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# Assessing the variability and predictability of adipokines (adiponectin, leptin, resistin and their ratios) in non-obese and obese women with anovulatory polycystic ovary syndrome

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## Abstract

**Objectives:** To assess the variability and predictability of adiponectin, leptin, resistin and their ratios in non-obese and obese women with anovulatory polycystic ovary syndrome (aPCOS).

**Results:** A total of 52 ovulatory controls (mean age =  $31.63 \pm 4.88$  years, BMI =  $25.33 \pm 2.68$  kg/m<sup>2</sup>); 54 non-obese (mean age =  $32.11 \pm 4.25$  years, BMI =  $25.72 \pm 2.95$  kg/m<sup>2</sup>) and 50 obese women with aPCOS (mean age =  $33.64 \pm 4.14$  years, BMI =  $39.19 \pm 2.99$  kg/m<sup>2</sup>) were recruited. The aPCOS group had lower adiponectin [13.0 (10.49–16.59) vs 18.42 (15.72–19.92)  $\mu$ g/ml,  $p < 0.0001$ ], adiponectin: leptin ratio (A:L) [0.60 (0.35–0.88) vs 1.19 (0.92–1.37),  $p < 0.0001$ ], and adiponectin: resistin ratio (A:R) [0.30 (0.21–0.43) vs 0.42 (0.32–0.62),  $p < 0.0001$ ] but a higher leptin [20.02 (14.54–26.80) vs 16.17 (14.51–18.36) ng/ml,  $p < 0.0001$ ] and leptin: resistin ratio (L:R) [0.53 (0.37–0.82) vs 0.40 (0.27–0.48),  $p < 0.0001$ ] compared to the controls. The obese aPCOS group had lower adiponectin [11.04 (5.66–13.25) vs 14.18 (11.04–18.02),  $p < 0.0001$  and 18.42 (15.72–19.92)  $\mu$ g/ml,  $p < 0.0001$ ], A:L [0.36 (0.27–0.44) vs 0.78 (0.61–1.16),  $p < 0.0001$  and 1.19 (0.92–1.37),  $p < 0.0001$ ], and A:R [0.24 (0.17–0.38) vs 0.40 (0.23–0.58),  $p < 0.0001$  and 0.42 (0.32–0.62),  $p < 0.0001$ ] but a higher leptin [26.80 (14.28–32.09) vs 17.95 (14.86–21.26),  $p < 0.05$  and 16.17 (14.51–18.36) ng/ml,  $p < 0.0001$ ] and L:R [0.63 (0.46–1.03) vs 0.41 (0.30–0.61),  $p < 0.0001$  and 0.40 (0.27–0.48),  $p < 0.0001$ ] compared to the non-obese aPCOS and control group, respectively. A:L showed the best discriminatory power in predicting aPCOS (AUC = 0.83), followed by adiponectin alone (AUC = 0.79), L:R and leptin alone (both AUC = 0.69). Resistin alone had the poorest discriminatory power (AUC = 0.48).

**Keywords:** Polycystic ovary syndrome, Anovulation, Adiponectin, Leptin, Resistin

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## Introduction

Overweight and obesity are pervasive conditions which are considered global epidemic and threat to public health [1, 2]. Evidence suggest that obesity is associated with the risk of metabolic diseases such as diabetes, hypertension, cardiovascular disease, cancers and overall mortality [3–5]. There have also been reports of associations between obesity and infertility [6, 7], particularly among women due to the risk of anovulation [1, 8]. Anovulation is a common cause of infertility in women; responsible for 25–50% of female infertility [9, 10], of which polycystic ovary syndrome (PCOS) accounts over 90% of cases [11].

PCOS is a multisystem, endocrinological, reproductive and metabolic disorder characterized by oligo- and/or anovulation, hyperandrogenism, and polycystic ovaries [12]. Obesity-related adverse alterations in adipose tissue that predispose to metabolic dysregulation has been implicated in PCOS pathogenesis. These adverse alterations include derangements in bioactive cytokines and adipokines such as adiponectin, leptin, and resistin [13, 14].

Adiponectin is an adipokine secreted by adipose tissues, with anti-inflammatory, anti-atherogenic, cardio-protective, and insulin-sensitizing properties. Reduced adiponectin levels have been linked with obesity, T2DM, and PCOS [15–17]. Nonetheless, the relationship between altered adiponectin levels and PCOS remains debatable. While some studies report lower adiponectin levels in PCOS independent of BMI [13, 18], others report similar adiponectin levels in BMI-matched PCOS and controls [19, 20]. Leptin is an anorexigenic peptide hormone secreted by white adipose tissue [21]. Likewise, whereas some studies report a significant positive association between circulating leptin levels with high body fat independent of PCOS [22], others report no significant difference in circulating leptin levels between PCOS and age- and BMI-matched controls [23, 24] as well as between ovulatory and anovulatory women with PCOS [25]. Resistin is an adipocyte-derived polypeptide which have been associated with obesity, insulin resistance (IR) and cardiovascular risk [26, 27]. Similarly, some studies report comparable resistin levels between women with PCOS and controls [17, 27, 28] while others indicate that, irrespective of PCOS, there are elevated resistin levels in obese women compared to non-obese [29].

