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Clinical Research Article

Serum Chemerin Levels Correlate With Severity of Dysglycemia in Young Adult Women With Polycystic Ovary Syndrome

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Abstract

Context: A subset of polycystic ovary syndrome (PCOS) individuals also have type 2 diabetes (T2D); an unmet need to identify this subgroup exists.

Objective: We looked at the potential role of serum chemerin, a proinflammatory adipokine, in identifying dysglycemic PCOS.

Methods: A total of 93 PCOS and 33 healthy controls were classified, based on fasting and 2-hour plasma glucose levels (2hPGPG) and glycated hemoglobin A_{1c} (HbA_{1c}) (%) into normoglycemic (n = 34), dysglycemic (n = 33), and T2D (n = 26). Serum chemerin were measured by enzyme-linked immunosorbent assay. Homeostatic model 2 assessment of insulin resistance (HOMA-2IR) and homeostatic model 2 assessment of β-cell function (HOMA-2β) were computed using serum C-peptide.

Results: Metabolic syndrome was present in 9.7% (National Cholesterol Education Program) of PCOS. Waist circumference, body fat (%), 2hPGPG, and HbA_{1c} levels were significantly higher in T2D group. Serum triglycerides/high-density lipoprotein cholesterol (TGs/HDL-c) ratio was increased in PCOS individuals with T2D; no significant changes in total cholesterol and LDL-c levels were seen. Serum chemerin levels were significantly higher ($P < .001$) in the PCOS group. Total body fat (%), 2hPGPG, HbA_{1c}, and TG/HDL-c ratio correlated positively with chemerin levels. Serum chemerin levels correlated positively with HOMA2IR and negatively with HOMA-2β. On receiver operating characteristic curve analysis, a serum chemerin cutoff level of greater than 309.3 ng/mL differentiated PCOS individuals with dysglycemia from those without (sensitivity 85.71%, specificity 89.47%). The Cohen kappa test revealed a substantial agreement ($P < .001$) between chemerin cutoff and 2hPGPG levels greater than 200 mg/dL. The present study is arguably the first ever to define a serum chemerin cutoff to distinguish PCOS individuals with T2D from those without.

Conclusion: Elevated serum chemerin levels reliably identify PCOS individuals with dysglycemia. Further, longitudinal studies with larger samples are required to confirm this association.

Key Words: PCOS, chemerin, type 2 diabetes

Abbreviations: 2hPGPG, 2-hour post glucose plasma glucose level; AUC, area under the curve; BMI, body mass index; ELISA, enzyme-linked immunosorbent assay; FG Score, Ferriman-Gallwey Score; FPG, fasting plasma glucose; HbA_{1c}, glycated hemoglobin A_{1c}; HDL, high-density lipoprotein; HOMA-2IR, homeostatic model 2 assessment of insulin resistance; HOMA-2β, homeostatic model 2 assessment of β-cell function; IGT, impaired glucose tolerance; IL-1β, interleukin-1β; IR, insulin resistance; LDL, low-density lipoprotein; MetS, metabolic syndrome; NGT, normal glucose tolerance; PCOS, polycystic ovary syndrome; ROC, receiver operating characteristic; T2D, type 2 diabetes; TC, total cholesterol; TGs, triglycerides; TNF-α, tumor necrosis factor α.

Polycystic ovary syndrome (PCOS), is a common endometabolic disorder of women of reproductive age, and is characterized by ovulatory dysfunction, menstrual irregularities, and clinical and/or biochemical hyperandrogenism, with a worldwide prevalence ranging from 10-15% [1, 2]. PCOS is also termed the *ovarian manifestation of metabolic syndrome* (MetS) [2] and gives rise to type 2 diabetes mellitus (T2D) [3-5] in around 25% of cases [6]. PCOS and T2D share insulin resistance (IR) as the common denominator [5, 7-9]. However, there is no reliable biomarker available to distinguish PCOS individuals having prediabetes and T2D from individuals without.

Adipose Tissue Secretes Many Adipokines That, Through Paracrine and Endocrine Effects, Regulate Systemic Insulin Resistance.

