

Higher Visceral and Lower Peripheral Adiposity Characterize Fat Distribution and Insulin Resistance in Asian Indian Women with Polycystic Ovary Syndrome in Mauritius

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Keywords

Obesity · Insulin resistance · Cardiovascular risks · Visceral fat · Body composition

Abstract

Introduction: There are controversies about whether women with polycystic ovary syndrome (PCOS) show a disproportionately higher visceral adiposity, and its relevance to their higher cardiometabolic risks. We investigated in women of Asian Indian descent in Mauritius, a population inherently prone to abdominal obesity, whether those with PCOS will show a more adverse cardiometabolic risk profile that could be explained by abnormalities in fat distribution. **Methods:** Young women newly diagnosed with PCOS ($n = 25$) were compared with a reference control cohort ($n = 139$) for the following measurements made after an overnight fast: body mass index (BMI), waist circumference (WC), body composition by dual-energy X-ray absorptiometry, and blood pressure and blood assays for glycemic (glucose, HbA1c, and insulin) and lipid (triglycerides and cholesterol) profiles. **Results:** Women with PCOS showed, on average, higher BMI, WC, fat mass and lean mass ($p < 0.01$) than controls, but linear regression analyses indicate that for the same BMI (or same WC), the two groups

showed no significant differences in fat mass and lean mass. By contrast, linear regression plots indicate that for the same total fat mass, women with PCOS showed higher trunk, android, and visceral fat ($p < 0.01$); no difference in abdominal subcutaneous fat; and lower peripheral (gynoid or limb) fat ($p < 0.05$). Furthermore, women with PCOS showed higher fasting plasma insulin, insulin resistance (HOMA-IR) index, and lower insulin sensitivity index (QUICKI) (all $p < 0.001$), which were completely or markedly abolished after adjusting for visceral fat or central-to-peripheral fat ratios. **Conclusion:** In Mauritius, young women of Asian Indian descent with PCOS show altered fat distribution characterized by a disproportionately higher visceral (hazardous) adiposity in parallel to lower peripheral (protective) adiposity, which together explain their exacerbated state of hyperinsulinemia and insulin resistance.

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Introduction

Polycystic ovary syndrome (PCOS), a common endocrine disorder in reproductive-age women, is a complex multifactorial disease whose predisposing factors

have been attributed to genetics, neuroendocrine dysfunction, obesity, and lifestyle/environment [1]. Besides their increased risk for menstrual irregularity and infertility, the vast majority of women with PCOS show a constellation of cardiometabolic risks which are centered upon hyperinsulinemia and insulin resistance [2–6].

The development of obesity, which often leads to increased circulating levels of insulin and androgen, may lead to increased PCOS prevalence and exacerbate its clinical features [4, 7–10]. There are, however, controversies about whether body fat distribution patterns in women with PCOS differ from controls, and about the relevance of differences in abdominal and visceral adiposity to the pathogenesis or exacerbation of their cardiometabolic risks [11–22]. While several studies have reported higher visceral fat in women with PCOS than in controls matched for age and body mass index (BMI) [12–15, 17, 19], other studies found no differences in their fat distribution patterns, including in visceral adiposity and abdominal subcutaneous adiposity [16, 18, 20–22]. In some of these latter studies, conducted in European Caucasians [16, 18], the lack of regional differences in adiposity between women with PCOS and controls was observed despite significant differences in insulin resistance between these two groups, thereby suggesting that excessive insulin resistance in PCOS may be independent of abdominal fat and visceral adiposity. Whether these contentions can be extended to women of South Asian origins, who are known for their inherent proneness to abdominal obesity [23] and cardiometabolic diseases [24–27], are uncertain. In fact, there are recent reports that South Asians living in India show higher visceral fat associated with higher insulin resistance than BMI-matched controls [28–30]. However, because of the limitations of BMI as an index of adiposity per se, and that BMI-matching does not necessarily translate into body fat-matching, there are still uncertainties about whether the reported higher visceral fat and insulin resistance in South Asian women with PCOS are driven by overall fatness or consequential to other abnormalities in fat distribution such as lower body adiposity.

To address these uncertainties, we report here studies conducted in Mauritius, a multi-ethnic island nation in which more than two-thirds of the population are from South Asian (Indian subcontinent) ancestry [31], and where type 2 diabetes and cardiovascular diseases are the leading causes of death, contributing 19% and 21% of total mortality, respectively [32]. Furthermore, the national prevalence of obesity is high, namely, 19.2%, using the World Health Organization (WHO) BMI cutoff ≥ 30 kg/m² [33] and even higher to reach 36% in men and 42% in women using ethnic-specific BMI cut-offs [32]. The specific aims of the study were two-folds:

- to explore potential differences in body fat distribution (relative to total body fat) between young Indian women with newly diagnosed PCOS and healthy controls and
- to investigate the extent to which differences in insulin resistance and cardiometabolic health markers between these young women with PCOS and controls may be explained by differences in visceral adiposity or other abnormalities in body fat distribution.

