

Exacerbated health related quality of life amid morbidly Obese PCOS women from Faisalabad, Pakistan

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Abstract

Background: Projected elevation rate of obesity, as feature of metabolic syndrome (MetS) among PCOS women, more likely intoxicated the women's health and quality of life (HRQoL). Whereas influence of its multifaceted dysfunctional profile on PCOS pathology can better be explained employing advance statistical approach, structural equation modeling (SEM).

Methods: PCOS women with MetS (N=500) were recruited to examine the impact of MetS on association of PCOS manifestation and HRQoL, recorded from normal weight, overweight, obese and morbidly obese women.

Results: An appreciable ($P<0.05$) boost in PCOS and MetS parameters was resulted in obese and morbidly obese women compared to normal weighed. Moreover suggested models for obese women delineated the confounding intricacy of variables from each construct and appropriateness was also ascertained via confirmatory factor analysis (CFA) and goodness of fit statistics ($\chi^2/df=1.68$, NFI=0.786, CFI=0.897, RMSEA=0.078). While positive significant (0.523, $P=0.001$) impact of MetS on PCOS but inverse noticeable (-0.196, $P=0.042$) effects of PCOS on physical satisfaction was examined in morbidly obese women. A close directional association between physical dissatisfaction and mental distress in women was also revealed.

Conclusion: In conclusion, metabolically blemished morbidly obese and obese women were found more threatened by PCOS manifestation as well as impaired HRQoL.

Introduction

Polycystic ovary syndrome (PCOS) is the most prevalent among all female reproductive problems [1]. Reproductive endocrinopathies and ovarian dysfunctions in PCOS are the profound causes of infertility [2] among couples mostly visiting clinics for their reproductive treatments. Heterogeneity due to combination of hyperandrogenism, cyclic dysfunction and polycystic ovary morphology among PCOS and deviated consequences on their reproductive health are well examined [3]. However PCOS causing infertility became more complicated when this heterogeneity defined through the most common medical problem metabolic syndrome (MetS) among the other potential PCOS's morbidities. Metabolic disorders with variable combinations of dyslipidemia, hyperglycemia and hypertension, are found more frequently among different medical problems [4].

In several reports, half of all PCOS women are found either obese or overweight [5, 6] which is implicating the contribution of obesity through dyslipidemia in PCOS manifestations [7]. Moreover hyperinsulinemia and obesity are providing the reasons of enhanced androgens and metabolic dysfunctions [8]. Among women both syndromes and related several malformations not only augmented the endocrinopathy [9], obesity, severity of PCOS manifestations and infertility but also quality of their lives.

A bulk of literature on quantitative determinations of disease-specific quality of life through questionnaire [10, 11] is now used to examine the disease load in a particular region and to devise coordinated health policies. Most of the health related quality of life (HRQoL) questionnaires addresses the association between disease, such as endometriosis, and physical, social and emotional outcomes [12]. A noticeable decline in HRQoL score was mostly observed when PCOS and non-PCOS women were compared [13]. This score is also found repressed under the influence of obesity [14, 15] and gynecological problems among PCOS women [16]. Low self-esteem is found more associated with sexual dysfunction [17] while a recent review also implicated the high prevalence of depression and anxiety among the PCOS women [18].

Scarce information about HRQoL scores of PCOS women with MetS from this region is so far available, hence the current cross-sectional study was designed to address the hypothesis, "MetS in morbidly obese PCOS women more likely intensifies PCOS manifestations and apparently reduces the psychological and physical satisfactions while these two SF-36 domains are likely associated".

Patients And Methods

All adult women with PCOS visiting hospitals during 2015-17 were requested to participate in a survey after proper endorsed consent of confidentiality. Assurance of prohibited disclosure of personal information was rendered to each participant. While details about processing of collected data, possible use and probable outcomes were shared in written consent and discussed personally with participants. Collected data compiled and interpreted according to guidelines of STROBE checklist. Prior to start the survey, the research proposal was reviewed and recommended by the institutional review board (IRB). Preliminarily 500 PCOS women were selected for interview and a comprehensive data sheet/ questionnaire was also filled in under the supervision of a gynecologist. The questionnaire comprised four sections, socio-demographic, medical and reproductive history, metabolic syndrome and health related quality of life sections.

