



Obstetrics & Gynaecology

A CASE CONTROL STUDY TO ASSESS C-REACTIVE PROTEIN/ALBUMIN RATIO IN WOMEN WITH AND WITHOUT POLYCYSTIC OVARIAN SYNDROME

Dr Aparna Priya	Department of Obstetrics and Gynaecology SMS Medical College, Jaipur
Dr Priyanka Meena	Assistant Professor, Department of Biochemistry, SMS Medical College, Jaipur
Dr Aakanksha Siwach	Department of Obstetrics And Gynaecology SMS Medical College, Jaipur
Dr Mohan Lal Meena*	Senior Professor and unit head, Department of Obstetrics And Gynaecology SMS Medical College, Jaipur.*Corresponding Author

ABSTRACT **A. AIM & OBJECTIVE:** To compare C-reactive protein/Albumin ratio in women with or without polycystic ovarian syndrome. **B. METHODOLOGY:** The present study is a hospital based comparative study conducted SMS Medical College, Jaipur Rajasthan. Total 168 subjects divided into two groups with case comprising of 84 subjects diagnosed on the basis of Rotterdam's criteria and 84 controls. The study aimed to find CRP/Albumin ratio in women with and without PCOS. **C. RESULT:** Mean CRP/albumin ratio was higher in PCOS cases (0.437 ± 0.222) as compared to controls (0.086 ± 0.112). A high AUC of 0.861 suggest that CRP is a good marker of PCOS ($p < 0.001$). At a cutoff value for CRP > 9.15 mg/dl, it identified PCOS with a sensitivity of 73.8% and specificity of 83.3%. The AUC for CRP/Albumin Ratio was higher (AUC=0.890), indicating that CRP/Albumin Ratio is a good marker of PCOS ($p < 0.001$). At a cutoff value for > 0.103 , CRP/Albumin Ratio identified PCOS with a sensitivity of 77.4% and specificity of 90.5%. **D. CONCLUSION:** CRP/albumin ratio, a marker for inflammation related to metabolic dysfunction, was found to have a stronger association with PCOS than either androgen excess or Insulin resistance. Inflammation is known to be influenced by adiposity, but relative to controls, women with PCOS have higher levels of CRP/albumin ratio irrespective of BMI. This supports the view that inflammation may play a central role in the pathophysiology of PCOS.

KEYWORDS : Polycystic Ovarian Syndrome (PCOS), C-Reactive Protein (CRP)

INTRODUCTION:

Polycystic Ovarian Syndrome (PCOS) is also referred to as hyperandrogenic anovulation (HA), or stein-Leventhal Syndrome is one of the most common endocrine system disorders that affect women in their reproductive age [1]. The Rotterdam 2003 criteria defines PCOS as incidence of any two of the three key criteria, namely, Oligoovulation and/or anovulation, excess androgen activity and polycystic ovaries (PCO) [1,2]. The most common symptoms of PCOS can range from menstrual disorders, infertility, hyperandrogenemia to metabolic syndrome [3]. Elevated insulin levels due to IR may lead to development of PCOS by contributing to the underlying abnormalities seen in the hypothalamic-pituitary ovarian axis. Elevated C-reactive protein (CRP) levels inflammatory cytokines (such as interleukin-6 and interleukin-18), and increased leucocyte count indicate on low-grade chronic inflammation in PCOS [4]. A high CRP level indicates increased risk for cardiovascular risk and is associated with metabolic disorder associated with obesity and insulin resistance [5]. Albumin is markedly reduced in women with PCOS due to being a negative acute phase protein. Reduced albumin levels can potentially contribute to higher free androgens in women with PCOS and exacerbation of disease phenotype [6].

AIM & OBJECTIVE:

To compare C-reactive protein/Albumin in women with or without polycystic ovarian syndrome.

METHODOLOGY:

All eligible women fulfilling inclusion criteria will be explained about nature and purpose of the study. After taking their informed written consent, detail history general and systemic examination will be done. Detail investigations will be done for all patients. All information and reports will be recorded on a pre-designed pro-forma and will be entered in Microsoft Excel Sheet to prepare master chart.

The present study is a hospital based comparative study conducted SMS Medical College, Jaipur Rajasthan over a duration of 1 year. Total 168 subjects divided into two groups with case comprising of 84 subjects diagnosed on the basis of Rotterdam's criteria and 84 controls. Diabetes mellitus hyperprolactinemia active thyroid disease, women on antihypertensive drugs and those who take OCP's were excluded from the study. The aim was to find CRP/Albumin ratio in women with and without PCOS.

HORMONAL ANALYSIS:

Peripheral venous fasting blood samples will be obtained following an overnight (more than 12 hour) fast during early follicular phase of the menstrual cycle (day 2+/-5) for control women and women with Polycystic Ovarian Syndrome who did not present with menstrual irregularities, or any day for women with Polycystic Ovarian Syndrome with menstrual irregularity. Serum luteinizing hormone (LH), follicular-stimulating hormone (FSH), thyroid-stimulating hormone (TSH), testosterone, glucose and insulin were measured by automated chemiluminescence immunoassays. Free testosterone, Progesterone and oestradiol serum levels were quantitated by radioimmunoassay. Concentrations of serum albumin were analysed by photospectrometry with albumin bromocresol purple assay on a COBAS c701. Measurement of plasma high-sensitivity CRP levels was done by latex-enhanced nephelometry on a BN II Nephelometer. Serial serum dilutions were made in measuring high CRP (>30 mg/L) levels. Percentile CRP values were estimated for comparison purposes.

STATISTICAL ANALYSIS:

All data will be analyzed using SPSS version 17.0 (SPSS Inc.). The Student's t-test and the Mann-Whitney U test will be used for the statistical analysis as appropriate. The AUC Graph will be used for analysis of C-Reactive protein/Albumin ratio in women with polycystic ovarian syndrome and P Value less than 0.05 will be considered statistically significant for all analysis.

