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Original Research Article

The association of serum C-reactive protein albumin ratio with polycystic ovarian syndrome

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a common endocrine disorder among women, characterized by various symptoms and long-term risks. Reliable diagnostic methods are needed to predict and diagnose PCOS. This study aimed to assess the serum C reactive protein/albumin ratio as a potential predictor and diagnostic tool for PCOS.
Methods: This cross-sectional analytical study was conducted at the department of obstetrics and gynecology, Sir Salimullah Medical College and Mitford Hospital, Dhaka, from September 2018 to August 2019. The study included 80 participants aged 18 to 45 years, with 40 healthy subjects in group I and 40 diagnosed cases of PCOS in group II. Serum C-reactive protein and serum albumin levels were measured, and data were analyzed using descriptive statistics and Unpaired t-tests.
Results: The study group had a mean age of 23.98±2.61, while the comparison group had a mean age of 23.85±2.79. Serum CRP levels were significantly higher in newly diagnosed PCOS cases (5.73±3.35) compared to non-PCOS cases (2.89±0.85) ($p<0.001$). The study group had a significantly higher mean CRP: albumin ratio (0.123±0.07) compared to the comparison group (0.067±0.02) ($p<0.001$).
Conclusions: This study found that serum CRP and the CRP/albumin ratio were increased in PCOS subjects, while serum albumin levels did not differ significantly from non-PCOS subjects. These findings suggest that the serum CRP/albumin ratio could be a potential marker for predicting and diagnosing PCOS.

Keywords: PCOS, CRP, Albumin, Anovulation, Infertility

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders among women of reproductive age characterized by chronic anovulation and infertility, hyperandrogenism (HA), and long-term metabolic, cardiovascular, and neoplastic risks.[1,2] In a study among young women in India, the prevalence of PCOS was reported to be varying from 3% to 22%.[3] Another study among adolescents found the prevalence to be 9% to 36%.[4] Worldwide, PCOS is one of the most common causes of infertility due to anovulation. In a study conducted among 16700 patients in 8 fertility centers in Bangladesh PCOS and anovulation accounted for infertility among 37% of cases.[5] According to the National Institutes of Health, basic diagnostic criteria includes the presence of hyperandrogenism and chronic oligo or anovulation, with the exclusion of other causes of hyperandrogenism such as adult-onset congenital adrenal hyperplasia, hyperprolactinemia, and androgen-secreting neoplasms. Rotterdam consensus meeting in 2003 relied on the presence of any two: Menstrual disturbance;

hyperandrogenism, and ultrasound finding polycystic ovary. In 2006 the androgen excess society (AES) criteria were defined, which stated that diagnosis required the presence of hyperandrogenism, with the associated findings of either menstrual irregularity and/or PCOS.[6] Diagnosing PCOS in adolescence comes across another set of issues arising from the pubertal changes as many of the signs and symptoms of PCOS overlap with the normal changes that occur during puberty.[7] The European society of human reproduction and embryology/American society for reproductive medicine-sponsored PCOS consensus workshop held in Amsterdam recommended considering all 3 of the Rotterdam consensus and not just 2 of 3 to avoid overdiagnosis PCOS in adolescents.[2] Endocrine society (ES) clinical practice guideline for the diagnosis and treatment of PCOS and the guideline from the pediatric endocrine society (PES) further clarified the diagnosis criteria for the adolescent and stated that ultrasonography is a poor criterion for the detection of PCOS in adolescents as the Rotterdam ultrasound polycystic ovary criteria have not been validated for adolescents and the PCOM might be a feature of normal puberty that subsides with the onset of regular menstrual cycling.[8,9] Overall, polycystic ovarian morphology (PCOM), oligo-anovulation (OA), and HA are accepted diagnostic criteria for PCOS with variations based on the age group. Despite the presence of set criteria, wide variances of detection have been reported which might be arising from the difficulties in defining the polycystic ovarian morphology and clinical hyperandrogenism due to technical characteristics of ultrasound devices, ultrasound operator dependence, and the interobserver variability of scoring. To overcome the issues a range of biochemical parameters and hormonal levels have been tested to objectively detect the presence of PCOS. PCOS has been reported to be a proinflammatory condition and its low-grade chronic inflammation causes metabolic derangements and ovarian dysfunction. Visceral adipose tissue secretes inflammatory promoters like adipokines and vasoactive substances. These interfere with insulin action and also result in the overactivity of androgens and inflammation of ovaries in PCOS. Circulating C-reactive protein (CRP) is an acute phase protein secreted from the liver, which is stimulated by interleukin-6, originating from the adipose tissue, was considered to estimate the low-grade chronic inflammation in PCOS, and the level was found to be as high as 96% among the PCOS cases compared to the control.[10] In contrast, serum levels of albumin are reduced in individuals experiencing chronic inflammation. Serum albumin also binds with sex steroids and provides the majority of the total antioxidant capacity of normal plasma. The ratio of serum CRP levels over serum albumin (CRP/albumin) was found to be strongly associated with more severe metabolic dysfunction in premenopausal women with induced alterations to their ovarian hormone status.[11] So, this study aimed to determine the association of serum CRP/abumin ratio with PCOS in Bangladeshi females who are in the reproductive age.