Participants Criteria

Rotterdam criteria for PCOS were used for the selection of all women with pre-diagnosis of PCOS from marked hospitals in Faisalabad territory through multistage sampling. Briefly Rotterdam criteria are the combination of cyclic dysfunctions; oligomenorrhea or amenorrhea, hyperandrogenism and polycystic ovary morphology (PCOM) [>12 with 2-9mm diameter follicles in ovarian ultrasonographic image]. In the second tier of recruitment, PCOS women were further examined under WHO criteria for MetS [19]. Briefly, HDL <50 mg/dL, waist-to-hip ratio >0.85 and fasting blood glucose >110 mg/dL. Subsequently, four BMI categories, from all recruited PCOS women with MetS, were made, Normal weight group (BMI: 18-24 kg/m²), overweight group (BMI: 25-29 kg/m²), obese group (BMI: 30-34 kg/m²) and morbidly obese group (BMI: >35 kg/m²).

Physical and biochemical assessments

Socio-demographic and reproductive history sections of the questionnaire were completed through direct interview during the first tier of PCOS women's selection. However PCOM recordings from both ovaries were taken through ultrasonographic imaging machine. Gynecologists and trained nurses assisted for Physical examination and the recording of modified Ferriman Gallways (F-G) hirsutism score, blood pressure, BMI and waist & hip circumferences and ratio were taken as routinely practiced and recommended in reports [20]. Whereas, a phlebotomist assisted to determine blood pressure and to draw blood for further biochemical analyses including fasting blood sugar, lipid (LDL, HDL, total cholesterol and triglycerides in mg/dL) and hormone (LH and FSH) profiles, under pathology lab optimized protocols.

Health related quality of life: SF-36

After the second tier of PCOS women's recruitment on MetS profile, 323 randomly requested women responded to the HRQoL SF36 questionnaire. This short form-36 (SF-36) comprised of physical and psychological domains scoring the eight aspects of quality of life including physical function, role limitation due to physical function, role limitation due to emotional problem, energy/fatigue, emotional function, social function, pain and general health perception.

Numerical analyses

All grouped data sets were statistically analyzed employing one way analysis of variance (ANOVA). Significance of difference, among and between the groups,

At first stage of simple modeling four constructs with un-recorded latent variables PCOS, MetS, SF36 physical domain and SF-36 psychological domain were developed separately and cronbach's reliability was also reckoned separately for four different BMI groups (18-24, 25-29, 30-34 & >35 kg/m²). These models were assessed under variances and maximum likelihood estimates for intricate structural equation modeling (SEM), while each complex model of the four BMI groups was also assessed for appropriateness through confirmatory factor analyses (CFA) and goodness of model fit indices. Discriminatory and convergent validity were also ensued for each construct to confirm that data used for each construct accommodate it well and separate from other construct. A set of goodness of fit statistics including CMIN, baseline comparisons GFI, normed fit index (NFI) and comparative fit index (CFI) were also estimated for each model from all BMI groups. Among these statistics, appropriateness of data accommodation of each model was ascertained by a complete picture of covariance in NFI and CFI indices, while model fitness and appropriateness was made through Parsimonious NIF (PNIF), parsimonious CFI (PCFI) and root mean square error of approximation (RMSEA). This RMSEA estimated for each raised model indeed scaffolds on error of approximations in study population. It emphasizes on how the proposed model fit the covariance matrix of population. All statistics were carried out using SPSS version 23 while AMOS 24 was used to establish SEM in the current study.

Results

PCOS, MetS and SF36 parameter recordings from four BMI groups (18-24, 25-29, 30-34 & >35 kg/m²) were statistically analyzed employing multifactorial analysis and resulted appreciably ($P < 0.001$) different (Table 1). Mean ovarian volume (ml), cycle duration (days) and Ferriman- Gallways scores were significantly ($P < 0.05$) increased in morbidly obese PCOS women compared to women with other BMI levels, normal weight, overweight and morbidly obese, while mean fasting blood glucose (mg/dL), LDL (mg/dL), waist to hip ratio, both systolic and diastolic blood pressures (mmHg) were also examined significantly ($P < 0.05$) high among morbidly obese PCOS women compared to other PCOS women. Both obese and morbidly obese PCOS women were found more affected from their metabolic dysfunctions when their physical domain of HRQoL was surveyed and compared to normal weight and overweight PCOS women. Whereas, these both type of PCOS women had non-significant ($P > 0.05$) lower scores of all variables from psychological domain than the other PCOS women.