Methods

The participants in the study conducted in Mauritius were young women of South Asian (Indian) ethnicity, whose ancestors originated from the Indian subcontinent, mostly from the North, East, and South-Eastern provinces of India [34]. They comprised a group of women with PCOS ($n = 25$) who were compared with a large cohort of healthy controls ($n = 139$); the subjects in both groups were living within the same geographic areas (central districts) on the island. All women in the PCOS group were newly diagnosed PCOS patients; the diagnosis was based on the Rotterdam criteria [35], i.e., presence of two of the following three criteria: androgen excess, oligomenorrhea, or polycystic ovaries. Women with PCOS were recruited from the gynecology unit of the main government hospitals on the island, within a few weeks after their diagnosis of PCOS, after approval from their consultant gynecologists and/or obstetricians. Participants (in both PCOS and control groups) were eligible if they were women of 18–40 years of age, without diabetes, not on medication, with relatively stable body weight (defined as $<3\%$ variation during the past 3 months), and non-physically active as defined by the Sedentary Behaviour Research Network [36]. Smokers, people who regularly consume alcoholic drinks, and pregnant or breastfeeding women were excluded. Control participants were recruited from the staff populations of two major hospitals on the island and among students at the nursing school. Participation was requested from healthy women with regular menstrual cycles and with no history of hirsutism. All participants (women with PCOS and controls) lived in urban and sub-urban areas. As Mauritius is a very small island with a high population density (634 per km²) [37], the distinction between urban, sub-urban, and rural is narrow.

Anthropometry

Body weight was measured using an electronic weighing scale (Tanita Corporation, Tokyo) and height was measured using a portable stadiometer (Tanita

Table 1. Age, anthropometry, and body composition of women with PCOS and controls (mean $\pm$ SD)

	Control (n = 139)	PCOS (n = 25)	p value
Age, years	26.6 $\pm$ 6.1	26.6 $\pm$ 5.6	NS
Height, m	1.59 $\pm$ 0.06	1.58 $\pm$ 0.07	NS
Weight, kg	62.7 $\pm$ 16.9	70.5 $\pm$ 17.6	*
BMI, kg/m ²	24.8 $\pm$ 6.2	28.1 $\pm$ 6.2	**
WC, cm	86.7 $\pm$ 13.6	93.1 $\pm$ 14.0	*
Body composition			
Fat-free mass index, kg/m ²	14.3 $\pm$ 2.4	15.6 $\pm$ 2.2	**
Appendicular lean mass index, kg/m ²	6.04 $\pm$ 1.22	6.66 $\pm$ 1.13	**
Fat mass index, kg/m ²	10.5 $\pm$ 3.9	12.4 $\pm$ 4.0	*
Bone mineral content, kg	1.84 $\pm$ 0.26	1.80 $\pm$ 0.26	NS
Bone mineral density, g/cm ²	1.04 $\pm$ 0.07	1.02 $\pm$ 0.07	NS
WHO BMI classification for Asians			
Percentage with overweight, BMI $\geq$ 23 to <27.5 kg/m ²	23.7	32	
Percentage with obesity, BMI $\geq$ 27.5 kg/m ²	30.2	52	
Percentage with overweight or obesity, BMI $\geq$ 23 kg/m ²	53.9	84	

* $p < 0.05$; ** $p < 0.01$; NS: not significant; SD, standard deviation.

Leicester Height Measure, Leicester, UK). Waist circumference (WC) was measured at the navel level using a non-stretchable tape and according to the Standardization Reference Manual of Lohman et al. [38].

Body Composition and Fat Distribution

Whole body composition was determined by dual-energy X-ray absorptiometry (DXA) using a HologicTM Horizon[®] QDR[®] WI System (Hologic Inc., Bedford, MA, USA) and according to guidelines for DXA procedures [39]. Scans were also analyzed to estimate the regional fat mass using the standardized regions specified by the manufacture for Trunk (region includes the neck, chest, and abdominal and pelvic areas), android (area overlying the abdomen between the ribs and the pelvis), gynoid (hips and upper thigh, and portion of the legs from the greater femoral trochanter, extending caudally to the mid-thigh), and appendicular or limb fat (the sum of fat mass of the arms and legs). The visceral adipose tissue mass (also referred to as visceral fat) was assessed in the visceral regions that occupy a band crossing the subject's abdominal cavity between the pelvis and the rib cage using the Hologic Visceral Fat software. Abdominal subcutaneous fat (i.e., subcutaneous fat in the android region) was calculated as the difference between android fat and visceral fat. Peripheral adiposity refers to gynoid fat or appendicular (limb) fat.