Thus far, reports regarding the alterations in adiponectin, leptin, and resistin in non-obese and obese women with PCOS remain inconclusive. Additionally, despite numerous previous studies highlighting the expediency of the ratios of these adipokines as a biomarker for obesity, IR, diabetes, coronary artery disease, and stroke [30–33], there is a dearth of information on their expediency

as predictors of PCOS. This study aimed at assessing the variability and predictability of adiponectin, leptin, resistin and their ratios in non-obese and obese women with anovulatory PCOS.

## Main text

### Materials and methods

#### Study design/setting

This was a case–control study. Consecutive consenting women clinically diagnosed of aPCOS visiting the Obstetrics and Gynaecology units of Trust Care, Ruma and Asbury were included in the study as cases. PCOS diagnosis was based on the 2003 Rotterdam criteria [12]. All PCOS participants were anovulatory. Fertile (eumenorrhic) women visiting the hospital for routine check-up were included as controls. Relevant clinical data of each participant was extracted from the hospital's archive. Women with Cushing syndrome, hyperprolactinemia, androgen-producing tumors, non-classic adrenal hyperplasia, active thyroid disease, and diabetes were excluded.

#### Study population and Anthropometric measurements

A total of 52 ovulatory, 54 non-obese and 50 obese women with aPCOS were included in this study. The weight was measured using a calibrated analogue scale (Seca, Hamburg, Deutschland). Height was measured using a stadiometer (Seca, Hamburg, Deutschland). Body mass index (BMI) was calculated by:  $BMI = \text{weight} / \text{height}^2$  ( $\text{kg}/\text{m}^2$ ) [34]. Obesity was defined according to the World Health Organization (WHO) criteria ( $BMI \geq 30 \text{ kg}/\text{m}^2$ ) [35]. Waist circumference (WC) and hip circumference (HC) were measured with a measuring tape; waist-to-height ratio (WHtR) =  $WC$  (m) / height (m), waist-to-hip ratio (WHR) =  $WC$  (m) /  $HC$  (m), body adiposity index (BAI) =  $(100 \times HC$  (m)) / ( $\text{height}$  (m)  $\times \sqrt{\text{height}$  (m)) - 18 [36] and visceral adiposity index (VAI) =  $(WC(m)) / (36.58 + (1.89 \times BMI)) \times (TG / (0.81)) \times ((1.52) / HDL-C)$  were calculated.

#### Blood sampling, processing and analysis

Five milliliters of venous blood was obtained from each participant and dispensed into gel separator tubes. The tubes were centrifuged at  $1500 \times g$  for 10 min at  $4^\circ\text{C}$  to obtain the serum which were stored at  $-20^\circ\text{C}$  until analysis. Serum levels of adiponectin, leptin, and resistin were measured based on solid-phase sandwich Enzyme Linked Immunosorbent Assay (ELISA) technique (standardized with an intra- and inter-assay %CVs < 10%) (Green Stone Swiss Co Limited, China) according to the manufacturer's instructions.

**Statistical analysis**

Statistical analysis was performed using the R Language for Statistical Computing version 3.6.0 [37]. Chi squared test was used to assess significance of association between the participant characteristics and fertility status. Distribution of adipokines were presented with density plots. Hierarchical clustering by Spearman’s correlation was used to assess relationship between adipokines (and their ratios) and obesity indices. Independent t-test and one-way ANOVA with Tukey test or Mann–Whitney U and Kruskal–Wallis with Dunn’s test were used to test for significance of difference between groups where applicable. The receiver operating characteristic (ROC) curve analysis was used to evaluate the performance of the adipokines (and their ratios) in predicting aPCOS. A p value < 0.05 was considered statistically significant.

**Results**

A total of 52 ovulatory controls (mean age = 31.63 ± 4.88 years, BMI = 25.33 ± 2.68 kg/m<sup>2</sup>); 104 aPCOS patients comprising 54 non-obese [mean age = 32.11 ± 4.25 years, BMI = 25.72 ± 2.95 kg/m<sup>2</sup>] and 50 obese women [mean age = 33.64 ± 4.14 years, BMI = 39.19 ± 2.99 kg/m<sup>2</sup>] were included in this study. A

higher proportion of the study participants had tertiary education, were employed and did not consume alcohol. There was no statistically significant association between fertility status and baseline characteristics (Table 1).

The aPCOS group had a significantly lower adiponectin [13.0 (10.49–16.59) µg/ml vs 18.42 (15.72–19.92) µg/ml, p < 0.0001], adiponectin: leptin ratio (A:L) [0.60 (0.35–0.88) vs 1.19 (0.92–1.37), p < 0.0001], and adiponectin: resistin ratio (A:R) [0.30 (0.21–0.43) vs 0.42 (0.32–0.62), p < 0.0001] but higher leptin [20.02 (14.54–26.80) ng/ml vs 16.17 (14.51–18.36) ng/ml, p < 0.0001] and leptin: resistin ratio (L:R) [0.53 (0.37–0.82) vs 0.40 (0.27–0.48), p < 0.0001] compared to the controls (Fig. 1a, b).