Model fit indices of four constructs including PCOS, MetS, SF-36 physical and psychological domains were estimated for PCOS women from normal weight, overweight, obese and morbidly obese groups are presented in table 2 and 3. Four of five tabulated goodness of fit indices were confirming the appropriateness of the constructs. While standardized regression coefficient were also estimated for all loading factors separately in each preliminary construct and presented in table 3. In latent variable PCOS, increased right ovary volume (ml) remarkably ($P < 0.05$) impacted the latent variable of all BMI groups. Moreover the drop in the number of reproductive cycles per year was reciprocally influencing the latent variable from all groups, normal weight ($\beta = -0.208$, $P < 0.05$), overweight ($\beta = -0.275$, $P < 0.05$), obese ($\beta = -0.045$, $P > 0.05$) and morbidly obese ($\beta = -0.253$, $P > 0.05$) PCOS women. Interestingly, however, increase in F-G score loading factor was negatively influencing the latent variable from obese and morbidly obese women while overweight women's

F-G score was very parallel to the latent variable. In MetS latent variable, elevated diastolic pressures (mmHg) and BMI (kg/m²) among overweight ($\beta = 0.561$, $P < 0.05$ and $\beta = 0.895$, $P > 0.05$ respectively) and morbidly obese ($\beta = 0.894$, $P < 0.05$ and $\beta = 0.475$, $P < 0.05$ respectively) women were appreciably parallel with latent variable. While, increase in pain loading factor positively contributed to SF-36 physical domains latent variables of overweight ($\beta = 0.819$, $P < 0.05$) and morbidly obese women ($\beta = 0.768$, $P > 0.05$). Whereas fall in the score of role limitation due to emotional problem and emotional functions loading factors among morbidly obese women hit reciprocally ($\beta = -0.300$, $P > 0.05$ and $\beta = -0.037$, $P > 0.05$ respectively) to the SF-36 psychological latent variable. The convergent validities of CFA including average variance extracted

(AVE) and composite reliability (CR) for all constructs were though not closed to the set criteria (Table4) however discriminant validities were strongly ascertained that each construct was built with suitable variables since the correlation coefficient values estimated for each pair of correlating latent variables were not greater than the difference between two estimated AVE (Supplementary table 1). While model fit statistics of correlation constructs established for each group were also stood appropriate on six indices which were according to required criteria.

Table 5 shows direct, though non-significant, effects between two latent variable constructs but the rationality of the hypothesis was ascertained. Such as PCOS women with normal weights showed an alternate association between MetS & PCOS, MetS&SF-36 physical and psychological domains, while a negative impact of PCOS on SF-36 physical domain was appreciable ($P=0.05$). Among morbidly obese PCOS women a highly appreciable ($P=0.042$) inverse relation was examined between latent variable PCOS and SF-36 physical domain, while overweight and morbidly obese PCOS women groups showed a remarkable ($P=0.003$, $P=0.001$ respectively) positive influence of MetS on PCOS latent variables. PCOS women from all BMI groups (18-24, 25-29, 30-34 & >35 kg/m²) had a positive association between SF-36 physical and psychological domains, whereas goodness of fit indices and chi-square results of all groups were ascertaining the association between theory and model (**Table 5**).

However, indirect effects of latent constructs were also depicting the rationality but significance was compromised (**supplementary table 2**). Among morbidly obese women, MetS was inversely impacted on physical and psychological domains of HRQoL through intermediary drift of PCOS. Similar physical domain.

Four intricate model diagrams using all latent variables were developed for all PCOS women with their BMI groups (Figure 1 A-D). Exogenous variables, defining each latent variable, were estimated with their exact effects by factor loading strength and error variance while a model modification opportunity was also applied where it was inevitable. All models, representing the four groups; normal weight, overweight, obese and morbidly obese, with their model fit statistics, were very according to hypothesis, MetS and PCOS had positive association. Whereas, MetS and PCOS had negative impact on physical and psychological scores. Moreover both of these HRQoL domains had a parallel association. All these latent variables had a progressive increment with increase in BMI of obese and morbidly obese PCOS women.

Discussion

Results of current study ascertained the synergistic exacerbated influence of PCOS and Metabolic syndrome endocrinopathy on physical and psychological domains of HRQoL in overweight, obese and morbidly obese PCOS women. Whereas the morbidly obese women were more susceptible to both syndromes and consequently challenged the physical and psychological satisfaction.

Most of disease-based epidemiological research, like current study, unveiled the adverse effects of abnormal BMI on body functions [21]. These adverse impacts were due to the abnormal accumulation of fat in body which is explained by WHO in terms of obesity [22].