Chemerin, a proinflammatory adipokine, is a critical regulator of adipogenesis, glucose homeostasis, food intake, and body weight [10, 11]. Increased chemerin messenger RNA

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expression has been reported in adipocyte cell lines as well as in adipose tissue isolated from diabetic animal models [12-15]. In vivo and in vitro studies on the effects of chemerin on glucose metabolism have yielded contradicting results. However, in humans, circulating chemerin concentration shows a consistently positive association with the components of MetS [12, 16-19]. Recently, elevated chemerin levels have also been reported in obese or lean PCOS women [12, 16-19]. However, whether circulating chemerin levels discriminate PCOS individuals with dysglycemia from those without is unknown. In this study, we compared serum chemerin levels along the glycemic spectrum of PCOS individuals. We also looked at the correlation of chemerin level with IR and pancreatic β-cell dysfunction.

Materials and Methods

Study Participants

Ninety-three participants fulfilling the inclusion/exclusion criteria as per Rotterdam Criteria, 2003(Supplementary Fig. S1) [20] were recruited from outpatient services. Written informed consent was obtained from each patient in their own vernacular. Sample size was calculated (33 each group) using the method as referred by Sami et al in 2013, anticipating the prevalence of PCOS is 10% and T2D is 8% [21-23]. Power of the study was calculated using G* Power software.

Studies were approved by the institutional ethics committee of the IPGME & R and SSKM Hospital, Kolkata, India (letter No. IPGME&R/IEC/2018/046) in accordance with the code of ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

Blood Collection and Processing of Samples:

A fast of 10 to 12 hours was recommended to the study participants before blood samples were collected. A total sample of 6 mL of venous blood was then collected in clot vials. The study participants were then asked to drink 75-g anhydrous glucose, dissolved in 300 mL of water over 5 minutes. Plasma glucose level was estimated in blood samples drawn 2 hours from the beginning of the glucose drink. For the estimation of glycated hemoglobin A_{1c} (HbA_{1c}) (%), a 50-µL whole-blood sample was used. To separate serum and cellular components in the remaining blood samples, centrifuges were run at 825*g* for 10 minutes at 4 °C. Serum samples were collected in cryovials for further biochemical and molecular assays.

Serum glucose level was measured for both FPG (fasting plasma glucose) and 2-hour post glucose plasma glucose (2hPGPG) test by the colorimetric method using a commercially available kit. HbA_{1c} % was measured by high-performance liquid chromatography method (Bio-Rad, full-line automated HbA_{1c} testing systems). Fasting plasma lipid profile components—total cholesterol (TC), triglycerides (TGs), high-density lipoprotein cholesterol (HDL-c), and low-density lipoprotein cholesterol (LDL-c)—were estimated spectrophotometrically. Serum C-peptide levels were measured by enzyme-linked immunosorbent assay (ELISA) (catalog No. E0009Hu, Bioassay Technology Laboratory, RRID: AB_3083012). Homeostatic model 2 assessment of insulin resistance (HOMA-2IR) and homeostatic model 2 assessment of β-cell function (HOMA-2β) were calculated from the C-peptide values using HOMA calculator version 2.2.3 from the Radcliffe Department of Medicine, University of Oxford. Serum levels of chemerin (sensitivity 7.8 ng/mL, detection range: 31.2-2000 ng/mL), tumor necrosis factor α (TNF-α) (sensitivity 1.52 ng/L, detection range: 3-900 ng/L), and interleukin-1β (IL-1β) (sensitivity 10.07 pg/mL, detection range: 20-6000 pg/mL) were measured by ELISA using commercial kits (CusaBio for chemerin, RRID: AB_3083462 and BT, Bioassay, for TNF-α, RRID: AB_3083463 and IL-1β, RRID: AB_3083464) as per the manufacturers' protocol. Intra-assay precision of chemerin and TNF-α is coefficient of variation (CV) (%) less than 8% and interassay precision CV (%) less than 10.

Anthropometric measurements, that is, height, weight, body mass index (BMI), and waist circumference were captured for all participants. Body fat level of the participants was measured by the TANITA UM-075 bioelectrical impedance method.

Blood pressure (systolic and diastolic) were recorded in the left arm in sitting posture after 15 minutes rest for all participants with a manual aneroid instrument. An average of 3 readings were taken to arrive at the final value.