Blood Assays and Blood Pressure

Resting blood pressure (BP) (systolic and diastolic) was measured by oscillometry using an OMRON[®] M2 automatic BP monitor (OMRON Healthcare Ltd., Milton Keynes, UK), after which a blood sample was collected. HbA1c was measured on the same day on whole blood by HPLC (TosohG8, Tosoh Bioscience Inc., Tokyo, Japan). The other blood parameters were measured from plasma or serum (obtained by centrifugation and stored at -20°C until later assays) using automated clinical analyzers (Abbott Architect c8000 and i2000, Illinois, USA), namely, plasma glucose and insulin, and serum concentrations of triglycerides, total cholesterol, and HDL cholesterol. The serum value for LDL cholesterol was calculated using the Friedewald formula [40]. The Homeostatic Model Assessment for insulin resistance (HOMA-IR) was used to determine the insulin resistance status of the subjects [41]. The Quantitative Insulin Sensitivity Check Index (QUICKI) was also used to calculate insulin sensitivity [42].

Data Analysis and Statistics

Data analyses were performed using statistical software (STATISTIX version 8.0; Analytical Software, St Paul, MN, USA), and the figures were made using Graphpad Prism Software (version 9.3.1 for Windows, San Diego, CA, USA). The tabulated data are presented as mean $\pm$ standard deviation.

Table 2. Analysis of DXA-derived central, peripheral, and central-to-peripheral adiposity indices in women with PCOS and in controls (mean $\pm$ SD)

	Control (<i>n</i> = 139)	PCOS (<i>n</i> = 25)	<i>p</i> value
Central adiposity, kg			
Trunk	11.8 $\pm$ 5.3	14.9 $\pm$ 5.7	**
Android	1.96 $\pm$ 0.96	2.55 $\pm$ 1.09	**
Visceral	0.402 $\pm$ 0.193	0.557 $\pm$ 0.248	**
Subcutaneous	1.56 $\pm$ 0.79	1.99 $\pm$ 0.87	**
Peripheral adiposity, kg			
Gynoid	4.86 $\pm$ 1.68	5.38 $\pm$ 1.80	NS
Limb (appendicular)	13.7 $\pm$ 5.3	15.4 $\pm$ 5.7	NS
Central-to-peripheral adiposity indices, ratio			
Trunk/gynoid	2.39 $\pm$ 0.46	2.73 $\pm$ 0.54	**
Android/gynoid	0.391 $\pm$ 0.09	0.464 $\pm$ 0.10	***
Visceral/gynoid	0.0819 $\pm$ 0.028	0.103 $\pm$ 0.037	**
Subcutaneous/gynoid	0.309 $\pm$ 0.072	0.361 $\pm$ 0.073	***
Trunk/limb	0.853 $\pm$ 0.159	0.963 $\pm$ 0.208	**
Android/limb	0.140 $\pm$ 0.033	0.164 $\pm$ 0.042	**
Visceral/limb	0.029 $\pm$ 0.010	0.036 $\pm$ 0.013	**
Subcutaneous/limb	0.111 $\pm$ 0.026	0.128 $\pm$ 0.030	**

p* < 0.01; *p* < 0.001; NS = not significant; SD, standard deviation.

The Wilcoxon rank-sum test was used to examine the significance of differences between the two groups (PCOS vs. control), and the analysis of variance and covariance was applied to examine the extent to which any between-group significant difference for a given cardiometabolic parameter is altered after adjustments for potential anthropometric and body composition covariants. Because of their skewed distributions, the values of blood triglycerides and insulin, as well as the HOMA-IR index, were logarithmically transformed to normalize the distribution prior to the application of statistical analyses. Linear model procedures were also applied for statistical comparisons of two regression lines for equality of variance, slopes, and elevations (that is, y-intercepts). The analytical software for comparison of regression lines utilizes the analysis of covariance. For all tests, significance was set at *p* < 0.05.