A Meta-analysis lately also implicated the time-dependent progressive trajectory in obesity among men and women through BMI fluctuations [23]. While among PCOS women, an anovulatory condition is found more complicated with BMI change [24] however, MetS features were associated with hyperandrogenism [25] despite of age related marked decline in ovarian steroidogenic capacity [26]. The SEM construct of the present study especially for overweight and morbid obese PCOS women revealed the linear progressive influence of MetS on PCOS manifestations. These findings supported the molecular role of adiponectin in ovarian dysfunctions and inflammatory impacts as reviewed by Sartori et al [27].

In 2012, the consensus of an ESHRE/ASRM workshop also indicated the requirement of research on PCOS among adolescents to expose their ovarian and cyclic dysfunctions and impacts on their quality of life [2]. Insulin resistance (IR) among obese individuals not only flared up the obesity and adipokines but also likely provides a potential reason of cardiovascular risks, diabetes, reproductive dysfunctions and physical and psychological impairments [28]. High insulin and BMI was also evidenced in all PCOS women either with common MetS or individual components of MetS [29]. A very recent fact sheet about overweight and obesity by the WHO also documented the adverse effects of overweight and obesity among both genders while an impairment of body functions was comprehensively found under the influences of an abnormal BMI [30]. Moreover an anti-fat attitude or health care discrimination for obese or morbidly obese subjects made them reluctant to seek medical assistance [31] and contributed to mental distress. Several studies on obese subjects of both genders also equivocally reported a correlation between BMI and marred emotional quality of life [32]. In the current study, SEM constructs from overweight, obese and morbidly obese women were also showed the inverse consequences on the mental health when direct influence of MetS and PCOS on quality of life was examined. Similarly, a significant mutual parallel influence was noticed between physical impairment and mental distress in PCOS patients from overweight, obese and morbidly obese groups.

An association between hyperandrogenism and metabolic disturbances [33] has revealed the negative impact on quality of life [18] as in current study. Whereas a relationship between obesity and HRQoL was found fluctuate among sub-groups of population and prominently based on gender and age [34]. Asian Muslim women with PCOS migrated to Austria were faced greater psychological problems [35] while another study on PCOS women from Brazil reported the psychological distress positively associated with changes in appearance like obesity, acne and hirsutism [36]. Lately studies from Spain [37] and UK have shown the prominent concern about weight and infertility among PCOS women [38] and reflected the poor quality of life among PCOS women with overweight or obesity [30].

A direct and indirect association between MetS characteristics of PCOS women and their quality of life is still equivocal since manifestation of modifiers and mediators were likely uncontrolled, which made the association more confounding. Moreover varying high collinearity among confounding variables were also unlikely explained employing simple statistics. SEM was found more reliable as confirmatory and exploratory statistics tool to manage the intricate paradigm of causes and effects dealt in any hypothesis or theory. Results of a comprehensive SEM study on PCOS womens' psychological distress, self-esteem, body image and sexual dysfunction [39] were very similar to those of current study. However estimated regressions weights of PCOS pathways were unique. Moreover in SEM paradigms for all groups in this study, estimated mediating impact of PCOS and SF-36 physical domain was though non-significant but also showed the adverse intermediary effects of PCOS under influence of MetS on physical and psychological satisfaction of all types of women.

Conclusion

The results of the current study implicated the remarkable impact of MetS on the PCOS women from obese and morbidly obese groups that can contribute in increase of reproductive dysfunction and decrease in quality of life. It is more likely that effects of both syndromes are combined and their endocrinopathy affects the mental and physical satisfaction. Whereas SEM was found to be a more appropriate statistical approach to establish the confirmatory analysis for suggested pathway validation but exploratory statistics unveiled the new dimensions of any well-defined principal pathway of any disease.

Abbreviations

χ^2 =Chi-square

ASRM=American Society for Reproductive Medicine AVE=Average variances extract

BMI=Body mass index CFA=Confirmatory factor analysis CFI=Comparative fit index CMIN= Chi-square CR=Composite reliability

ESHRE= European Society of Human Reproduction and Embryology. F-G hirsutism score= Ferriman Gallwey score

FMIN= Minimum discrepancy function FSH=Follicle stimulating hormone GFI= Goodness of fit index HDL=High density lipoprotein HRQoL= Health related quality of life IR= Insulin resistance

IRB= Institutional review board

LDL=Low density lipoprotein

LH=Luteinizing hormone

MetS=Metabolic syndrome

NCP= Non-centrality parameter

NFI= Normed fit index

PCFI=Parsimonious comparative fit index PCOS= Polycystic ovary syndrome PHY=SF-36 physical domain PNIF=Parsimonious normed fit index PSY=SF-36 psychological domain