Statistical Analysis

To evaluate the normality of continuous variables, the D'Agostino and Pearson test were performed. Data were represented using mean ±SD. More than 2 normally distributed groups were compared by ordinary 1-way analysis of variance/Brown-Forsythe and Welch analysis of variance test, depending on the equal or different SD value, respectively. For nonnormally distributed groups, the Kruskal-Wallis test was used to compare. Unpaired *t* test was performed for comparison between 2 normally distributed groups and Mann-Whitney *U* test for nonnormally distributed groups. Depending on the distribution, the correlation between 2 variables was represented using the Pearson or Spearman correlation coefficient. Binary logistic regression was performed between PCOS (normal glucose tolerance [NGT]) and PCOS (impaired glucose tolerance [IGT]/T2D) to distinguish the contribution of serum chemerin as a predictor of dysglycemia in PCOS. An analysis of receiver operating characteristics (ROC) was performed to determine the area under the curve (AUC), the cutoff value, and the sensitivity and specificity of serum chemerin level for discriminating PCOS (T2D) individuals from PCOS (NGT) individuals. The Cohen kappa test was performed to identify the agreement between chemerin-detected T2D with 2hPGPG. A *P* value less than .05 was considered to be statistically significant. GraphPad Prism (version 9) and SPSS 26 (trial version) were used to perform statistical analyses.

Results

Of 93 PCOS individuals, 34 had NGT, 33 had IGT, and 26 had T2D (see Supplementary Fig S1) [20]. A family history of T2D was present in 41.8% (paternal: 20.4%, maternal: 13.1%, biparental: 8.1%). MetS (defined by National Cholesterol Education Program, 2004 criteria) was present in 9.7% of participants with PCOS but was absent in the control group, although 3 controls matched 2 out of 3 criteria. Waist circumference, body fat (%), 2hPGPG, and HbA_{1c} levels were significantly higher in the T2D group compared to those with IGT and NGT; no significant difference in BMI

Table 1. Characteristics of the study participants: measurement of anthropometric, metabolic parameters in control and polycystic ovary syndrome subgroups

Parameters	Control (n = −33)	PCOS (NGT) (n = 34)	PCOS (IGT) (n = 33)	PCOS (T2D) (n = 26)	*P*
BMI	24.90 ± 3.50	24.89 ± 4.28	24.24 ± 2.56	27.71 ± 5.91	.0681
Body fat, %	**31.67 ± 3.38**	**32.91 ± 6.42**	**33.06 ± 4.04**	**38.97 ± 4.46**	**.0008**
Waist circumference, cm	**83.16 ± 9.85**	**86.47 ± 8.85**	**83.98 ± 10.15**	**94.89 ± 11.68**	**.0028**
FPG, mg/dL	88.67 ± 10.59	89.13 ± 9.71	91.28 ± 10.64	96.95 ± 14.37	.0856
2hPGPG, mg/dL	**119.8 ± 15.63**	**115.8 ± 5.61**	**155.2 ± 19.52**	**270.3 ± 47.11**	**<.0001**
HbA_{1c}, % (mmol/mol)	**5.37 ± 0.22 (35 ± 2.4)**	**5.38 ± 0.33 (35 ± 3.6)**	**5.53 ± 0.54 (37 ± 5.9)**	**6.29 ± 0.91 (45 ± 9.9)**	**.0002**
Triglycerides, mg/dL	**117.2 ± 19.58**	**128.7 ± 25.50**	**133.1 ± 38.34**	**176.7 ± 60.53**	**.0023**
Cholesterol, mg/dL	152.2 ± 24.37	173.1 ± 41.27	163.6 ± 27.94	174.4 ± 42.92	.2332
LDL, mg/dL	79.94 ± 18.02	93.93 ± 28.87	96.33 ± 23.66	91.13 ± 33.89	.3317
HDL, mg/dL	**53.70 ± 7.14**	**45.64 ± 10.27**	**43.97 ± 8.78**	**43.54 ± 6.49**	**.0010**
TNF-α, ng/L	106.7 ± 25.68	92.84 ± 32.01	106.3 ± 31.11	125.8 ± 49.42	.2557
IL-1β, pg/L	**757.1 ± 115.6**	**721.6 ± 120.1**	**807.9 ± 187.3**	**881.4 ± 197.3**	**.0474**
Chemerin, ng/mL	**154.3 ± 58.17**	**181.4 ± 61.53**	**360.9 ± 166.5**	**479.3 ± 138.9**	**<.0001**

Data are expressed as mean ± SD. *P* less than .05 is considered statistically significant. Statistically significant values were represented in bold. "n" represents the number of participants in respective groups.
Abbreviations: 2hPGPG, postglucose plasma glucose level; BMI, body mass index; FPG, fasting plasma glucose; HbA_{1c}, glycated hemoglobin A_{1c}; HDL, high-density lipoprotein; IGT, impaired glucose tolerance; IL-1β, insulin-1β; LDL, low-density lipoprotein; NGT, normal glucose tolerance; PCOS, polycystic ovary syndrome; T2D, type 2 diabetes; TNF-α, tumor necrosis factor α.