Results

Anthropometry

The subjects in the PCOS and control groups were of the same age (mean/median ~26.5 years) and age range (19–40 years), and did not differ significantly in height (Table 1). The PCOS group, however, weighed more than the control group, with a mean body weight difference of 7.8 kg (*p* < 0.05), and had a higher mean BMI (+3.3 units, *p* < 0.001) and a greater mean WC (+6.4 cm, *p* < 0.05). The proportion of participants classified as being with overweight or obesity

using BMI cut-off for Asians (BMI $\geq$ 23 kg/m²) was greater in the PCOS group than in controls (84% vs. 54.5%). Furthermore, the proportion of subjects classified with central (abdominal) obesity, as defined by WC $\geq$ 80 cm, was also high in both groups but higher in those with PCOS than in controls (84.0% vs. 65.5%).

Body Composition

The data on whole-body composition measured by DXA are also presented in Table 1. Compared to the control group, the PCOS group shows significantly higher mean values for fat mass, fat-free mass, and appendicular (soft) lean mass, even after adjusting for height, as shown by their higher values for fat mass index, fat-free mass index, and appendicular lean mass index. Similarly, compared to controls, women with PCOS, on average, showed significantly higher values for various measures or indices of central adiposity and for central-to-peripheral adiposity ratios (Table 2).

However, the application of linear regression analyses indicates no significant between-group differences in their relationships between fat-mass index (or fat-free mass index) and BMI, as well as between trunk fat and WC, as judged by the lack of statistically significant y-intercepts (elevations) when comparing the PCOS and control groups, as shown in Figure 1 (panels a–c respectively). Similarly, no significant between-group differences are observed in the relationships between the appendicular lean mass index and BMI or between trunk lean mass and WC (data not shown). These results thus indicate that for

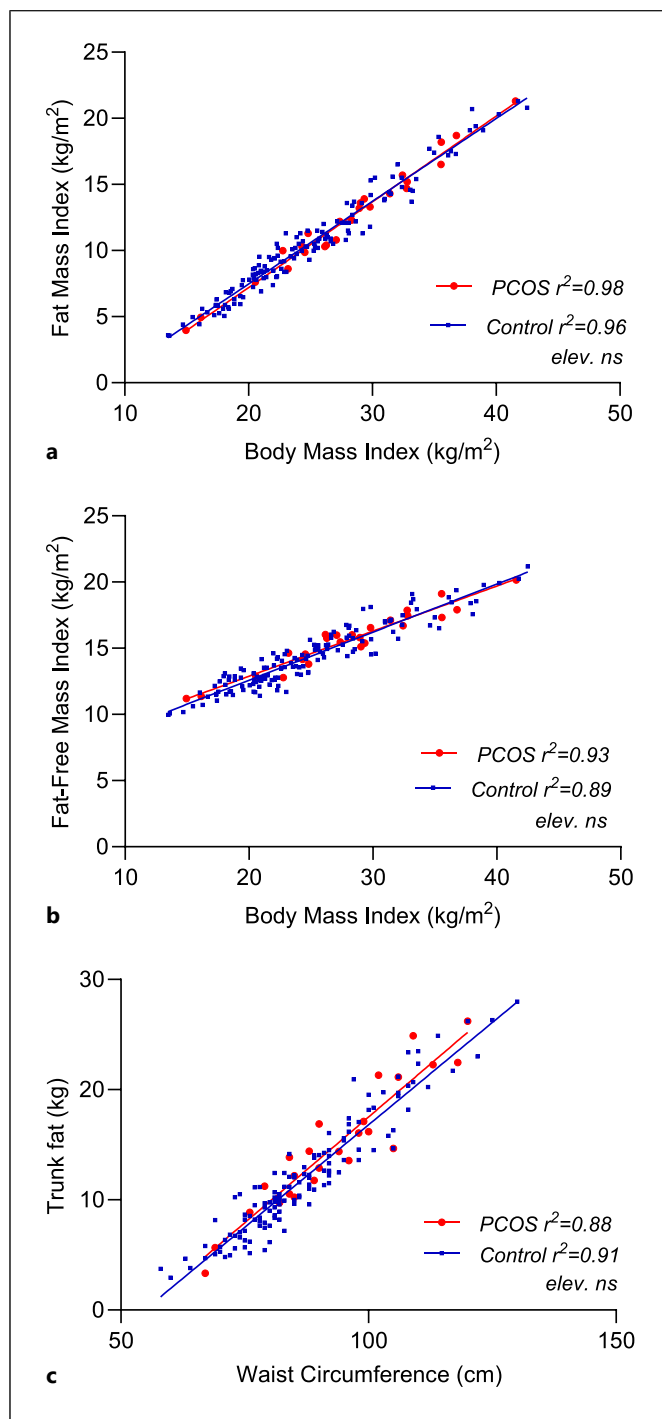


Fig. 1. Relationship between adiposity and anthropometry. Plots of total body fat as fat mass index vs. body mass index (**a**), total fat-free mass as fat-free mass index vs. body mass index (**b**), and trunk fat vs. waist circumference (**c**). Within each panel, *elev.* refers to statistical significance in the elevation between the two regression lines, that is, in their y-intercepts.

the same BMI, women with PCOS show similar total fat mass and lean mass as control subjects, and that for the same WC, women with PCOS show similar trunk fat mass and trunk lean mass as the controls.