The obese aPCOS group had a significantly lower adiponectin [11.04 (5.66–13.25) µg/ml vs 14.18 (11.04–18.02) µg/ml, p < 0.0001 and 18.42 (15.72–19.92) µg/ml, p < 0.0001], A:L [0.36 (0.27–0.44) vs 0.78 (0.61–1.16), p < 0.0001 and 1.19 (0.92–1.37), p < 0.0001], and A:R [0.24 (0.17–0.38) vs 0.40 (0.23–0.58), p < 0.0001 and 0.42 (0.32–0.62), p < 0.0001] but higher leptin [26.80 (14.28–32.09) ng/ml vs 17.95 (14.86–21.26) ng/ml, p < 0.05 and 16.17 (14.51–18.36) ng/ml, p < 0.0001] and L:R [0.63 (0.46–1.03) vs 0.41 (0.30–0.61), p < 0.0001 and 0.40 (0.27–0.48), p < 0.0001] compared to the non-obese aPCOS and control group, respectively (Fig. 1c, d).

**Table 1 Baseline characteristics of the study population**

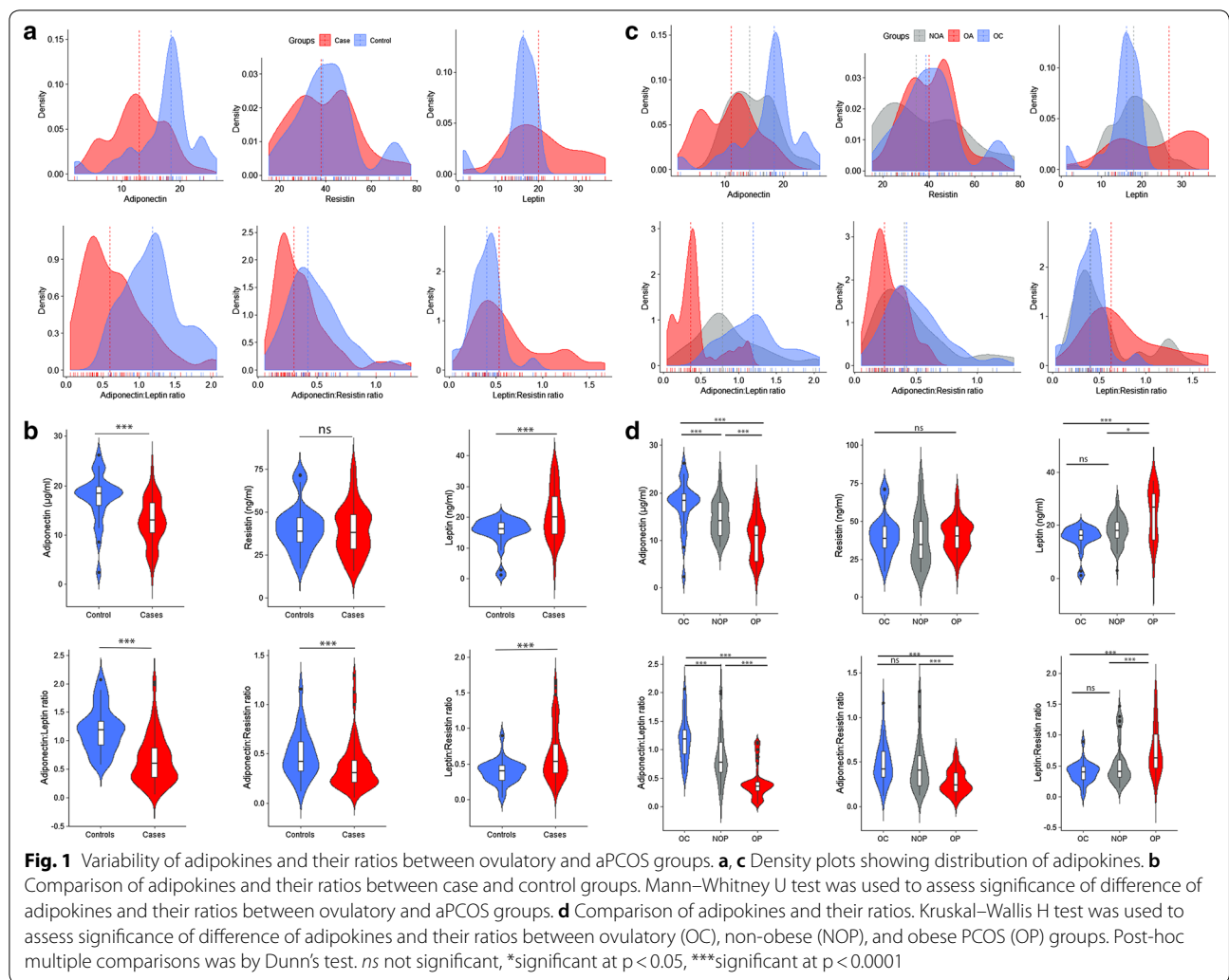
Variable	Ovulatory control (n = 52)	PCOS (n = 104)	p-value	Non-obese PCOS (n = 54)	Obese PCOS (n = 50)	p-value
Age (years)	31.63 ± 4.88	32.85 ± 4.25	0.112 <sup>‡</sup>	32.11 ± 4.25	33.64 ± 4.14	0.062 <sup>†</sup>
Educational level			0.312			0.219
None/basic	5 (21.7)	18 (78.3)		12 (52.2)	6 (26.1)	
Secondary	14 (41.2)	20 (58.8)		12 (35.3)	8 (23.5)	
Tertiary	33 (33.3)	66 (66.7)		30 (30.3)	36 (36.4)	
Occupation			0.197			0.093
Unemployed	9 (47.4)	10 (52.6)		8 (42.1)	2 (10.5)	
Employed	43 (31.4)	94 (68.6)		46 (33.6)	48 (35.0)	
Informal	10 (29.4)	24 (70.6)		10 (29.4)	14 (41.2)	
Formal	33 (32.0)	70 (68.0)		36 (35.0)	34 (33.0)	
Frequency of exercise			0.073			0.064
Rarely	17 (25.4)	50 (74.6)		22 (32.8)	28 (41.8)	
1/week	22 (34.9)	41 (65.1)		26 (41.3)	15 (23.8)	
> 1/week	13 (50.0)	13 (50.0)		6 (23.1)	7 (26.9)	
Alcohol consumption			0.235*			0.405*
No	36 (30.5)	82 (69.5)		42 (35.6)	40 (33.9)	
Yes	16 (42.1)	22 (57.9)		12 (31.6)	10 (26.3)	
Smoking status						
No	52 (33.3)	104 (66.7)		54 (34.6)	50 (32.1)	–

