R. Rossini
Research Center for Reproductive Medicine, Gynecological Endocrinology and Menopause,
IRCCS San Matteo Foundation, Pavia, Italy

impact on HRQoL, followed by infertility and menstrual irregularity [7]. Thus, the subjectively perceived impact of PCOS symptoms on women's lives, as well as cultural considerations or women's expectations, provides a basis for a better understanding of this large variability in QoL.

The polycystic ovary syndrome health-related quality of life questionnaire (PCOSQ) is the only specific validated instrument to measure QoL in these women population. It includes 26 items categorized into five domains, i.e., hirsutism, emotions, body weight, infertility, and menstruation [8]. Subsequently, the PCOSQ was modified by adding four questions to evaluate issues associated with acne [9]. Even generic questionnaires, validated for chronic diseases, have been used to assess HRQoL in PCOS women.

8.1.1 Hirsutism and Acne

Symptoms affecting appearance and body image, as hair and skin problems, reduce self-confidence and self-esteem causing marked psychological distress. The symptom of acne was reported in very few studies, probably because it is not included as a domain in the PCOSQ. Hirsutism, together with menstruation, is the most affected domain of HRQoL in PCOS women [3], but QoL may vary through different populations according to differences in cultural heritage, value systems, and family structure. In a German PCOS population, an elevated Ferriman-Gallwey score for hirsutism was associated with a low SF-36 scale including bodily pain, general health and physical domains, as well as decreased sexual satisfaction, but no correlation was detected between hirsutism and psychological or emotional distress [10]. On the other hand, a UK study involving PCOS women with self-reported facial hair showed an elevated incidence of depression and anxiety; the subsequent randomization to a laser treatment revealed a positive impact upon HRQoL with reduction in self-reported severity of hirsutism, time spent on hair removal, and depression and anxiety scores [11]. Thus, as demonstrated in a sample of adolescent girls with PCOS [12], self-perceived severity of illness such as hirsutism might correlate more directly with HRQoL than clinical assessment, further supporting the importance of measuring HRQoL from the patient's perspective. The pathogenesis of skin issues (hirsutism and acne) includes both hyperandrogenemia and insulin-resistance; therefore, it was demonstrated that both combined hormonal contraceptives and lifestyle changes have a positive effect on QoL [13].

8.1.2 Body Weight

PCOS is associated with higher rates of obesity and metabolic syndrome, leading to an increased prevalence of cardiovascular risk factors, such as insulin resistance, dyslipidemia, and diabetes. Weight gain appears to exert the greatest negative influence upon HRQoL in women with PCOS, and many of them report frustration with inability to lose weight, low self-esteem, and consequently a poor body image [8]. Cultural

influences are likely involved in body image distress, as the android fat pattern commonly associated with PCOS is considered unattractive in many context. Moreover, social expectations of thinness in Western countries may also play a role. However, the role of body mass index (BMI) in self-reported QoL of women with PCOS appears to be complex. Some studies have shown that reductions in HRQoL are associated with an elevated BMI [10, 14], not only in the adult population but also in PCOS adolescents [15]. Other studies do not suggest a relationship between BMI status and HRQoL in PCOS women. For example, Hashimoto et al. [16] found similar HRQoL weight scores comparing two ethnicities (Austrian and Brazilian women) with significant differences in BMI (Austrian women were leaner than Brazilians); the weight domain resulted the worst area of HRQoL in both populations. These findings indicate that all women with PCOS have weight concerns regardless of their BMI; therefore, relying on this clinical measurement alone as an indicator of poor QoL would overlook the difficulties experienced by PCOS women who have a "normal" weight. One potential explanation of the reduction in HRQoL may be that PCOS women with normal BMI struggle to maintain their weight at this level. There is also the need to look beyond BMI and measure waist circumference which is more directly proportional to total body fat and to metabolically active visceral fat, a more accurate measure of metabolic risk. In any case, a reduction in weight appears to improve HRQoL significantly. A combined treatment with lifestyle interventions and hormonal contraceptives was associated with improvement in all domains of HRQoL in overweight/obese PCOS women [13], confirming some findings previously obtained in obese adolescents with or without the addiction of metformin [17]. Even if changes in insulin sensitivity did not correlate with changes in HRQoL [13], Hahn et al. [18] showed that treatment with metformin induces an improvement in SF-36 HRQoL scores significantly correlated with a reduction in weight. In women with multiple comorbidities, such as depression, even cognitive-behavioral therapy added to an intensive lifestyle intervention showed a positive impact on PCOSQ scores [19]. Therefore, efforts to identify appropriate long-term weight loss programs and treatments would be beneficial to these women, and physicians must provide early interventions because young, obese adolescents with PCOS have a high prevalence of early endocrine, metabolic, and cardiovascular characteristics.