Objectives

General objective study was to evaluate the association of serum CRP: albumin ratio with the polycystic ovarian syndrome.

Specific objectives of the study were to determine serum C-reactive protein and albumin levels in study subjects; to estimate the ratio of serum C-reactive protein to albumin in PCOS cases and control subjects; and to compare the C-reactive protein: albumin ratio in patients with PCOS and healthy subjects.

METHODS

This cross-sectional analytical study was conducted in the department of obstetrics and gynecology at Sir Salimullah Medical College andMitford Hospital, Dhaka from September 2018 to August 2019. A total of 80 cases aged 18 to 45 years were included, with 40 healthy subjects in group I and 40 diagnosed cases of PCOS in group II. Written informed consent was obtained from each participant or their authorized representative. Demographic information was collected through a questionnaire, and a detailed history, physical examination, and biochemical investigations were performed. Serum CRP and albumin levels were estimated at the Biochemistry department of BSMMU. The data were analyzed and expressed as percentages and mean±standard deviation (SD). Unpaired t-tests were used for between-group comparisons, with a significance level set at $p<0.05$. The statistical analysis was conducted using the statistical package for social sciences (SPSS). Confidentiality of all information was ensured, and ethical clearance for the study was obtained from the institutional review board of Sir Salimullah Medical College and Mitford Hospital, Dhaka. The inclusion criteria for the study group included newly diagnosed patients of PCOS aged 18 to 45 years, while the comparison group comprised age and BMI-matched healthy females. Participants were required to provide consent for participation. Exclusion criteria encompassed subjects with acute illness and infection, Cushing's syndrome, Cushing's disease, congenital adrenal hyperplasia, diabetes mellitus, hypertension, dyslipidemia, hyperthyroidism, hypothyroidism, cardiovascular disease, liver disease, renal failure, and those receiving hormonal or non-hormonal treatment for PCOS. Individuals who did not give consent were also excluded from the study.

RESULTS

The clinical parameters of the two-group matched by age and BMI. The mean age for the study group and comparison group was 23.98±2.61 and 23.85±2.79. The mean BMI was 27.16±3.49 and 27.1±3.53 for the study and comparison group. The mean systolic blood pressure of the study groups was significantly comparable ($p<0.05$).

Differences in mean diastolic blood pressure were not found to be significant (Table 1).

Table 1: General characteristics of the study population (N=80).

Parameter	Comparison group (n=40), mean±SD	Study group (n=40), mean±SD	P value
Age (year)	23.98±2.61	23.85±2.79	0.837
Height (cm)	153.73±6.41	154.24±6.47	0.72
Weight (kg)	63.38±10.32	63.55±10.45	0.94
BMI	27.16±3.49	27.1±3.53	0.94
WC (cm)	74.71±5.17	75.28±5.56	0.635
SBP (mm of Hg)	107.27±10.08	113.00±10.43	<0.05
DBP (mm of Hg)	76.06±6.09	77.00±6.48	0.529

BMI=body mass index; WC=waist circumference; SBP=systolic blood pressure; DBP=diastolic blood pressure

The majority of the health cases without PCOS (n=19, 47.5%) were from the low-income class. Compared to this newly diagnosed PCOS cases were mostly from solvent (n=12, 30%) and non-poor class (n=14, 35%) (Table 2).

Table 2: Socioeconomic profile of the study groups (N=80).

Socioeconomic status	Comparison group (n=40)		Study group (n=40)		Diff (x^2)
	n	%	n	%	
Low-income class	19	47.5	14	35.0	0.512
Non-poor class	12	30.0	14	35.0	
Solvent class	9	22.5	12	30.0	

Table 3: Serum CRP, albumin, and CRP: albumin ratio of the study population (N=80).

Parameter	Comparison group	Study group	Significance
	Mean±SD	Mean±SD	
Serum CRP (mg/dl)	2.89±0.85 (1.42-4.6)	5.73±3.35 (0.18-14.41)	<0.001
Serum albumin (g/l)	43.58±2.92 (38.00-50.00)	44.94±3.35 (38.00-53.00)	0.082
CRP: albumin	0.067±0.02 (0.03-0.11)	0.123±0.07 (0.00-0.31)	<0.001

P value reached from unpaired t-test

The mean values of serum CRP were significantly raised among the newly diagnosed PCOS cases (5.73±3.35) compared to the non-PCOS cases (2.890.85) (p≤0.001). Serum albumin was slightly increased (44.94±3.35 versus 43.58±2.92) and was not significant (p=0.080). The mean CRP: albumin ratio was also found to be significant (0.123±0.07 in the study group versus 0.067±0.02 in the comparison group) (p<0.001) (Table 3).