and FPG was seen (Table 1). Serum TGs/HDL-c ratio level was significantly increased in PCOS individuals with T2D compared to those with IGT and NGT; no significant changes in TC and LDL-c levels were seen (see Table 1). Among the PCOS participants, 45.16% of individuals had an FG score greater than 8; only 1 healthy individual had an FG score greater than 8 (Supplementary Table S1) [20]. Serum testosterone level was significantly higher in the PCOS group (37.52 ± 29.65 ng/dL) compared to controls (22.09 ± 3.51 ng/dL; $P < .05$) (see Supplementary Table S1) [20]. Although serum testosterone levels were higher in the PCOS groups, the levels did not correlate with serum chemerin. In the post hoc analysis, chemerin level was found to be significantly higher in the overall PCOS group compared to controls ($P < .001$) (Fig 1A), and chemerin level significantly correlated with the metabolic and anthropometric parameters. A highly significant positive correlation was seen between chemerin and total body fat ($r = 0.4492$; $P = .0047$), 2hPGPG ($r = 0.5755$; $P = .0021$), HbA_{1c} ($r = 0.4187$; $P = .0058$), TGs/HDL-c level ($r = 0.5491$; $P = .0001$), and a partially significant correlation was seen with waist circumference ($r = 0.2863$; $P = .0733$) (Fig 2 and Supplementary Table S2) [20]. In this context, serum TG level was significantly correlated with body fat percentage ($r = 0.3898$; $P = .0039$) but did not correlate strongly with waist circumference (*P* value not significant). Additionally, we further classified the PCOS individuals based on their body fat percentage as lean PCOS and obese PCOS (obese PCOS ≥ 30). Our results suggest that mean serum chemerin level is significantly higher in the obese PCOS (381.6 ± 268.6 ng/mL) group compared to the lean PCOS (199.2 ± 151 ng/mL) group. But there was no significant change in serum chemerin levels between healthy individuals and the lean PCOS group (Supplementary Fig S2) [20]. Also, serum chemerin level had a significantly negative correlation with HOMA-2β ($r = -0.5326$; $P = .0004$) and a partial significantly positive correlation with HOMA 2IR ($r = 0.3499$; $P = .0798$) (see Fig 2 and Supplementary Table S2)

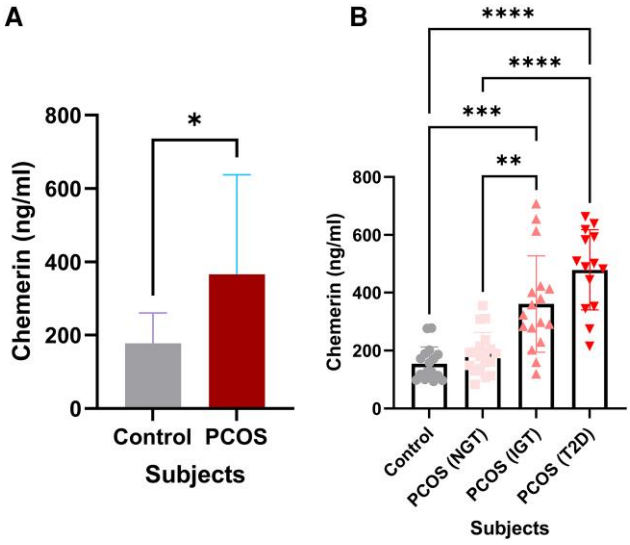


Figure 1. Measurement of circulating chemerin level. A, Comparison of serum chemerin level between the control and polycystic ovary syndrome (PCOS) group. Mann-Whitney *U* test was performed to compute the statistical significance. *P* value less than .05 is considered significant. B, Measurement of serum chemerin level in control and subgroups of PCOS. One-way analysis of variance was performed to compute the *P* value among the groups. *P* value less than .05 is considered significant. All data are represented as mean ± SD.