By contrast, significant between-group differences are observed for linear regression plots of central or peripheral adiposity as a function of total fat mass. As shown in Figure 2 (panels a–c), significant differences are observed in the y-intercepts for trunk fat vs. total fat (PCOS more elevated than controls, $p = 0.01$), as well as for gynoid fat or limb fat vs. total fat (PCOS less elevated than controls, $p < 0.05$ and $p < 0.01$, respectively). Linear regression plots, presented in Figure 2 (panels d, e), also show significant differences between android fat or visceral fat vs. total fat (PCOS more elevated than controls, $p < 0.01$), which contrast with the lack of significant differences (NS) between the two groups in the relationship between abdominal subcutaneous fat vs. total fat (Fig. 2, panel f). Taken together, these results indicate that relative to total body fat, the subjects with PCOS show disproportionately higher central adiposity (characterized by higher visceral fat) and lower peripheral adiposity (characterized by lower gynoid and limb fat) than controls.

Cardiometabolic Health Markers

The results, shown in Table 3, indicate that compared to the control group, the group with PCOS showed no significant differences in fasting plasma glucose and HbA1c (a marker of chronic glycemic control), but a significantly higher plasma insulin (+5.4 units, $p < 0.001$), higher HOMA-IR index (+1.5 units, $p < 0.001$), and lower QUICKI (0.32 vs. 0.34, $p < 0.001$). No significant between-group differences are found in the plasma lipid profile (triglycerides and cholesterol) and in BP (systolic or diastolic).

The application of co-variance analysis, with various measures or indices of body composition as covariants, indicates that the highly significant differences observed between women with PCOS vs. controls for plasma insulin, HOMA-IR index, and QUICKI (all $p < 0.001$) were completely abolished (NS) only after adjusting for visceral fat among the various central adiposity indices, as well as after adjusting for the android/gynoid fat ratio (Table 4). They were also markedly reduced after adjusting for the other ratios of central-to-peripheral adiposity, but only marginally reduced after adjusting for indices of peripheral adiposity or for whole-body fat mass and lean mass. Furthermore, in a multiple regression analysis, in which independent variables that are too highly correlated with a linear combination of other independent variables in the