Unless otherwise indicated, Chi squared test was used to assess significance of association between the baseline characteristics and fertility status

\* Fisher exact test for test of association

<sup>‡</sup> Significance of difference comparing Ovulatory control and PCOS group using Independent t-test

<sup>†</sup> Significance of difference comparing Ovulatory control, Non-obese PCOS, and Obese PCOS group using One-way ANOVA



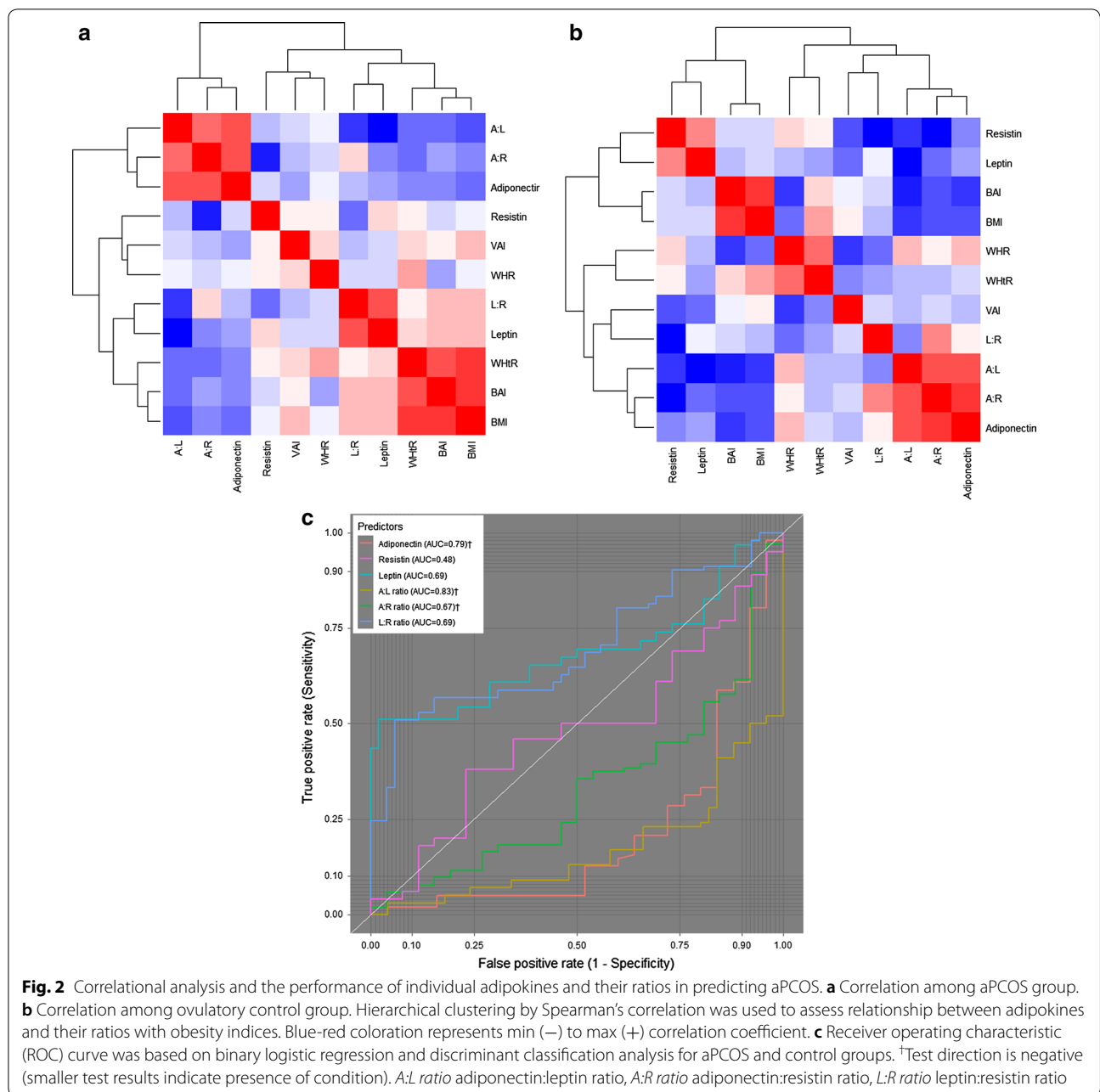
Among the aPCOS group, adiponectin showed a significant negative correlation with BMI ( $r_s = -0.43$ ,  $p < 0.0001$ ), WHtR ( $r_s = -0.36$ ,  $p < 0.0001$ ), BAI ( $r_s = -0.35$ ,  $p < 0.0001$ ), and VAI ( $r_s = -0.19$ ,  $p = 0.049$ ). Leptin had a positive correlation with BMI ( $r_s = 0.31$ ,  $p = 0.001$ ), WHtR ( $r_s = 0.27$ ,  $p = 0.007$ ), and BAI ( $r_s = 0.29$ ,  $p = 0.003$ ). There was no statistically significant correlation between resistin and obesity indices. A:L showed a negative correlation with BMI ( $r_s = -0.48$ ,  $p < 0.0001$ ), WHtR ( $r_s = -0.38$ ,  $p < 0.0001$ ), and BAI ( $r_s = -0.40$ ,  $p < 0.0001$ ). A:R showed similar correlations while L:R showed a positive correlation with BMI ( $r_s = 0.27$ ,  $p = 0.005$ ) and BAI ( $r_s = 0.29$ ,  $p = 0.003$ ) (Fig. 2a and Additional file 1: Table S1). Among the controls, adiponectin showed a significantly negative correlation with BAI ( $r_s = -0.33$ ,  $p = 0.017$ ) while resistin showed a positive correlation with WHR ( $r_s = 0.31$ ,  $p = 0.028$ ) and WHtR ( $r_s = 0.28$ ,  $p = 0.044$ ). There was no statistically significant correlation between leptin and