[20]. HOMA 2IR and HOMA-2β were calculated from C-peptide measured by Ethe LISA method with a CV of less than 8% for intra-assay and less than 10% for interassay. Serum chemerin level did not correlate with BMI or FPG (see Supplementary Table S2) [20]. Serum chemerin level was significantly higher ($P < .001$) in PCOS participants with T2D (479.3 ± 138.9 ng/mL) and IGT (360.9 ± 166.5 ng/mL) compared to NGT (181.4 ± 61.53 ng/mL) and controls (154.3 ± 58.17 ng/mL) (see Table 1). No significant

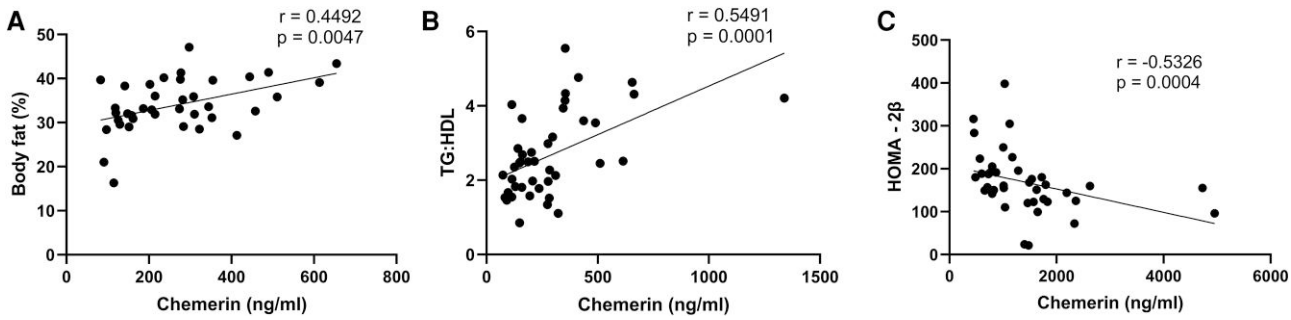
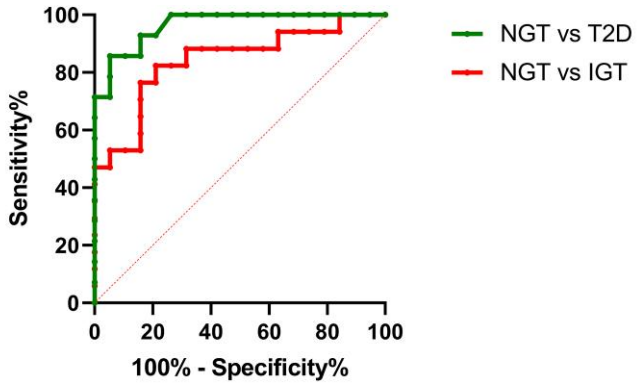


Figure 2. Correlation of serum chemerin level with anthropometric and metabolic parameters. A, Graphical representation of serum chemerin level positively correlated with body fat (%); chemerin as independent variable (x-axis). B, Graphical representation of serum chemerin level positively correlated with triglycerides/high-density lipoprotein cholesterol (TG/HDL-c). C, Graphical representation of serum chemerin level negatively correlated with homeostatic model 2 assessment of β-cell function (HOMA-2β).



Chemerin Level	Cut-off Value	Sensitivity (%)	Specificity (%)	AUC (%)	P-value
@ T2D	>309.3 ng/ml	85.71	89.47	96.43	<0.0001
@ IGT	>222.5 ng/ml	82.35	78.95	84.21	0.0005

Figure 3. Receiver operating characteristic (ROC) curve of chemerin. ROC curve analysis of serum chemerin for the diagnosis of type 2 diabetes (T2D) and impaired glucose tolerance (IGT).

change was observed in the chemerin level between the control and PCOS group without dysglycemia (*P* value nonsignificant) (Fig 1B). ROC curve analysis showed that the cutoff value of serum chemerin level to predict dysglycemia in PCOS individuals is greater than 309.3 ng/mL with 85.71% sensitivity and 89.47% specificity (Fig 3). Chemerin level in control vs T2D individuals had an AUC of 0.9643 ($P < .0001$) with a 95% CI of 0.9112 to 1 and a likelihood ratio of 8.143. Using the aforementioned cutoff, 89.5% of the T2D participants and 14.3% of individuals with NGT had a higher value of chemerin. Similarly, serum chemerin at a cutoff value greater than 222.5 ng/mL had an AUC of 0.8421 with a sensitivity of 82.35% and specificity of 78.95% for IGT (see Fig 3). Using this cutoff, 82.35% of the IGT participants and 21.05% of NGT had a higher value of chemerin. Intra-assay precision of chemerin is CV (%) less than 8% and interassay precision is CV (%) less than 10. We further ran binary logistic regression analysis in which the Nagelkerke R Square value for differentiating PCOS individuals having T2D from the women having only PCOS was 0.793 and for differentiating PCOS individuals having dysglycemia (either T2D or prediabetes) from individuals having only PCOS was 0.589 (with insignificant Hosmer and Lemeshow test). This indicates that the model is good for testing; chemerin detects 79.8% of the PCOS individuals having T2D correctly and 58.9% of any dysglycemic individuals correctly with sufficient power (>0.95).

