ORIGINAL RESEARCH

Assessment of serum copeptin as a biomarker of polycystic ovarian syndrome and its correlation with metabolic syndrome components

[1]Satya Kumari, [2]Pratibha Kumari, [3]Sangeeta Pankaj

[1,2]Senior Resident, [3]Professor and Head, Department of Gynecological Oncology, IGIMS, Patna, Bihar, India

Corresponding Author
Pratibha Kumari
Senior Resident, Department of Gynecological Oncology, IGIMS, Patna, Bihar, India

Received Date: 21 May, 2022 Accepted Date: 18 June, 2022

ABSTRACT

Background: Copeptin is a useful and practical surrogate marker for AVP in clinical settings since it is co-secreted in equimolar amounts with AVP, the stable and physiologically inactive C-terminal part of pro-vasopressin. The present study was conducted to assess serum copeptin as a biomarker of polycystic ovarian syndrome and its correlation with metabolic syndrome components. **Materials & Methods:** The present study was conducted at Department of Gynae Oncology, IGIMS, Patna, Bihar, India during January 2019 to December 2021. 50 patients of polycystic ovarian syndrome of both genderswere divided into two groups: Group I subjects with PCOS having metabolic syndrome, and group II subjects with PCOS but not having metabolic syndrome. Serum insulin, total cholesterol, high- density lipoprotein cholesterol (HDL-C), and triglycerides (TG), low- density lipoprotein cholesterol (LDL-C) and Homeostasis Model Assessment Insulin Resistance Index (HOMA-IR)were measured. **Results:** In group I and group II, the mean BMI (kg/m2) was 31.4 and 23.7, waist HIP ratio was 0.89 and 0.81, serum copeptin (ng/mL) was 7.5 and 8.4, SBP (mmHg) was 123.5 and 112.6, DBP (mmHg) was 84.5 and 74.2, fasting plasma glucose (mg/dL) was 95.4 and 91.3, fasting serum insulin (uIU/mL) was 24.6 and 91.0, HOMA- IR was 5.6 and 2.6, total cholesterol (mg/dL) was 192.6 and 170.5, triglycerides (TG) (mg/dL) was 165.2 and 122.8, HDL-cholesterol (mg/dL) was 44.7 and 53.1 and LDL-cholesterol (mg/dL) was 125.2 and 102.8 respectively. The difference was significant (P< 0.05). Serum copeptin levels showed a significant correlation with fasting serum insulin (p=0.006) and HOMA-IR (p=0.012). There was a significant negative moderate correlation between serum copeptin and serum insulin levels, and between serum copeptin and HOMA-IR. **Conclusion:** Copeptin measures in plasma have very low sensitivity, hence the serum copeptin cannot be utilized as an independent diagnostic for the diagnosis of metabolic syndrome in PCOS patients.

Keywords: Copeptin, diabetes, metabolic syndrome

INTRODUCTION

Recent studies have connected the onset of type 2 diabetes, metabolic syndrome, chronic renal diseases, and cardiovascular ailments to elevated plasma concentrations of arginine vasopressin (AVP).[1] Nevertheless, AVP's limited therapeutic usefulness as a biomarker is due to its small size, poor stability, and short half-life in plasma (16–20 minutes). These factors also make direct testing difficult.[2] Copeptin is a useful and practical surrogate marker for AVP in clinical settings since it is co-secreted in equimolar amounts with AVP, the stable and physiologically inactive C-terminal part of pro-vasopressin. In healthy adults, the concentration of copeptin plasma ranges from 1 to 13.8 pmol/L, with an average of 4.2 pmol/L. The concentration of copeptin varies significantly between genders, with lower values in females.[3]

There has been an increase in interest lately in the function of the AVP system in regulating human metabolic homeostasis.[4] Elevated levels of circulating plasma copeptin have been associated with multiple metabolic syndrome components, such as dyslipidemia, insulin resistance, glucose intolerance, hyper-insulinemia, hypertension, and abdominal obesity. In a population-based investigation with a mixed ethnic group, Enhorning S et al.[5] demonstrated a substantial correlation between elevated copeptin and a greater frequency of Non-Alcoholic Fatty Liver Disease (NAFLD). Additionally, copeptin had a positive link with elevated BMI, vasopressin, just like

AVP and neurophysin II. Copeptin is considered a reliable and practical clinical surrogate for AVP in conditions affecting the body's fluid equilibrium. Copeptin and AVP levels have been discovered to strongly positively correlate in both healthy individuals and patients with various cardiovascular diseases.[6]The present study was conducted to assess serum copeptin as a biomarker of polycystic ovarian syndrome and its correlation with metabolic syndrome components.