obesity indices. A:L had a significant negative correlation with BMI ( $r_s = -0.36$ ,  $p = 0.008$ ) and BAI ( $r_s = -0.39$ ,  $p = 0.004$ ) while A:R showed a significant negative correlation with BMI ( $r_s = -0.29$ ,  $p = 0.038$ ) (Fig. 2b and Additional file 1: Table S2).

A:L presented with the best discriminatory power in predicting aPCOS (AUC=0.83) followed by adiponectin alone (AUC=0.79), and L:R and leptin alone (both AUC=0.69). Resistin alone presented with the poorest discriminatory power (AUC=0.48) (Fig. 2c).

### Discussion

Evidence suggest that, in PCOS, high body fat coupled with dysfunction of adipose tissue result in over-production of leptin, resistin and reduced expression of adiponectin. Levels of adiponectin have been shown to decrease in obesity and increase with weight loss [29]. It is considered a ‘beneficial’ adipokine in reproduction [38]. Leptin is constitutively secreted by adipocytes



in proportion to the adipose mass [39]. In obesity, the levels of leptin are even more elevated due to leptin resistance [40]. Additionally, increased expression of the resistin gene has been observed in human preadipocytes, which decreased during adipocyte differentiation. Some studies report comparable adiponectin, leptin and resistin levels in PCOS [19, 24, 28] while others report lower adiponectin [18], higher leptin [22] and resistin levels [29] among women with PCOS than controls in relation to obesity. Thus, reports regarding

the levels of adiponectin, leptin, and resistin in PCOS remain unresolved.

In this study, aPCOS patients had significantly lower levels of adiponectin, A:L, and A:R but higher leptin and L:R compared to the controls. Our finding is comparable to a study by Sarray et al. [28], who reported significantly lower levels of adiponectin, A:L, and A:R among women with PCOS compared to controls in Bahrain. A recent study by Baldani et al. also found significantly lower adiponectin and higher leptin among



women with PCOS compared to controls in Croatia [41]. Upon stratification of aPCOS group by obesity status, we found the obese aPCOS group to have a significantly lower adiponectin, A:L, and A:R but higher leptin and L:R compared to the non-obese aPCOS and ovulatory group, respectively. This finding is in harmony with a study by Olszanecka-Glinianowicz et al. [17] who found serum adiponectin and A:R to be lowest in the obese PCOS subgroup compared to both the normal weight PCOS subgroup and the controls in Poland. In their study, serum resistin levels did not differ significantly between both non-obese and obese PCOS subgroups and the controls which is comparable to our study findings. Studies by Xiu et al. [42], Arikan et al. [43], and Seow et al. [44] also found similar serum resistin levels among controls, non-obese, obese women with PCOS. Furthermore, Sarray et al. [28] found markedly reduced A:L and A:R among obese women with PCOS compared to non-obese women with PCOS and controls. They also found lower L:R among obese women with PCOS though not statistically significant. Together with previous findings, our results corroborate the deposition that high body fat indeed play pivotal roles in the pathogenesis of PCOS.