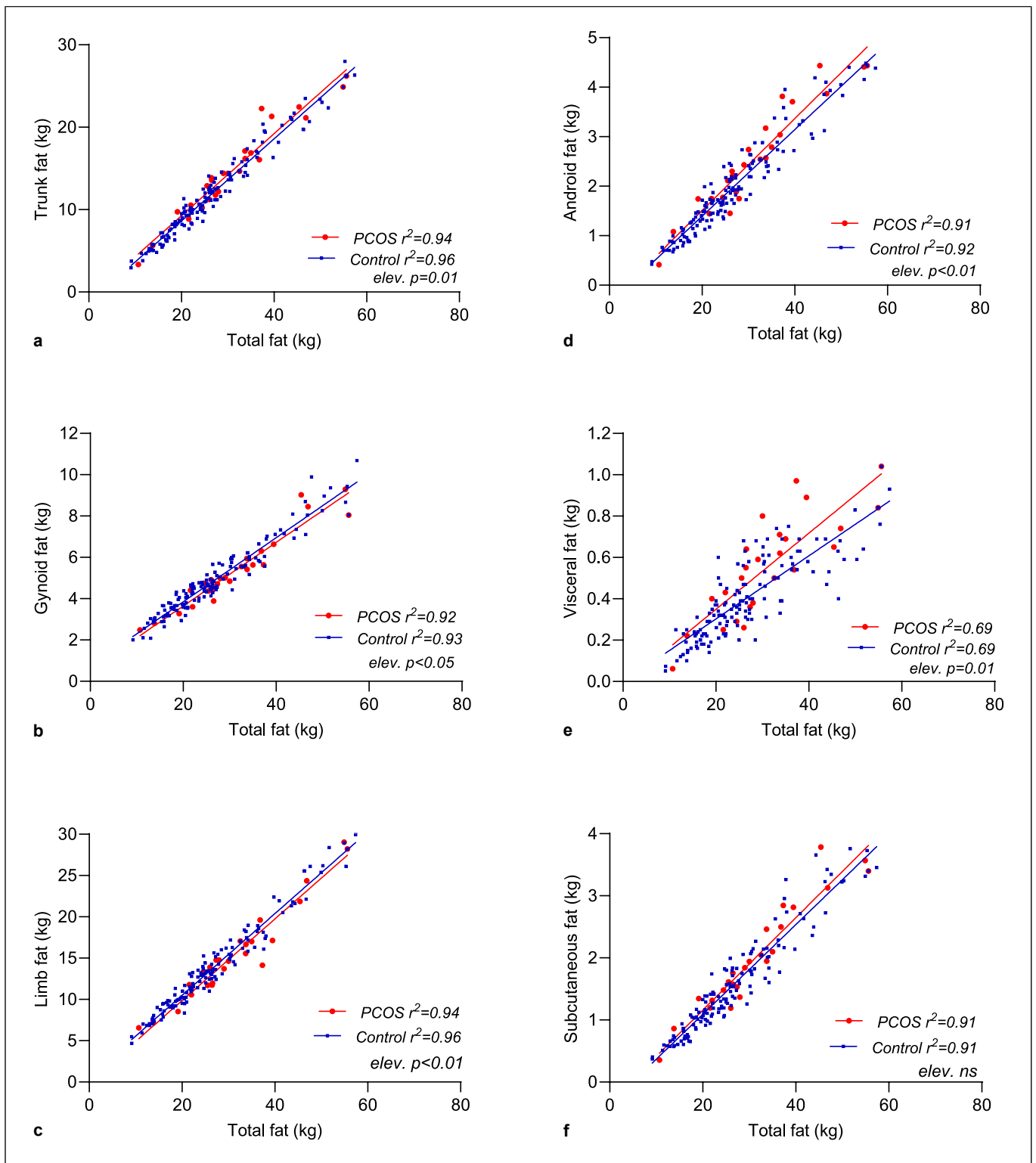


Fig. 2. Relationship between adiposity compartments and total body fat. Plots of trunk fat (**a**), gynoid fat (**b**), and limb fat (**c**) vs. total fat. Plots of android fat (**d**), visceral fat (**e**), and subcutaneous android fat (**f**) vs. total fat. Within each panel, elev. refers to statistical difference in the elevation between the two regression lines, that is, in their y-intercepts.

Table 3. Cardiometabolic parameters in women with PCOS compared to a control group

Fasting plasma/serum concentration	Control (n = 139)	PCOS (n = 25)	p value
Glycemic profile			
Glucose, mmol/L	5.10±0.97	5.43±1.78	NS
HbA1c, %	5.60±0.69	5.78±1.20	NS
Insulin, µU/mL	10.8±5.8	16.2±9.0	***
HOMA-IR	2.54±1.78	3.99±2.75	***
QUICKI	0.342±0.026	0.322±0.027	***
Lipid profile			
Triglycerides, mmol/L	0.995±0.48	1.14±0.59	NS
Total cholesterol, mmol/L	4.61±0.89	4.66±1.14	NS
HDL-cholesterol, mmol/L	1.29±0.25	1.27±0.29	NS
LDL-cholesterol, mmol/L	2.92±0.79	2.93±1.06	NS
BP			
Systolic BP, mm Hg	106±12	101±12	NS
Diastolic BP, mm Hg	75.6±9.3	72.3±10.0	NS
***p < 0.001; NS, not significant.			

model (collinearity) are dropped from the model, both visceral fat and the android/gynoid fat ratio were retained as statistically significant independent predictor variables for plasma insulin, HOMA-IR index, and QUICKI (Table 5).

Sensitivity Analysis

It should be noted that the above results are based on participants who were recruited a priori without known type 2 diabetes, but that a few of these young adults (5 among the controls and 2 among those with PCOS) were subsequently diagnosed with type 2 diabetes (HbA1c >6.5%). However, sensitivity analysis indicated that their inclusion or exclusion has no impact on the above results.