MATERIALS & METHODS

The present study was conducted at Department of Gynae Oncology, IGIMS, Patna, Bihar, India during January 2019 to December 2021. The present study was conducted on 50 patients of polycystic ovarian syndrome of both genders. All were informed regarding the study and their written consent was obtained.

Data such as name, age, gender etc. was recorded. Patients were divided into two groups: Group I subjects with PCOS having metabolic syndrome, and group II subjects with PCOS but not having metabolic syndrome. Blood samples for serum copeptin were taken under aseptic precautions, and levels were analysed using a commercially available Enzyme-Linked Immunosorbent Assay (ELISA) kit. The copeptin ELISA kit had an assay range of 0-100 pmol/L and results were expressed in ng/mL. Serum insulin levels were measured using specific Electro-chemiluminescence immunoassays. Levels of total cholesterol, High-Density Lipoprotein Cholesterol (HDL-C), and Triglycerides (TG) were determined with enzymatic colorimetric assays by spectrophotometry. Low-Density Lipoprotein Cholesterol (LDL-C) was calculated using the Friedewald formula. Insulin resistance was calculated using the Homeostasis Model Assessment Insulin Resistance Index (HOMA-IR).Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table I Comparison of parameters

Parameters	Group I	Group II	P value
BMI (kg/m2	31.4	23.7	0.02
Waist HIP Ratio	0.89	0.81	0.05
Serum copeptin (ng/mL)	7.5	8.4	0.01
SBP (mmHg)	123.5	112.6	0.05
DBP (mmHg)	84.5	74.2	0.05
Fasting plasma glucose (mg/dL	95.4	91.3	0.04
Fasting serum insulin (uIU/mL)	24.6	91.0	0.001
HOMA- IR	5.6	2.6	0.001
Total cholesterol (mg/dL)	192.6	170.5	0.03
Triglycerides (TG) (mg/dL)	165.2	122.8	0.05
HDL-cholesterol (mg/dL)	44.7	53.1	0.04
LDL-cholesterol (mg/dL)	125.2	102.8	0.05

Table I shows that in group Iand group II, the mean BMI (kg/m2) was 31.4 and 23.7, waist HIP ratio was 0.89 and 0.81, serum copeptin (ng/mL) was 7.5 and 8.4, SBP (mmHg) was 123.5 and 112.6, DBP (mmHg) was 84.5 and 74.2, fasting plasma glucose (mg/dL) was 95.4 and 91.3, fasting serum insulin (uIU/mL) was 24.6 and 91.0, HOMA- IR was 5.6 and 2.6, total cholesterol (mg/dL) was 192.6 and 170.5, triglycerides (TG) (mg/dL) was 165.2 and 122.8, HDL-cholesterol (mg/dL) was 44.7 and 53.1 and LDL-cholesterol (mg/dL) was 125.2 and 102.8 respectively. The difference was significant (P< 0.05).