Also consistent with previous reports [39, 40, 45–47], we found that, with the exception of resistin, all other adipokines including their ratios were strongly and more correlated with various obesity indices among women with aPCOS compared to the controls. Specifically, adiponectin, A:L, and A:R showed a negative associations whereas leptin, and L:R correlated positively with the obesity indices. This finding is also coherent with studies by Sarray et al. [28] and Golbahar et al. [48].

In order to assess the predictive capabilities of the adipokines and their ratios, we employed the ROC curve analysis with reference to aPCOS. We found A:L to have the best discriminatory power in predicting aPCOS with an AUC of 0.83, followed by adiponectin alone (AUC = 0.79). Adiponectin and leptin are adipose tissue-derived hormones with contrasting relationship with the metabolic dysregulation [48]. Previous studies have highlighted A:L as a biomarker for obesity IR, and stroke [30–33]. Given the high AUC, our finding suggest that A:L could be a useful marker for aPCOS. This finding corroborates with a study by Golbahar et al. who found A:L to have a similarly high discriminatory power with comparable AUC of 0.86 among Bahraini women with PCOS [48]. Sarray et al. found a much higher discriminatory power (AUC of 0.94) for A:L in predicting PCOS in Bahrain [28]. The discrepancy in the predictive power may be attributed to differences in characteristics of the study population, sample size, and methods for biochemical analysis.

## Conclusion

This study shows significantly altered serum adiponectin and leptin levels but not resistin in Ghanaian women with aPCOS compared to healthy subjects. Obese aPCOS patients have the most altered levels of adipokines compared to non-obese aPCOS and healthy subjects. Adiponectin: leptin ratio is the best predictor of aPCOS compared to individual adipokines.

## Limitations

We did not assess androgens levels of the participants. Also, levels of insulin or IR was not evaluated. Furthermore, the relatively small sample size is a limitation of this present study. We recommend the use of larger sample size in future studies.

## Additional file

**Additional file 1.** Correlation co-efficient, lipid profile and anthropometric characteristics of the study population.

## Abbreviations

aPCOS: anovulatory polycystic ovary syndrome; BMI: body mass index; WHO: World Health Organization; T2DM: type 2 diabetes mellitus; WC: waist circumference; HC: hip circumference; WHR: waist to hip ratio; WHtR: waist to height ratio; BAI: body adiposity index; VAI: visceral adiposity index; ELISA: Enzyme Linked Immunosorbent Assay.

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## Authors' contributions

CO and WKBAO designed the study, supervised the research and laboratory analysis, drafted and revised the manuscript. SAA, EA, EAA and EKAB were involved in the design of the study, collection of data, laboratory analysis, drafting and revision of the manuscript. EWO was involved in the design of the study, collection of data, laboratory analysis, statistical analysis and interpretation, drafting and revision of the manuscript. All authors read and approved the final manuscript.

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## Availability of data and materials

The datasets supporting the conclusions of this article are included within the article and its additional file.

## Ethics approval and consent to participate

Ethical approval for this study was obtained from the committee on Human Research, Publications and Ethics (CHRPE), School of Medical Sciences, Kwame Nkrumah University of Science & Technology (CHRPE/AP/564/17), Ruma Fertility Hospital, Asbury Fertility Hospital and Trust Care Hospital. Written informed consent was obtained from all participants who opted to participate after the aims and objectives of the study had been explained to them. Participation was voluntary, and respondents were assured that the information obtained

was strictly for research and academic purposes only and were guaranteed the liberty to opt out from the study at their own convenience.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare that they have no competing interests.