Discussion

An inherently high susceptibility to develop abdominal obesity is believed to be a key factor in the proneness of people of South Asian origins to develop type 2 diabetes and cardiovascular diseases [23–27]. In the reference control cohort in the present study and consisting of young Mauritian women of Asian Indian ethnicity, two-thirds of these participants showed abdominal obesity (defined as WC in excess of 80 cm), and a third could be characterized as people with pre-diabetes (HbA1c 5.7–6.5%). Such high prevalence of abdominal obesity and pre-diabetes in this reference cohort reflects the outcome of national surveys of the past 2 decades in their characterization of Mauritian of Indian ethnicity as a population with a high predisposition to abdominal obesity and type 2 diabetes [43–48]. The main

findings of the present study is that when compared with this reference control group, the Mauritian Indian women with PCOS show further abnormalities in fat distribution characterized by a disproportionately higher abdominal and visceral adiposity in parallel to lower peripheral adiposity, and that this shift in fat distribution could explain their higher insulin resistance. Furthermore, as the inclusion or exclusion of the few subjects diagnosed with type 2 diabetes has no impact on our results, this research outcome and conclusions can be viewed as one based on young Mauritian women essentially without type 2 diabetes.

Body Composition and Fat Distribution

The observation in our study that women in the PCOS group showed higher mean values for BMI, WC, and for various indices of adiposity and lean mass than the control group reflects the greater proportion of subjects with high BMI or high WC, and hence an obesity-driven greater fat mass and lean mass in those with PCOS. However, as the application of regression analyses indicates, when total fat mass (or lean mass) indices are linearly regressed against BMI, as well as when trunk fat mass (or lean mass) is regressed against WC, there are no significant differences between those with PCOS and controls. These findings therefore suggest that for the same BMI (or same WC) across the wide range studied, the Mauritian Indian women with PCOS are not different from the controls in whole-body composition (fat mass and lean mass).

By contrast, regression analyses of the measures of central adiposity (trunk and android), or peripheral adiposity (gynoid and limb), against total body fat indicate that

Table 4. Analysis of the effect of PCOS on cardiometabolic risk markers before adjustments (“unadjusted” row, $p < 0.001$) and after adjustments for various adiposity and lean mass parameters as covariates

PCOS versus control	Insulin	HOMA-IR	QUICKI
<i>Unadjusted</i>	***	***	***
<i>Adjusted for covariates</i>			
Whole-body adiposity			
Fat mass	**	**	**
Fat mass index	**	**	**
Central adiposity			
Trunk	**	**	*
Android	*	*	*
Visceral	NS	NS	NS
Subcutaneous	**	**	*
Peripheral adiposity			
Gynoid	**	**	**
Limb (appendicular)	**	**	**
Central-to-peripheral adiposity			
Trunk/gynoid	*	*	*
Android/gynoid	NS	NS	NS
Visceral/gynoid	*	*	*
Subcutaneous/gynoid	*	*	*
Trunk/limb	*	*	*
Android/limb	*	*	*
Visceral/limb	*	*	*
Subcutaneous/limb	*	*	*
Lean mass and lean mass indices			
Fat-free mass	**	**	**
Fat-free mass index	**	**	**
Appendicular lean mass	**	**	**
Appendicular lean mass index	**	**	**

A marginal and modest impact of the covariate in abolishing partially is shown as $p < 0.01$ and $p < 0.05$, respectively, while the impact of covariate in abolishing completely the significant effect is shown as “NS.”
 * $p \leq 0.05$; ** $p \leq 0.01$; *** $p < 0.001$; NS, not significant.

Table 5. Multivariate regression analysis of log-transformed plasma Insulin and HOMA-IR, as well as QUICKI against indices of adiposity

Predictors	Plasma insulin		HOMA-IR		QUICKI	
	β value	p value	β value	p value	β value	p value
Visceral fat	0.84	<0.001	0.86	<0.01	−0.041	<0.01
Android/gynoid fat	1.80	<0.001	2.14	<0.001	−0.11	<0.001
Overall model						
Adjusted r^2	0.45		0.44		0.45	
ANOVA p value	$p < 0.001$		$p < 0.001$		$p < 0.001$	

compared to controls, women with PCOS show a different fat distribution pattern that is characterized by a disproportionately greater central adiposity in parallel to a lower

peripheral adiposity. Furthermore, the findings that women with PCOS differ from controls in their more elevated line of regression for visceral fat vs. total body fat, but not for

abdominal subcutaneous fat in the android region vs. total fat mass, underscore an intrinsic android pattern of adiposity that is characterized by a disproportionately higher visceral adiposity in women with PCOS.

Taken together, the higher central and visceral adiposity, concomitant to lower peripheral adiposity, could thus constitute a “double hazard” for cardiometabolic risks in women with PCOS. On the one hand, an expansion of abdominal adiposity, and in particular visceral adiposity, through the secretion of fatty acids and pro-inflammatory cytokines, can lead to insulin resistance and increased risks for cardiometabolic disease [49]. On the other hand, a reduction in peripheral adiposity can also be hazardous since subcutaneous adipose tissue in periphery (e.g., gluteofemoral) has been shown to be protective against cardiometabolic risks through the release of anti-inflammatory cytokines, and by its capacity to metabolize and store (and hence buffer against) excess circulating glucose and free fatty acids [50–52].