RESULT:

The present study is a hospital based comparative study conducted in a total of 168 subjects divided into two groups with case comprising of 84 subjects diagnosed on the basis of Rotterdam's criteria and 84 controls. It was conducted in Gynecology OPD of Department of Obstetrics and Gynecology, SMS Medical College and Attached Hospitals, Jaipur, Rajasthan.

Table 1: Distribution of study subjects in relation to CRP: Albumin ratio

CRP : Albumin ratio	Case		Control		Total	
	N	%	N	%	N	%
Ratio >0.103	65	77.4	08	9.5	73	43.4
Ratio <0.103	19	22.6	76	90.5	95	56.6

Total	84	100	84	100	168	100
Chi-square = 75.969 with 1 degree of freedom; P < 0.001 (S)						

True positive – 65 False positive - 08

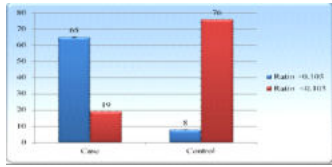


Figure 2: Distribution of study subjects in relation to CRP: Albumin ratio

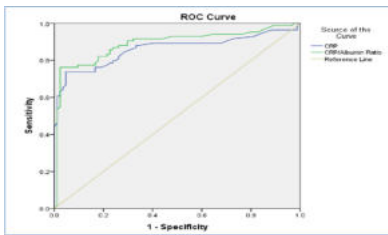
Mean CRP/albumin ratio was higher in PCOS cases (0.437 ± 0.222) as compared to controls (0.086 ± 0.112), this difference was found to be statistically significant ($p < 0.001$).

Table 3: ROC Curve for CRP and CRP: Albumin Ratio for identifying PCOS

	CRP	CRP : Albumin Ratio
AUC (95% CI)	0.861 (0.800 – 0.922)	0.890 (0.836 - 0.944)
P value	<0.001 (S)	<0.001 (S)
Critical cutoff	9.15	0.103
Sensitivity	73.8%	77.4%
Specificity	83.3%	90.5%

A high AUC of 0.861 indicates that CRP is a good marker of PCOS ($p < 0.001$). At a cutoff value for CRP > 9.15 mg/dl, it identified PCOS with a sensitivity of 73.8% and specificity of 83.3%.

The AUC for CRP: Albumin Ratio was higher (AUC=0.890), indicating that CRP : Albumin Ratio is a good marker of PCOS ($p < 0.001$). At a cutoff value for > 0.103, CRP: Albumin Ratio identified PCOS with a sensitivity of 77.4% and specificity of 90.5%.



DISCUSSION:

Mean Albumin level was lower in PCOS cases (26.85 ± 10.03 g/dL) as compared to controls 46.84 ± 7.67 g/dL), this difference was found to be statistically significant ($p < 0.001$). Mean CRP/albumin ratio was higher in PCOS cases (0.437 ± 0.222) as compared to controls (0.086 ± 0.112), this difference was found to be statistically significant ($p < 0.001$). A high AUC of 0.861 indicates that CRP is a good marker of PCOS ($p < 0.001$). At a cutoff value for CRP > 9.15 mg/dl it identified PCOS with a sensitivity of 73.8% and specificity of 83.3%. The AUC for CRP: Albumin Ratio was higher (AUC=0.890), indicating that CRP: Albumin Ratio is a good marker of PCOS ($p < 0.001$). At a cutoff value for > 0.103, CRP: Albumin Ratio identified PCOS with a sensitivity of 77.4% and specificity of 90.5%. Shirin Kalyan et al [A] observed that Independent of body mass index (BMI), receiver operating characteristic curve for CRP/albumin ratio as a selective biomarker for PCOS was 0.865 (95% CI 0.824 to 0.905). CRP/albumin ratio, a marker for inflammation related to metabolic dysfunction, was found to have a stronger association with PCOS than either androgen excess or insulin resistance.

CONCLUSION:

CRP/albumin ratio, a marker for inflammation related to metabolic dysfunction, was found to have a stronger association with PCOS than either androgen excess or Insulin resistance. Inflammation is known to be influenced by adiposity, but relative to controls, women with PCOS have higher levels of CRP/albumin ratio irrespective of BMI. This supports the view that inflammation may play a central role in the pathophysiology of PCOS. PCOS patients often have increased BMI resulting in increased inflammatory markers. CRP/albumin ratio remains unaffected by the raised BMI and serves as a better and economical potential biomarker.

REFERENCES:

- 1) Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of the polycystic ovary syndrome in an unselected population. *J. Clin. Endocrinol. Metab.* 2004.
- 2) Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group: Revised 2003 consensus on diagnostic criteria and longterm health risks related to polycystic ovary syndrome. *Fertil. Steril.* 2004;81:19-25.
- 3) Teede H, Deeks A, Moran L. Polycystic ovary syndrome: a complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan. *BMC. Med.* 2010; 8: 41
- 4) Hirschfield GM (June 2003). "C-reactive protein: a critical update". *The Journal of Clinical Investigation.* 111 (12):1805–12. doi:10.1172/JCI18921. PMC 161431. PMID 12813013
- 5) Koenig, Wolfgang (2006). "C-reactive protein - a critical cardiovascular risk marker". *CRPhealth.com*.
- 6) Kalyan S, Patel MS, Kingwell E, et al.. Competing factors link to bone health in polycystic ovary syndrome: Chronic low-grade inflammation takes a toll. *Sci Rep* 2017;7:3432 10.1038/s41598-017-03685-x [PMC free article] [PubMed] [CrossRef] [Google Scholar].