RMSEA=Root mean square error of approximation SEM=Structure equation modeling

SF-36= Short form-36

STROBE= Strengthening the reporting of observational studies in epidemiology WHO= World health organization

Declarations

Ethical Approval and Consent to participate

Prior to start the survey, research proposal entitled, "study the impacts if PCOS patients clinical manifestation on quality of life: A hospital trial in Faisalabad territory" for fulfillment of MPhil degree that later approved as dissertation title, was reviewed and recommended by the institutional review board (IRB). Hardcopy of the recommendation from committee will be provided on demand.

Consent for publication

In this study all adult women with PCOS were requested to participate in a survey after proper endorsed consent of confidentiality of personal information and possible use of scientific information for publication.

Competing interests

There is no any financial and non financial competing interests to declare from each author.

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Authors' contributions

1. First author, wrote the main manuscript text and carried out statistics used in this manuscript.

2. Second author Ehsan-ul-Haq was MPhil student who helped much in data collection and its sorting.

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Conflict of interest:

Author states that there is no conflict of interest.

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Tables

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Figures

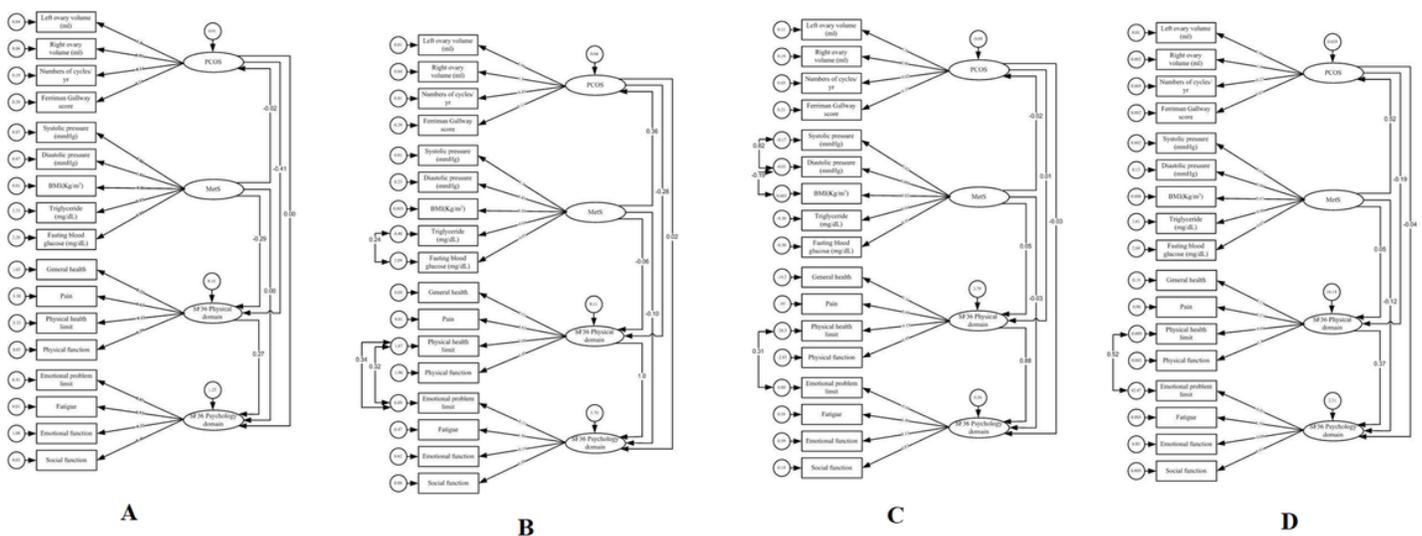


Figure 1

A paradigm of four constructs; polycystic ovary syndrome (PCOS), metabolic syndrome (MetS), SF-36 physical domain and SF-36 psychological domains developed for PCOS women from A) normal weight group (BMI: 18-24 kg/m²), B) overweight group (BMI: 25-29kg/m²), C) obese group (BMI: 30-34 kg/m²) and D) morbidly obese group (BMI: >35 kg/m²)using AMOS 24. Strong inverse impact of MetS was ensued with, mental and physical well-beingness while positive impact resulted in PCOS manifestation. Oval shapes are latent variable, rectangles are estimated variables connected with error variances in circles, and values on arrows are the factor loading.

Supplementary Files

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