Impact of Fat Distribution and Insulin Resistance

Indeed, the significant effect of PCOS on plasma insulin and HOMA-IR index (higher in women with PCOS than in controls), as well as in a lower insulin sensitivity index (QUICKI), was found to be completely abolished or markedly reduced after adjusting for the visceral component of android adiposity or for the various ratios of central-to-peripheral adiposity. In fact, the outcome of a multiple regression analysis revealed that both visceral fat and the ratio of android/gynoid fat were retained as independent predictor variables for both plasma insulin and the insulin resistance (HOMA-IR) index, as well as for QUICKI. Taken together, these findings underscore the tendency in women with PCOS for a “masculinized” body fat distribution pattern, characterized by less of the protective gluteofemoral and thigh subcutaneous adiposity in the gynoid region and more hazardous visceral adiposity, thereby contributing to their increased susceptibility for insulin resistance and compensatory hyperinsulinemia. Such findings are consistent with a recent report that differences in atherogenic cardiometabolic risks due to sex in young Mauritians are best defined by a higher ratio of visceral-to-peripheral adiposity [53]. From a mechanistic standpoint, our findings are also strongly supported by the recent report that the gluteofemoral adipose tissues of women with PCOS show impaired adipogenesis (and hence limited expansion capacity) characterized by abnormal adipose-derived stem cell transcriptome and methylome, in parallel with a more pronounced pro-inflammatory state of their adipose-derived stem cells in the abdominal adiposity depot [54].

Study Limitations and Strength

A main limitation in this exploratory study is the relatively small number of Asian Indian women in the PCOS group. However, this limitation is partly offset by a relatively homogeneous and well-defined population sample, with participants selected as young women with no known diabetes, taking no medication, not smoking, not consuming alcohol regularly, and having a relatively sedentary lifestyle. These selective criteria thus obviate the need to adjust for these well-known clinical and lifestyle confounders for body composition and cardiovascular risk, and thus the need for a large sample size. Furthermore, the wide range of BMI and WC (and hence body composition) in women with PCOS and in the reference control cohort is consistent with the conditions for an appropriate analytical procedure centered on regression models and analysis of co-variance. Because of limitations of BMI and WC as indices of total adiposity and central adiposity per se, and in particular BMI-matching and WC matching do not necessarily translate into body fat-matching, these regression approaches are more sensitive than comparing women matched for BMI and/or WC in revealing group differences in fat distribution patterns and their impact on cardio-metabolic risk. Another limitation of this study is that the possibility of undiagnosed or undetected PCOS among the control participants cannot be ruled out. If present, however, it would have contributed to the underestimation of the true magnitude of differences observed between the two groups.

Conclusions

This study in young Mauritian women of Asian Indian ethnicity indicates that those with PCOS have an intrinsic android pattern of adiposity characterized by a disproportionately higher visceral adiposity and in parallel to a lower peripheral adiposity, which together could contribute to their more adverse state of insulin resistance. The limited number of subjects used in this first exploratory study would need to be expanded to confirm such abnormalities in fat distribution among Asian Indian women with PCOS. To what extent such abnormalities in fat distribution of women with PCOS is specific to young adults of South Asian origins or also occur among those of other ethnicities in Mauritius and in other countries warrants further investigations. Furthermore, and of particular relevance to Small Island Developing States like Mauritius, where the populations tend to exhibit a higher biological expression of disease phenotypes [55], there is a need to address the causes of the adverse fat distribution pattern in the context of non-communicable diseases

intersecting with an environment characterized by rapid urbanization, environmental pollution, food insecurity, and climatic change.

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Statement of Ethics

This study was conducted in accordance with the guidelines of the Declaration of Helsinki. This study was approved by the following ethical review board: the Ethics Committee of the Ministry of Health and Wellness, Republic of Mauritius; the ethical approval reference number/code: MHC/CT/NETH/RAME. Written informed consent was obtained from participants to participate in the study.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

N.J., V.R., and A.D. were involved in the study planning and design; V.R., B.N.R., N.J., and S.H. contributed to data collection and sample analysis; A.D., V.R., J.-P.M., and Y.S. contributed to data analysis and interpretation; A.D. and V.R. wrote the initial draft of the manuscript; and J.-P.M., Y.S., N.J., and S.H. contributed towards its final version. All authors read and approved the final version.

Data Availability Statement

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the corresponding author (A.D.) upon reasonable request.

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