Graph I Comparison of parameters

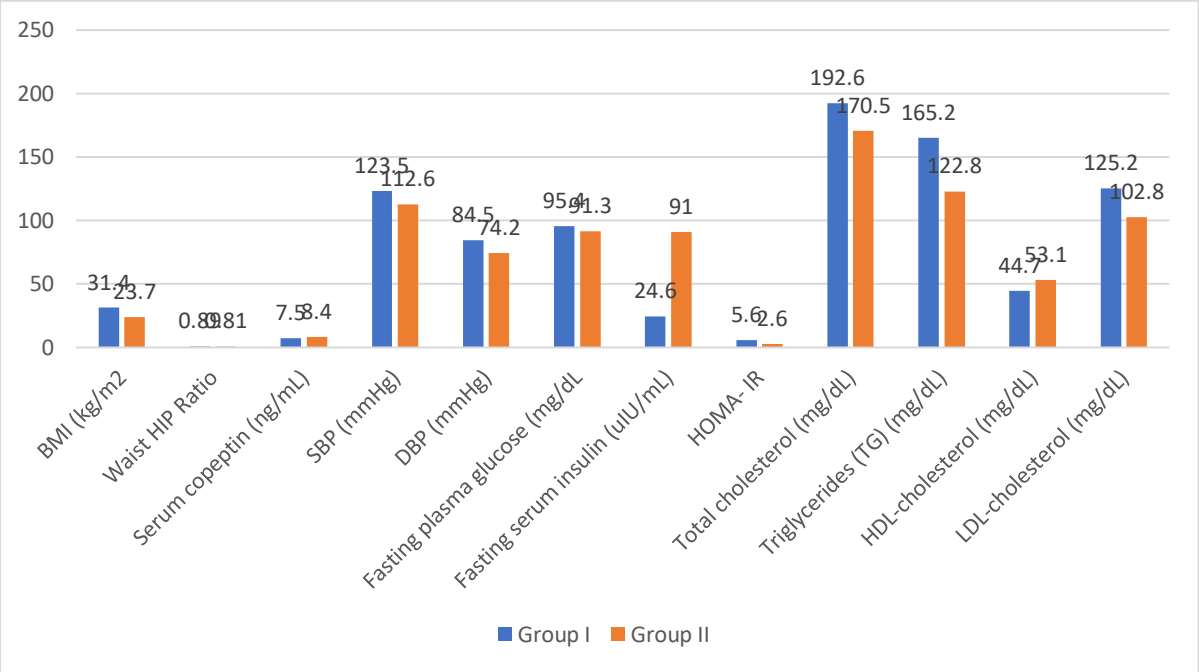

Table II Assessment ofCorrelation of serum copeptin level with metabolic syndrome components in women with PCOS

Parameters	Serum copeptin	
	R value	P value
Copeptin- BMI (kg/m2)	-0.2	0.73
Copeptin-Waist Hip Ratio	-0.13	0.15
Copeptin- SBP	-0.07	0.26
Copeptin- DBP	-0.17	0.49
Copeptin-fasting plasma glucose	-0.11	0.52
Copeptin-fasting serum insulin	-0.36	0.05
Copeptin- HOMA-IR	-0.34	0.03
Copeptin- serum total cholesterol	-0.26	0.02
Copeptin- serum Triglycerides (TG)	-0.08	0.82
Copeptin-serum HDL Cholesterol	-0.05	0.91
Copeptin-serum LDL Cholesterol	-0.07	0.84

Table II shows that serum copeptin levels showed a significant correlation with fasting serum insulin (p=0.006) and HOMA-IR (p=0.012). There was a significant negative moderate correlation between serum copeptin and serum insulin levels, and between serum copeptin and HOMA-IR.

DISCUSSION

Copeptin and the likelihood of high HOMAI-IR ≥2.5 are related, according to a case-control study involving women with PCOS. Serum copeptin levels have been reported to be raised in PCOS patients, especially those who are obese.[7] Additionally, there is a positive correlation between serum copeptin concentrations and cardiometabolic markers such total testosterone, HOMA-IR, WHR, BMI, and hirsutism score. This implies that copeptin could be useful in determining a patient's future cardiovascular risk if they have PCOS.[8]The present study was conducted to assess serum copeptin as a biomarker of polycystic ovarian syndrome and its correlation with metabolic syndrome components.

We found that in group I and group II, the mean BMI (kg/m2) was 31.4 and 23.7, waist HIP ratio was 0.89 and 0.81, serum copeptin (ng/mL) was 7.5 and 8.4, SBP (mmHg) was 123.5 and 112.6, DBP (mmHg) was 84.5 and 74.2, fasting plasma glucose (mg/dL) was 95.4 and 91.3, fasting serum insulin (uIU/mL) was 24.6 and 91.0, HOMA- IR was 5.6 and 2.6, total cholesterol (mg/dL) was 192.6 and 170.5, triglycerides (TG) (mg/dL) was 165.2 and 122.8, HDL-cholesterol (mg/dL) was 44.7 and 53.1 and LDL-cholesterol (mg/dL) was 125.2 and 102.8 respectively. Coelho et al[9]assessed the utility of copeptin as a diagnostic marker of PCOS and to evaluate the correlation of serum copeptin levels with metabolic syndrome components in women with PCOS. A total of 60 subjects with PCOS were selected through convenient sampling and divided into two groups: Group 1-subjects with PCOS having metabolic syndrome, and Group 2-subjects with

PCOS but not having metabolic syndrome. The mean age of the study participants was 24.24±4.721 years, ranging from 15 to 43 years. The mean age of patients with metabolic syndrome was 23.96±6.3 years, while those without metabolic syndrome was 24.40±3.52 years. The mean Body Mass Index (BMI) was 31.17±5.38 in those with metabolic syndrome and 23.2±4.7 in those without (p=0.0001). The Waistto-Hip Ratio (WHR) of Group 1 was significantly higher than Group 2 (p=0.001). The two groups did not differ significantly with regard to serum copeptin level, i.e., 7.386±4.58 in Group 1 and 8.66±6.03 in Group 2 (p=0.736). Serum copeptin levels showed a significant correlation with fasting serum insulin (0.006) and Homeostatic Model Assessment - Insulin Resistance (HOMA-IR) (0.012).