8.1.3   Menstruation

Menstrual irregularity (oligomenorrhea and amenorrhea) is one the most distressing symptoms in PCOS women determining a reduced feeling of femininity and a significant concern about fertility [9]. In a US sample, menstrual cycle disorders were the second most important factor after obesity in reducing QoL in women with PCOS [14], whereas by comparing Asian and Caucasian PCOS women, menstrual problems were found to be of least concern for Asians [6]. Indeed, different studies display a variability in the distribution and frequency of PCOSQ sub-scale domains, which is probably determined not only by ethnicity and culture but also by the enrollment of women with different phenotypes of PCOS [20].

8.1.4 Infertility

PCOS is the most common endocrine disorder causing female anovulatory infertility regardless of ethnicity. Infertility has been reported as the worse domain of HRQoL in some studies [21], but selection bias must be considered as women could have been referred to clinic due to infertility problems. Several factors modulate the emotional consequences of infertility, including duration of infertility, previous treatment failure, age, and socio-cultural background. Reproductive history predicted scores in the infertility domain of the PCOSQ: women with PCOS who had given birth to at least one viable infant exhibited better functioning in this domain in comparison to women without children. Moreover, women who experienced spontaneous abortions reported the lowest scores in the infertility domain, exceeding those of women who had been unsuccessful in establishing pregnancy [14]. Infertility is not only a concern of women trying to conceive since it has been shown that even adolescent girls with PCOS are worried about their future ability to become pregnant with an impact on their QoL [22].

8.1.5 Psychological Distress (Depression and Anxiety)

Women with PCOS have higher levels of emotional distress with excessive weight, hirsutism, and infertility having a strong influence on the psychological experience of women because they evoke negative emotions of low self-esteem, frustration, and anxiety [23]. A recent meta-analysis showed that PCOS women have over three times the risk of depressive symptoms and over five times the risk of anxiety symptoms if compared to controls [24]. The association remained significant also restricting the analysis to moderate and severe depressive and anxiety scores [24]. Other psychiatric disorders have been found to correlate with PCOS, with increased odds of personality disorder, schizoaffective disorder, withholding anger, obsessive compulsive disorder, panic disorder, and attention deficit disorder [25]. Disordered eating behaviors, as bulimia and binge eating disorder, are also more prevalent in adult women with PCOS.

The exact mechanism underlying the increased prevalence of depressive and anxiety symptoms in women with PCOS is unclear, but many potential factors may play a role. In the general population, some meta-analyses have shown association between depression and factors such as obesity, insulin resistance, and diabetes [26]. In PCOS, although weight concerns are common and are associated with low QoL scores, a meta-analysis showed only a modest impact of weight on depression and anxiety scores [27]; in addition, women maintained higher odds of psychological disturbances after matching for BMI, suggesting an independent relationship. Insulin resistance, common in both obese and lean PCOS women, showed a bidirectional relationship with depression, but not with anxiety [28]. Infertility does not seem to correlate with an increased risk of depression or anxiety. The relationship between androgens and mood in women is controversial. Biochemical hyperandrogenemia, in particular higher free testosterone, was observed in PCOS women with anxiety compared to PCOS women without anxiety [29], whereas no association

was seen between testosterone and depression [24]. Clinical hyperandrogenism was associated with elevated depression and anxiety scores, when the Ferriman-Gallwey scale is self-administered. By contrast, when the clinician filled-in the same scale of hirsutism, there was no correlation with depression, indicating the importance of the subjective experience of hirsutism. Stress and increased activity of hypothalamic-pituitary-adrenal axis have been implicated as a possible mechanism contributing to depression both in the general population and in PCOS patients ([30]), but very few studies are available.