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#### References

- de Mola Loret J. Obesity and its relationship to infertility in men and women. *Obstet Gynecol Clin N Am*. 2009;36(2):333–46, ix.
- Talmor A, Dunphy B. Female obesity and infertility. *Best Pract Res Clin Obstet Gynaecol*. 2015;29(4):498–506.
- Hensrud DD, Klein S, editors. *Extreme obesity: a new medical crisis in the United States*. In: Mayo Clinic Proceedings. Amsterdam: Elsevier; 2006.
- Brown CH III. *Obesity and cancer*. Obesity. Boca Raton: CRC Press; 2012. p. 360–71.
- Bastien M, Poirier P, Lemieux I, Després J-P. Overview of epidemiology and contribution of obesity to cardiovascular disease. *Prog Cardiovasc Dis*. 2014;56(4):369–81.
- Pasquali R, Patton L, Gambineri A. Obesity and infertility. *Curr Opin Endocrinol Diabetes Obes*. 2007;14(6):482–7.
- Best D, Bhattacharya S. Obesity and fertility. *Horm Mol Biol Clin Invest*. 2015;24(1):5–10.
- Koning A, Kuchenbecker W, Groen H, Hoek A, Land J, Khan K, et al. Economic consequences of overweight and obesity in infertility: a framework for evaluating the costs and outcomes of fertility care. *Human Reprod Update*. 2010;16(3):246–54.
- Eijkemans MJ, Imani B, Mulders AG, Habbema JDF, Fauser BC. High singleton live birth rate following classical ovulation induction in normogonadotrophic anovulatory infertility (WHO 2). *Hum Reprod*. 2003;18(11):2357–62.
- Rowe PJ, Comhaire FH, Hargreave TB, Mellows HJ, Organization WH. *WHO manual for the standardized investigation and diagnosis of the infertile couple*. London: Cambridge University Press; 1993.
- Weiss RV, Clapauch R. Female infertility of endocrine origin. *Arquivos Brasileiros de Endocrinologia & Metabologia*. 2014;58(2):144–52.
- ESHRE TR, Group A-SPCW, Raji T. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertil Steril*. 2004;81(1):19–25.
- Mannerås-Holm L, Leonhardt H, Kullberg J, Jennische E, Odén A, Holm G, et al. Adipose tissue has aberrant morphology and function in PCOS: enlarged adipocytes and low serum adiponectin, but not circulating sex steroids, are strongly associated with insulin resistance. *J Clin Endocrinol Metab*. 2011;96(2):E304–11.
- Mitchell M, Armstrong D, Robker R, Norman R. Adipokines: implications for female fertility and obesity. *Reproduction*. 2005;130(5):583–97.
- Cao H. Adipocytokines in obesity and metabolic disease. *J Endocrinol*. 2014;220(2):T47–59.
- Lee S, Kwak H-B. Role of adiponectin in metabolic and cardiovascular disease. *J Exerc Rehabil*. 2014;10(2):54.
- Olshanecka-Glinianowicz M, Kuglin D, Dąbkowska-Huć A, Skałba P. Serum adiponectin and resistin in relation to insulin resistance and markers of hyperandrogenism in lean and obese women with polycystic ovary syndrome. *Eur J Obstet Gynecol Reprod Biol*. 2011;154(1):51–6.
- Spranger J, Möhlig M, Wegewitz U, Ristow M, Pfeiffer AF, Schill T, et al. Adiponectin is independently associated with insulin sensitivity in women with polycystic ovary syndrome. *Clin Endocrinol*. 2004;61(6):738–46.
- Lecke S, Morsch D, Spritzer P. Association between adipose tissue expression and serum levels of leptin and adiponectin in women with polycystic ovary syndrome. *Genet Mol Res*. 2013;12(4):4292–6.
- Lecke SB, Mattei F, Morsch DM, Spritzer PM. Abdominal subcutaneous fat gene expression and circulating levels of leptin and adiponectin in polycystic ovary syndrome. *Fertil Steril*. 2011;95(6):2044–9.
- Yannakoulia M, Yiannakouris N, Blüher S, Matalas A-L, Klimis-Zacas D, Mantzoros CS. Body fat mass and macronutrient intake in relation to circulating soluble leptin receptor, free leptin index, adiponectin, and resistin concentrations in healthy humans. *J Clin Endocrinol Metab*. 2003;88(4):1730–6.
- Plati E, Kouskouni E, Malamitsi-Puchner A, Boutsikou M, Kaparos G, Baka S. Visfatin and leptin levels in women with polycystic ovaries undergoing ovarian stimulation. *Fertil Steril*. 2010;94(4):1451–6.
- Barber T, Franks S. Adipocyte biology in polycystic ovary syndrome. *Mol Cell Endocrinol*. 2013;373(1–2):68–76.
- Svendsen PF, Christiansen M, Hedley PL, Nilas L, Pedersen SB, Madsbad S. Adipose expression of adipocytokines in women with polycystic ovary syndrome. *Fertil Steril*. 2012;98(1):235–41.
- Carmina E, Bucchieri S, Mansueto P, Rini G, Ferin M, Lobo RA. Circulating levels of adipose products and differences in fat distribution in the ovulatory and anovulatory phenotypes of polycystic ovary syndrome. *Fertil Steril*. 2009;91(4):1332–5.
- Steppan CM, Brown EJ, Wright CM, Bhat S, Banerjee RR, Dai CY, et al. A family of tissue-specific resistin-like molecules. *Proc Natl Acad Sci*. 2001;98(2):502–6.
- Filková M, Haluzik M, Gay S, Šenolt L. The role of resistin as a regulator of inflammation: implications for various human pathologies. *Clin Immunol*. 2009;133(2):157–70.
- Sarray S, Madan S, Saleh LR, Mahmoud N, Almawi WY. Validity of adiponectin-to-leptin and adiponectin-to-resistin ratios as predictors of polycystic ovary syndrome. *Fertil Steril*. 2015;104(2):460–6.
- Escobar-Morreale H, Villuendas G, Botella-Carretero J, Alvarez-Blasco F, Sancho R, Luque-Ramirez M, et al. Adiponectin and resistin in PCOS: a clinical, biochemical and molecular genetic study. *Hum Reprod*. 2006;21(9):2257–65.
- Jung C-H, Rhee E-J, Choi J-H, Bae J-C, Yoo S-H, Kim W-J, et al. The relationship of adiponectin/leptin ratio with homeostasis model assessment insulin resistance index and metabolic syndrome in apparently healthy Korean male adults. *Korean Diabetes J*. 2010;34(4):237–43.
- Hall J, Vora N, Langworthy R, Stock S, Momin A, Sherwood R, et al. Leptin/adiponectin ratio in patients with coronary heart disease: comparing subjects with and without metabolic syndrome. *Ann Clin Biochem*. 2011;48(4):327–31.
- Mojiminiyi O, Abdella N, Al Arouj M, Nakhi AB. Adiponectin, insulin resistance and clinical expression of the metabolic syndrome in patients with Type 2 diabetes. *Int J Obes*. 2007;31(2):213.
- Norata GD, Raselli S, Grigore L, Garlaschelli K, Dozio E, Magni P, et al. Leptin: adiponectin ratio is an independent predictor of intima media thickness of the common carotid artery. *Stroke*. 2007;38(10):2844–6.
- Owiredu E-W, Dontoh E, Essuman SE, Bazanfara BB. Demographic and lifestyle predictors of prehypertension: a cross-sectional study among apparently healthy adults in Kumasi, Ghana. *BioMed Res Int*. 2019;2019:9.
- WHO. Obesity and overweight: World Health Organization; 2018. <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>. Accessed 06 June 2019.
- Freedman D, Thornton J, Pi-Sunyer F, Heymsfield S, Wang J, Pierson R, et al. The body adiposity index (hip circumference÷height<sup>1.5</sup>) is not a more accurate measure of adiposity than is BMI, waist circumference, or hip circumference. *Obesity*. 2012. <https://doi.org/10.1038/oby.2012.81>.
- Team RC. R: a language and environment for statistical computing. Vienna: R Foundation for Statistical Computing; 2013.
- Campos D, Palin M, Bordignon V, Murphy B. The 'beneficial' adipokines in reproduction and fertility. *Int J Obes*. 2008;32(2):223.
- Budak E, Sánchez MF, Bellver J, Cerveró A, Simón C, Pellicer A. Interactions of the hormones leptin, ghrelin, adiponectin, resistin, and PYY3-36 with the reproductive system. *Fertil Steril*. 2006;85(6):1563–81.
- Dong M, Ren J. What fans the fire: insights into mechanisms of leptin in metabolic syndrome-associated heart diseases. *Curr Pharm Des*. 2014;20(4):652–8.