Discussion

PCOS, often considered as the ovarian manifestation of MetS, increases the risk of T2D. The identification of biomarkers that predict dysglycemia in PCOS could play an important role in preventing T2D in a young population with PCOS. The gold-standard protocol for detecting IGT, the 2hPGPG, has its limitations, including high cost, being labor-intensive, and variability issues. Therefore, identifying a biomarker for population studies remains an unmet need.

Chemerin, a recently identified adipocytokine, regulating adipocyte differentiation and gene expression, has been reported to regulate glucose and lipid homeostasis [13].

While studies have shown serum chemerin levels to be significantly increased in PCOS individuals [24], the present study shows increased serum chemerin levels only in the subset of PCOS participants having dysglycemia. To find out whether the higher chemerin levels in the PCOS individuals

with dysglycemia could be attributed to higher body fat percentage alone, we classified the study population based on their body fat content as follows: control, lean PCOS, and obese PCOS. The obese PCOS group had significantly higher mean serum chemerin levels compared to the lean PCOS group. But there was no significant difference in mean serum chemerin level between the control and lean PCOS groups. These findings also strengthen our observation that elevated serum chemerin level has no association with PCOS. Previous studies have reported increased chemerin levels in MetS, nonalcoholic fatty liver disease, and T2D, but no diagnostic cutoffs of chemerin for dysglycemia in PCOS have been reported. In our study, ROC curve analysis showed that the cutoff value of serum chemerin level greater than 309.3 ng/mL predicts dysglycemia in PCOS individuals with 85.71% sensitivity and 89.47% specificity and an AUC of 0.9643. Similarly, serum chemerin at a cutoff value greater than 222.5 ng/mL had an AUC of 0.8421 with sensitivity of 82.35% and specificity of 78.95% for IGT. The Cohen kappa showed a substantial agreement (0.767; $P < .001$) between the chemerin cutoff greater than 309.3 ng/mL and postglucose plasma glucose levels greater than 200 mg/dL. The present study is arguably the first ever to define a serum chemerin cutoff to distinguish PCOS individuals with T2D from those without and raises the possibility of it being used as a biomarker for dysglycemia in PCOS patients.

A study by Fatima et al in 2015 [25] found that 73% of newly diagnosed T2D individuals (n = 23) can be discriminated by chemerin value greater than 13.7 ng/mL (91% sensitivity and 96% specificity, respectively). Difference may be attributed either to smaller sample size or ethnicity differences of the population.

Another study by Hamza and colleagues in 2016 [26] addressed elevated chemerin level as a noninvasive, reproducible diagnostic marker for fatty liver in obese children and adolescent patients. They predicted that the serum chemerin level at a cutoff value greater than 350 ng/mL discriminates cases from controls with 93.3% of sensitivity and 88% specificity .

We also looked at the correlation between biochemical hyperandrogenism, a defining feature of PCOS, and serum chemerin levels, but did not find any, further indicating that increased serum chemerin levels correlate only with the presence and severity of dysglycemia, rather than the level of hyperandrogenism.

In contrast to Yang et al [24], we have not found any significant correlation of chemerin level with BMI. This difference in findings may happen because in India, multiple studies have shown BMI to be a poor predictor of obesity and IR. Rather, it is total body fat that correlates best with IR [27, 28]. In context, we have shown significantly higher positive correlation of chemerin levels with body fat percentage but not with BMI. Chemerin level was measured in women with PCOS as well as women without PCOS in a study by Guvenc et al [29]. According to that study, no significant difference was observed in serum chemerin level between individuals with and without PCOS. However, circulating serum chemerin level was elevated in overweight PCOS women regardless of serum glucose levels.

Strong positive correlations between chemerin levels on the one hand and 2hPGPG and HbA_{1c} on the other suggest chemerin levels to be a biomarker for IR. A negative correlation between serum chemerin levels and HOMA-2β is also indicative of a predictive role of chemerin in identifying pancreatic β-cell dysfunction. A partial correlation between serum chemerin levels and C-peptide HOMA2IR is in agreement with Kort et al [30], who suggested that chemerin might play a role in IR pathogenesis.