Distribution of serum CRP, serum albumin, and CRP: albumin ratio of the study population is given in Figure 1.

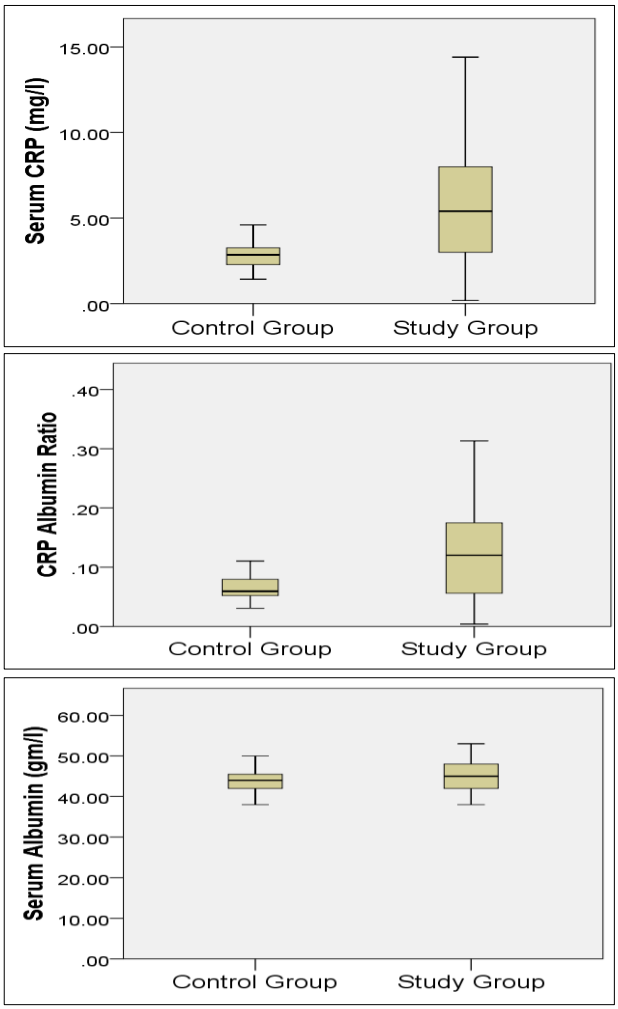

Figure 1: Box plots showing serum CRP, albumin and CRP: albumin ratio among two groups of study subjects (N=80).

DISCUSSION

The prevalence of PCOS in adolescents and young in our subcontinent has been reported as high as 22%. PCOS is commonly related to overweight, obesity, metabolic syndrome, dyslipidemia, and hypertension. Patients with PCOS have also reported suffering from diabetes, cardiovascular (CV) related morbidity, and mortality. Various studies have investigated the role of CRP in diagnosing PCOS as CRP also serves as one of the most sensitive predictors of CV morbidity and has shown to have a positive correlation with PCOS as a result of low-grade chronic inflammation. Recent studies also looked into CRP albumin and its correlation with PCOS and found it to have a stronger correlation in comparison to CRP alone. The ratio of serum CRP levels over serum albumin

(CRP/albumin) was found to be strongly associated with more severe metabolic dysfunction in premenopausal women with induced alterations to their ovarian hormone status.[11] In this study, the mean age of participants was 23.98±2.61 years in the comparison group and 23.85±2.79 years in the study group. It was proposed that women who are from high socio-economic status and have transitioned from one status to another might have experienced more peripubertal stress, a greater incidence of obesity, and early disruption in their menstrual cyclicity, and thus may contribute to this result. In this study mean serum CRP was found to be 2.89±0.85 in healthy patients while it was 5.73±3.35 in PCOS patients and the difference was significant ($p<0.05$) between the two groups. This is in favor of findings from previous related studies showing significantly higher CRP levels in PCOS patients compared to the control and non-PCOS cases.[10,12-14]

PCOS women are prone to ultimately suffer CVD when they get older. This enforces the claim to use CRP levels as a biomarker for PCOS. The differences in mean serum albumin between the two groups were also significant ($p<0.05$) in the present study (43.58±2.92 in the comparison group versus 44.94±3.35 in the study group). The mean CRP/albumin ratio between the two groups was also significant (0.067±0.02 in the comparison group versus 0.123±0.07 in the study group).