Depression and anxiety, as well as other psychiatric disturbances, should be routinely screened in PCOS patients. Indeed, some of PCOS specific treatments have shown favorable emotional effects, but there are no studies evaluating antidepressant or anti-anxiety medications specifically in the PCOS population. Lifestyle interventions (i.e., dietary, exercise) have been shown to decrease weight, testosterone, and hirsutism, potentially improving depressive and anxiety symptoms. The addition of hormonal contraception regulating the menstrual cycle and reducing hyperandrogenism showed a better efficacy [13]. On the other hand, hormonal contraceptives given to lean PCOS women showed no improvement in psychological domains [17]. Other potential treatments are laser hair removal, which improved psychological aspects related to hirsutism without changes in androgen levels [11], and pioglitazone, an insulin sensitizer which determined a greater decrease in depression scores if compared to metformin, probably because of its anti-inflammatory properties (in the general obese population, dysregulation of inflammatory pathways is associated to depression). Finally, cognitive behavioral therapy is one of the first-line treatments for patients with depression, with data confirming an improvement in weight loss and stress responsiveness and a small improvement in depression and anxiety scores [19].

Body image distress (BID) is an important mediator and predictor of depression and anxiety, and, in PCOS women, skin problems and obesity are the main determinants of body dissatisfaction. BID is defined as a distortion of perception, behavior, or cognition related to body weight or shape. The Multidimensional Body Self Relations-Appearance Subscales (MBSRQ-AS) (a 34-item questionnaire) and the Stunkard Figure Rating Scale (an image of multiple female silhouettes increasing in size) are validated instruments to measure body image distress. The most recent and larger controlled study by Alur-Gupta [31] confirmed a worse body image score on all subscales of MBSRQ-AS in PCOS patients, and this result is maintained even after adjustment for BMI and other confounders. Moreover, PCOS women expressed greater differences between ideal and perceived images of their own body, also indicative of BID. These results point to the need for screening and counseling women with PCOS regarding the higher predisposition for BID and the associated depressive and anxiety symptoms which may jeopardize motivation and compliance to treatments. Management of BID includes cognitive behavioral therapy, stress management training, and psychoeducation, associated with specific therapies for PCOS. Thus, a strict collaboration with nutritionists, endocrinologists, and behavioral health specialists is essential to provide a comprehensive care, and early intervention decreases psychological disturbances by improving QoL.

8.2   Sexual Health

In PCOS women, body image issues (i.e., obesity, hirsutism, and acne), irregular menstrual bleeding, and infertility may influence the feminine identity with consequent frustration, unhappiness, and psychological distress. In addition, the perceived unattractiveness may induce alteration of sexual behavior and loss of self-esteem with effects on both intimate and social relationships. Sexual function depends on the integration of physical, emotional, cognitive, and socio-cultural aspects. Female sexual dysfunction (FSD) may affect any phase of the sexual response cycle preventing the individual or the couple from experiencing satisfactory sexual behavior. The Female Sexual Function Index (FSFI) is the most used self-reporting instrument to assess six domains of sexual function (desire, arousal, lubrication, orgasm, satisfaction, pain) and has been largely used even in PCOS.

Current opinions about sexual function in women with PCOS are controversial; contrasting results observed in different studies might be explained by the multifactorial nature of women's sexual function, different phenotypes, and characteristics of study populations, as well as the spectrum of PCOS severity.

8.2.1   Impact of PCOS Traits on Sexual Function

Changes in appearance might impair feminine identity and compromise sexual satisfaction. In the general population, it has been shown that obesity affected several aspects of sexual function (except desire and pain) in women with FSD, whereas no correlation was demonstrated between BMI and FSFI in women without FSD. This finding indicates that obesity might be an important factor once sexual dysfunction is already manifested [32]. In PCOS women, some studies reported a weak correlation between BMI and FSD. For example, increasing BMI resulted in diminished FSFI scores on desire and sexual satisfaction domains [33]. In another study, high BMI had only a minor effect on sexual function, determining a lower satisfaction with sexual life [34]. Whereas obese healthy women had low FSFI score, PCOS women yielded borderline FSFI scores regardless of their obesity status [35]. On the other hand, Elsenbruch et al. [23] concluded that in PCOS women BMI had no impact on sexual satisfaction and no effect on the frequency of sexual intercourse or sexual thought and fantasies. The same results were found in Brazilian [4] and in North American PCOS women with a lack of correlation between BMI and sexual function, apart a mild association with orgasmic dysfunction [36].