Our study suggests that chemerin may be strongly associated with dysglycemia in PCOS patients. Individuals having chemerin levels greater than 309.3 ng/mL have a higher likelihood of having oral glucose tolerance test–confirmed T2D. A correlation study of chemerin with anthropometric and metabolic parameters confirms the involvement of chemerin in the pathogenesis of IR in PCOS individuals; however, the molecular mechanism of chemerin signaling needs to be further studied.

Limitations of the Study

We acknowledge that our study has some limitations. First, it is a cross-sectional study and all study participants belong to the same geographical area and were recruited by the clinic-based method. Although the power of the study is sufficient enough to conclude, still the sample size is small. However, further longitudinal studies with larger samples are required to confirm the association of serum chemerin levels with the severity of glycemia in adult women with PCOS.

In our study testosterone was measured by automated methos not by liquid chromatography–mass spectrometry, and free androgen index was not performed. IR was measured only by C-peptide hOMA-IR and body fat was measured by the bioelectrical impedance method, not by dual-energy x-ray absorptiometry.

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We declare that the manuscript has been approved by all named authors and there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of the authors listed in the manuscript has been approved by all of us. We confirm that the work is original and has neither been published elsewhere nor is it currently under consideration for publication elsewhere.

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Author Contributions

S.M. conceptualized the study; S.M. and C.B. designed the study; C.B. and B.M. investigated and performed analysis and data validation; B.M. wrote the manuscript; A.Mu. assisted in the recruitment of study participants; S.P. and C.S.

assisted in statistical analysis; A.Mo. assisted in performing a few of the experiments; and S.M. supervised the work and critically reviewed and edited the manuscript.

Disclosures

The authors declare no potential conflict of interest.

Data Availability

Data are available on request from the corresponding author. Supplementary data are available in the data repositories mentioned in "References."