We found that serum copeptin levels showed a significant correlation with fasting serum insulin (p=0.006) and HOMA-IR (p=0.012). There was a significant negative moderate correlation between serum copeptin and serum insulin levels, and between serum copeptin and HOMA-IR. Aly et al[10]investigated the correlations between the serum levels of copeptin and obestatin, carotid artery intima-media thickness (CIMT), and brachial artery flow mediated dilatation (FMD) in obese and non-obese women with PCOS. They analyzed 54 patients with PCOS and 20 normal women as controls. PCOS patients were divided into two groups based on body mass index (BMI): obese group (BMI > 30 kg/m2, n = 28) and non-obese group (BMI < 30 kg/m2, n = 26). Serum Copeptin and Obestatin levels, Insulin Homeostasis Model Assessment for Insulin Resistance (HOMA-IR), CIMT and brachial artery FMD were determined and compared among both groups.Serum Obestatin levels were significantly lower in obese PCOS group than non-obese and control. While Serum Copeptin levels were significantly higher in obese PCOS group than non-obese and control. Brachial artery FMD was lower in the PCOS groups than control. Obestatin was positively correlated with cardiovascular risk factor (FMD), whereas Copeptin was negatively correlated with FMD.

The shortcoming of the study is small sample size.

CONCLUSION

Authors found that copeptin measures in plasma have very low sensitivity, hence the serum copeptin cannot be utilized as an independent diagnostic for the diagnosis of metabolic syndrome in PCOS patients.

REFERENCES

1. Carmina E, Napoli N, Longo RA, Rini GB, Lobo RA. Metabolic syndrome in polycystic ovary syndrome (PCOS): Lower prevalence in southern Italy than in the USA and the influence of criteria for the diagnosis of PCOS. Eur J Endocrinol. 2006;154(1):141-45. Doi: 10.1530/eje.1.02058.
2. Norman RJ, Dewailly D, Legro RS, Hickey TE. Polycystic ovary syndrome. Lancet. 2007;370(9588):685-97.
3. Morgenthaler NG, Struck J, Jochberger S, Dünser MW. Copeptin: Clinical use of a new biomarker. Trends Endocrinol Metab. 2008;19(2):43-49.
4. Parizadeh SM, Ghandehari M, Parizadeh MR, Ferns GA, Ghayour-Mobarhan M, Avan A. The diagnostic and prognostic value of copeptin in cardiovascular disease, current status, and prospective. J Cell Biochem. 2018;119(10):7913- 23.
5. Enhörning S, Wang TJ, Nilsson PM, Almgren P, Hedblad B, Berglund G, et al. Plasma copeptin and the risk of diabetes mellitus. Circulation. 2010;121(19):2102-08.
6. Guelinckx I, Vecchio M, Perrier ET, Lemetais G. Fluid intake and vasopressin: Connecting the dots. Ann Nutr Metab. 2016;68 (Suppl 2):06-11.
7. Łukassyk E, Małyssko J. Copeptin: Pathophysiology and potential clinical impact. Adv Med Sci. 2015;60(2):335-41.
8. Szmygin H, Szydełko J, Matyjaszek-Matuszek B. Copeptin as a novel biomarker of cardiometabolic syndrome. Endokrynol Pol. 2021;72(5):566-71.
9. Jyotsna Mirabel Coelho, Prema D'Cunha, AR Shivashankara. Serum Copeptin as a Biomarker of Polycystic Ovarian Syndrome and its Correlation with Metabolic Syndrome Components: A Cross-sectional Analytical Study. Journal of Clinical and Diagnostic Research. 2024 Jul, Vol-18(7): QC01-QC04.
10. Aly AE, Elfeshawy MS, Elfatah AA, Saeed AM. Copeptin and obestatin levels in polycystic ovary women and their relation to obesity, insulin metabolism and cardiovascular diseases. Al-Ashar International Medical Journal. 2020;1(4):44-49