As already mentioned, hirsutism is another important trait of PCOS able to alter body image and affect one's perception of sexual attractiveness. In an Iranian sample of infertile PCOS women, Eftekhar et al. [33] found significantly lower scores in all FSFI domains using the Ferriman-Gallwey score, while in other studies [10, 23] PCOS women believed more than controls that their excessive body hair negatively affected their sexuality and caused difficulty in making social

contacts due to appearance. Instead, Stovall et al. [36] did not find an association between hirsutism and sexual dysfunction in PCOS. Hashemi et al. [37] reported a lower but not significant score of sexual function in hirsute women with PCOS, while alopecia, another distressful characteristic of PCOS, correlated to sexual dysfunction. In a study including lean PCOS and control women, those with clinical hyperandrogenism showed higher scores in the Visual/Proximity domain of the Cues of Sexual Desire Scale in respect with those with biochemical hyperandrogenism [38].

Concerning infertility, in an Iranian sample of married PCOS women a 10% wider prevalence of FSD in the infertile group compared to fertile counterpart was reported [37]. On the other hand, another study concluded that having children or not was not associated with sexual function in women with PCOS [34]. That being so, the wide variability in the perception of PCOS symptoms according to sociocultural factors may explain such controversial results.

Finally, sexual debut and behavior have been also investigated in adolescent with PCOS. These girls were less likely to be sexually active than their healthy peers, but the mean ages of initiation of sexual activity were not significantly different [22].

8.2.2   General Impact of PCOS on Sexual Function

We have stated that several studies have reported a possible association between PCOS and sexual dysfunction. However, a recent meta-analysis by Zhao et al. [39] concluded that PCOS did not significantly impair sexual functioning and the prevalence rate of FSD was similar in PCOS women and in healthy controls (34.6% and 33.5%, respectively). These results confirm the findings of a pilot study including PCOS women and controls with normal weight in order to avoid the bias of obesity on psychological distress and sexual function [40]. The incidence of FSD was similar in PCOS and control women even in the context of partnership (i.e., partner's sexual health and feelings, relationship) [40]. Other studies reported that women with PCOS felt less sexually attractive, were less satisfied with their sex life, and thought their partners were less satisfied too, even if they did not differ in the frequency of sexual intercourses and sexual thoughts and fantasies when compared to controls [10, 23]. Treatment with metformin increased the frequency of sexual intercourses, improved the satisfaction with sexual life, reduced pain during sexual intercourses, and diminished the self-reported impact of hirsutism on sexuality [18].

According to Zhang et al. [39], even if the total FSFI score did not differ between the PCOS group and the control group, women with PCOS had significantly lower values in the arousal and lubrication domains. A possible explanation is the relationship between arousal disorder and physical appearance (i.e., obesity, hirsutism) and between vaginal lubrication and psychological inhibition during sexual intercourse.

8.2.3 Androgens and Sexual Function in PCOS

Hyperandrogenemia is the hallmark of PCOS, and it is associated with a reduction of sexual hormone binding globulin (SHBG) levels that increase free circulating androgens. Androgens seem deeply involved in the modulation of sexual function by positively acting on sexual desire (thoughts and fantasies); however, the exact role of androgens in sexual response remains controversial and not completely understood because normal sexual function has been documented even in women with low androgen levels across the menstrual cycle [41]. Several studies have found that hyperandrogenemia had a negative effect on sexual function, probably because of the clinical signs of hyperandrogenism (hirsutism, acne, alopecia) which impair body image. On the contrary, some investigators suggested that hyperandrogenemia might act as a protecting factor for sexual function: Stovall et al. [36] reported that PCOS women with the lowest total serum testosterone levels tended to have the lowest sexual function scores, while higher testosterone levels were associated with greater desire/frequency. Discrepancies in linking androgen circulating levels and sexual function are well known and may be due to a variety of mechanisms, including intracrinology, bioavailability, and enzymatic and receptor activity [42]. Indeed, high testosterone levels in PCOS women did not produce any beneficial effects on their sexual function [35]; similarly, higher circulating androgen levels in PCOS women did not influence sexual function nor modify clitoral body volume if compared to women without PCOS showing normal androgen levels [40]. Consistent with this, Rellini et al. [38] demonstrated that clinical signs of hyperandrogenism, rather than biochemical signs of hyperandrogenemia, were associated with specific cues of sexual desire levels, implying that the link between androgens and sexual desire relies on individual androgen sensitivity.

8.3 Conclusions

The multifaceted aspects of PCOS coupled to the multidimensional nature of QoL and sexual function offer a complex view to the readers, fully opened to further research. It is likely that genetic and epigenetic mechanisms play a crucial role in setting different phenotypes of PCOS women giving origin to a multitude of behavioral patterns.

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