References

1. Lizneva D, Suturina L, Walker W, Brakta S, Gavrilova-Jordan L, Azziz R. Criteria, prevalence, and phenotypes of polycystic ovary syndrome. *Fertil Steril*. 2016;106(1):6-15.
2. Zhao H, Zhang J, Cheng X, Nie X, He B. Insulin resistance in polycystic ovary syndrome across various tissues: an updated review of pathogenesis, evaluation, and treatment. *J Ovarian Res*. 2023;16(1):9.
3. Shim U, Oh JY, Lee HJ, Hong YS, Sung YA. Long menstrual cycle is associated with type 2 diabetes mellitus in Korean women. *Diabetes Metab J*. 2011;35(4):384-389.
4. Kelestimur F, Unluhizarci K, Baybuga H, Atmaca H, Bayram F, Sahin Y. Prevalence of polycystic ovarian changes and polycystic ovary syndrome in premenopausal women with treated type 2 diabetes mellitus. *Fertil Steril*. 2006;86(2):405-410.
5. Ehrmann DA. Polycystic ovary syndrome. *N Engl J Med*. 2005;352(12):1223-1236.
6. Kakoly NS, Khomami MB, Joham AE, *et al*. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. *Hum Reprod Update*. 2018;24(4):455-467.
7. Hudnut-Beumler J, Kaar JL, Taylor A, *et al*. Development of type 2 diabetes in adolescent girls with polycystic ovary syndrome and obesity. *Pediatr Diabetes*. 2021;22(5):699-706.
8. Forslund M, Landin-Wilhelmsen K, Trimpou P, Schmidt J, Brännström M, Dahlgren E. Type 2 diabetes mellitus in women with polycystic ovary syndrome during a 24-year period: importance of obesity and abdominal fat distribution. *Hum Reprod Open*. 2020;2020(1):hoz042.
9. Jayasena CN, Franks S. The management of patients with polycystic ovary syndrome. *Nat Rev Endocrinol*. 2014;10(10):624-636.
10. Li Y, Shi B, Li S. Association between serum chemerin concentrations and clinical indices in obesity or metabolic syndrome: a meta-analysis. *PLoS One*. 2014;9(12):e113915.
11. Roman AA, Parlee SD, Sinal CJ. Chemerin: a potential endocrine link between obesity and type 2 diabetes. *Endocrine*. 2012;42(2):243-251.
12. Bozaoglu K, Bolton K, McMillan J, *et al*. Chemerin is a novel adipokine associated with obesity and metabolic syndrome. *Endocrinology*. 2007;148(10):4687-4694.
13. Goralski KB, McCarthy TC, Hanniman EA, *et al*. Chemerin, a novel adipokine that regulates adipogenesis and adipocyte metabolism. *J Biol Chem*. 2007;282(38):28175-28188.
14. Roh SG, Song SH, Choi KC, *et al*. Chemerin–a new adipokine that modulates adipogenesis via its own receptor. *Biochem Biophys Res Commun*. 2007;362(4):1013-1018.
15. Takahashi M, Takahashi Y, Takahashi K, *et al*. Chemerin enhances insulin signaling and potentiates insulin-stimulated glucose uptake in 3T3-L1 adipocytes. *FEBS Lett*. 2008;582(5):573-578.
16. Luangsay S, Wittamer V, Bondue B, *et al*. Mouse ChemR23 is expressed in dendritic cell subsets and macrophages, and mediates an anti-inflammatory activity of chemerin in a lung disease model. *J Immunol*. 2009;183(10):6489-6499.
17. Gu P, Cheng M, Hui X, Lu B, Jiang W, Shi Z. Elevating circulation chemerin level is associated with endothelial dysfunction and early atherosclerotic changes in essential hypertensive patients. *J. Hypertens*. 2015;33(8):1624-1632.
18. Sell H, Divoux A, Poitou C, *et al*. Chemerin correlates with markers for fatty liver in morbidly obese patients and strongly decreases after weight loss induced by bariatric surgery. *J Clin Endocrinol Metab*. 2010;95(6):2892-2896.
19. Mansoori A, Amoochi-Foroushani G, Zilaee M, Hosseini SA, Azhdari M. Serum and follicular fluid chemerin and chemerin mRNA expression in women with polycystic ovary syndrome: systematic review and meta-analysis. *Endocrinol Diabetes Metab*. 2022;5(1):e00307.
20. Bose C, Mukherjee B, Mukherjee A, *et al*. Supplemental data for "Serum Chemerin levels correlate with the severity of dysglycemia in young adult women with polycystic ovary syndrome". *Figshare*. Dataset. 2024. https://doi.org/10.6084/m9.figshare.25018244.v1
21. Sami W, Al-Rukban M, Almansour M, Waqas T, Afzal K, Asad M. How many subjects should be studied: sample size determination through hypothesis testing and confidence interval. *Majmaah J Health Sci*. 2013;1(2):43-48.
22. Bozdag G, Mumusoglu S, Zengin D, Karabulut E, Yildiz BO. The prevalence and phenotypic features of polycystic ovary syndrome: a systematic review and meta-analysis. *Hum Reprod*. 2016;31(12):2841-2855.
23. Pradeepa R, Mohan V. Prevalence of type 2 diabetes and its complications in India and economic costs to the nation. *Eur J Clin Nutr*. 2017;71(7):816-824.
24. Yang S, Wang Q, Huang W, *et al*. Are serum chemerin levels different between obese and non-obese polycystic ovary syndrome women? *Gynecol Endocrinol*. 2016;32(1):38-41.
25. Fatima SS, Butt Z, Bader N, Pathan AZ, Hussain S, Iqbal NT. Role of multifunctional chemerin in obesity and preclinical diabetes. *Obes Res Clin Pract*. 2015;9(5):507-512.
26. Hamza RT, Elkabbany ZA, Shedid AM, Hamed AI, Ebrahim AO. Serum chemerin in obese children and adolescents before and after L-carnitine therapy: relation to nonalcoholic fatty liver disease and other features of metabolic syndrome. *Arch Med Res*. 2016;47(7):541-549.
27. Ahirwar R, Mondal PR. Prevalence of obesity in India: a systematic review. *Diabetes Metab Syndr*. 2019;13(1):318-321.
28. Gupta RD, Tamanna N, Siddika N, Haider SS, Apu EH, Haider MR. Obesity and abdominal obesity in Indian population: findings from a nationally representative study of 698,286 participants. *Epidemiologia (Basel)*. 2023;4(2):163-172.
29. Guvenc Y, Var A, Goker A, Kuscu NK. Assessment of serum chemerin, vaspin and omentin-1 levels in patients with polycystic ovary syndrome. *J Int Med Res*. 2016;44(4):796-805.
30. Kort DH, Kostolias A, Sullivan C, Lobo RA. Chemerin as a marker of body fat and insulin resistance in women with polycystic ovary syndrome. *Gynecol Endocrinol*. 2015;31(2):152-155.