Changes in albumin are known to be associated with severe metabolic dysfunction in premenopausal women along with changes to their ovarian hormone status.[15] In this study mean CRP/albumin ratio was also found to be significant (0.123±0.07 in group 2 versus 0.067±0.02 in group I). One recent study has shown that CRP/albumin ratio is a more accurate and stronger correlate of PCOS compared with both free androgens and insulin resistance.[16] These investigators have found that the CRP/albumin ratio had a higher specificity and sensitivity for inflammation associated with metabolic dysfunction than insulin resistance and level of androgens.

Limitations

The study was conducted in a single hospital with a small sample size for a short duration. So, the results may not represent the whole community and the study was not able to longitudinally track and assess the biomarker in predicting PCOS and related morbidity. Moreover, this study excluded cases that increase the CRP and abumin levels, resulting in a skewed population sample, as these cases can also present as comorbid conditions of PCOS.

CONCLUSION

It can be concluded from the study that serum CRP and CRP/albumin ratio were significantly increased in PCOS subjects. However, serum albumin did not differ from those of non-PCOS subjects. Higher CRP: albumin ratio was associated with PCOS.

Recommendations

Ulticentric large-scale research is recommended including confounding factors to establish the power of association between serum CRP and serum CRP/albumin ratio as a biomarker of PCOS. Cost-effectiveness analysis is required to understand the role of CRP and the CRP/albumin ratio as a predictor or diagnostic marker of PCOS for the Bangladeshi population.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Boomsma CM, Eijkemans MJ, Hughes EG, Visser GH, Fauser BC, Macklon NS. A meta-analysis of pregnancy outcomes in women with polycystic ovary syndrome. Hum Reprod Update. 2006;12(6):673-83.
2. Fauser BC, Tarlatzis BC, Rebar RW, Legro RS, Balen AH, Lobo R, et al. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. Fertil Steril. 2012;97(1):28-38.
3. Gill H, Tiwari P, Dabadghao P. Prevalence of polycystic ovary syndrome in young women from North India: A Community-based study. Indian J Endocrinol Metab. 2012;16:S389.
4. Nidhi R, Padmalatha V, Nagarathna R, Amritanshu R. Prevalence of polycystic ovarian syndrome in Indian adolescents. J Pediatr Adolesc Gynecol. 2011;24:223-7.
5. Fatima P, Ishrat S, Rahman D, Banu J, Deeba F, Begum N, et al. Quality and quantity of infertility care in Bangladesh. Mymensingh Med J. 2015;24:70-3.
6. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. Positions statement: criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: an Androgen Excess Society guideline. J Clin Endocrinol Metab. 2006;91(11):4237-45.
7. Rosenfield RL. The diagnosis of polycystic ovary syndrome in adolescents. Pediatrics. 2015;136:1154-65.
8. Legro RS, Arslanian SA, Ehrmann DA, Hoeger KM, Murad MH, Pasquali R, et al. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2013;98(12):4565-92.
9. Witchel SF, Oberfield S, Rosenfield RL, Codner E, Bonny A, Ibáñez L, et al. The Diagnosis of Polycystic Ovary Syndrome during Adolescence. Horm Res Paediatr. 2015;1.
10. Escobar-Morreale HF, Luque-Ramírez M, González F. Circulating inflammatory markers in polycystic ovary syndrome: a systematic review and metaanalysis. Fertil Steril. 2011;95(3):1048-58.

11. Kalyan S, Patel MS, Kingwell E, Côté HCF, Liu D, Prior JC. Competing Factors Link to Bone Health in Polycystic Ovary Syndrome: Chronic Low-Grade Inflammation Takes a Toll. Sci Rep. 2017;7(1):3432.
12. Boulman N, Levy Y, Leiba R, Shachar S, Linn R, Zinder O, Blumenfeld Z. Increased C-reactive protein levels in the polycystic ovary syndrome: a marker of cardiovascular disease. J Clin Endocrinol Metab. 2004;89(5):2160-5.
13. Kelly CC, Lyall H, Petrie JR, Gould GW, Connell JM, Sattar N. Low grade chronic inflammation in women with polycystic ovarian syndrome. J Clin Endocrinol Metab. 2001;86(6):2453-5.
14. Spritzer PM, Lecke SB, Satler F, Morsch DM. Adipose tissue dysfunction, adipokines, and low-grade chronic inflammation in polycystic ovary syndrome. Reproduction. 2015;149(5):R219-27.
15. Kalyan S, Hitchcock CL, Sirrs S, Pudek M, Prior JC. Cardiovascular and metabolic effects of medroxyprogesterone acetate versus conjugated equine estrogen after premenopausal hysterectomy with bilateral ovariectomy. Pharmacotherapy. 2010;30(5):442-52.
16. Kalyan S, Goshtesabi A, Sarray S, Joannou A, Almawi WY. Assessing C reactive protein/albumin ratio as a new biomarker for polycystic ovary syndrome: a case-control study of women from Bahraini medical clinics. BMJ Open. 2018;8(10):e021860.

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