41. Baldani DP, Skrgatic L, Kasum M, Zlopasa G, Kralik Oguic S, Herman M. Altered leptin, adiponectin, resistin and ghrelin secretion may represent an intrinsic polycystic ovary syndrome abnormality. *Gynecol Endocrinol*. 2019;35:1–5.
42. Xiu-e L, He-feng H, Mei-gen L, Yi-min Z, Yu-li Q, Min-yue D. Resistin levels of serum and follicular fluid in non-obese patients with polycystic ovary syndrome during IVF cycles. *J Zhejiang Univ Sci B*. 2005;6(9):897–902.
43. Arikan Ş, Bahceci M, Tuzcu A, Kale E, Gökalp D. Serum resistin and adiponectin levels in young non-obese women with polycystic ovary syndrome. *Gynecol Endocrinol*. 2010;26(3):161–6.
44. Seow KM, Juan CC, Wu LY, Hsu YP, Yang WM, Tsai YL, et al. Serum and adipocyte resistin in polycystic ovary syndrome with insulin resistance. *Hum Reprod*. 2004;19(1):48–53.
45. Azuma K, Oguchi S, Matsubara Y, Mamizuka T, Murata M, Kikuchi H, et al. Novel resistin promoter polymorphisms: association with serum resistin level in Japanese obese individuals. *Horm Metab Res*. 2004;36(08):564–70.
46. Lee JH, Chan JL, Yiannakouris N, Kontogianni M, Estrada E, Seip R, et al. Circulating resistin levels are not associated with obesity or insulin resistance in humans and are not regulated by fasting or leptin administration: cross-sectional and interventional studies in normal, insulin-resistant, and diabetic subjects. *J Clin Endocrinol Metab*. 2003;88(10):4848–56.
47. Chen C-C, Li T-C, Li C-I, Liu C-S, Wang H-J, Lin C-C. Serum resistin level among healthy subjects: relationship to anthropometric and metabolic parameters. *Metabolism*. 2005;54(4):471–5.
48. Golbahar J, Das NM, Al-Ayadhi MA, Gumaa K. Leptin-to-adiponectin, adiponectin-to-leptin ratios, and insulin are specific and sensitive markers associated with polycystic ovary syndrome: a case–control study from Bahrain. *Metab Syndr Related Disorders*. 2012;10(2):98–102.

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