Neck Circumference Is a Reliable Predictor for Hyperuricemia in Women With Polycystic Ovary Syndrome: a Case Control Study

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Research

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Abstract

Background: The prevalence of hyperuricemia in the women with polycystic ovary syndrome (PCOS) is almost threefold higher than that in women without PCOS. Both PCOS and hyperuricemia are considered risk factors of metabolic disorders, including hypertension, diabetes and cardiovascular diseases. Previous study has indicated that neck circumference (NC) is a good predictor for insulin resistance in women with PCOS. The present analysis thus aims to assess the predictive value of NC for hyperuricemia in women with PCOS.

Methods: This is a cross-sectional study that recruited one hundred ninety women with PCOS from January 2018 to December 2019. PCOS was diagnosed according to the Rotterdam definition. Hyperuricemia was defined as serum uric acid level of at least 357 $\mu\text{mol/L}$.

Results: PCOS females with hyperuricemia had significantly greater values of NC, body mass index (BMI), waist circumference (WC) and hip circumference (HC). NC was positively associated with serum uric acid levels, with a standardized regression coefficient of 0.34 after adjusting for confounding factors. Furthermore, logistic regression analysis showed that NC was significantly associated with an increased risk of hyperuricemia, with an adjusted odds ratio of 1.58. The associations between NC and serum uric acid levels were more evident in those with medium BMI ($22.02 \text{ kg/m}^2 \leq \text{BMI} < 25.08 \text{ kg/m}^2$), low WC ($\text{WC} < 85 \text{ cm}$) or medium HC ($90 \text{ cm} \leq \text{HC} < 96 \text{ cm}$). The optimal cutoff point of NC in predicting hyperuricemia was 32.0 cm (Youden index = 0.48), with the sensitivity and negative predictive value of 87.23% and 93.68%, respectively.

Conclusions: Neck circumference is positively correlated with hyperuricemia and has a high negative predictive value for hyperuricemia in women with PCOS. Therefore, we suggest NC as a simple, novel, and reliable anthropometric measure to be used in the routine clinical assessment of women with PCOS to screen those at high risk of hyperuricemia.

Background

Polycystic ovary syndrome (PCOS) is one of the most common endocrine and metabolic disorders in reproductive-aged individuals, with an incidence of 3%-20% according to different diagnostic criteria(1–3). Women with PCOS are characterized by symptoms of hirsutism or oligo/amenorrhea or when resorting to infertility care in early adulthood(4). In addition to reproductive disorders, PCOS is also closely related to a variety of metabolic abnormalities, including insulin resistance, diabetes, dyslipidemia and cardiovascular disease, which exert negative and life-long impacts on quality of life(5).

Uric acid is a metabolite produced during purine metabolism, and elevated serum uric acid levels have been demonstrated as a risk factor of metabolic disorders, including hypertension, diabetes and cardiovascular diseases(6). In addition to the effect on metabolism, recent review suggests that there is a close relationship between serum levels of uric acid and female reproductive disorders(7). Previously, our study demonstrated that the prevalence of hyperuricemia in the PCOS population was almost threefold

higher than that in women without PCOS(8). Moreover, serum uric acid can be used as a predictor of adverse pregnancy and foetal outcomes(9, 10). Therefore, the early detection and intervention of hyperuricemia is of great significance for the health of women with PCOS. However, the detection of serum uric acid levels is time-consuming, and it requires professional personnel and specific equipment, which is unapplicable to clinical practice on a large scale, especially in some rural places. In contrast, measuring anthropometric indices such as body mass index (BMI), neck circumference (NC), waist circumference (WC) and hip circumference (HC) using tape or a scale is relatively easy(11). It has been confirmed that BMI(12–14), waist circumference(15–17) and hip circumference are positively correlated with the risk of hyperuricemia in different populations. However, it is not always feasible and accurate to measure WC, HC and BMI in the winter with heavy clothes or postprandially. Therefore, there is a need for a reliable, simple and fast method to identify hyperuricemia early in clinical practice.

Neck circumference (NC) is a convenient anthropometric parameter that reflects the subcutaneous fat tissue of the upper body(18). Our previous study found that in PCOS women with obesity, the prevalence of hyperuricemia was approximately threefold higher than that in PCOS women with normal BMI(8). Therefore, we hypothesized that NC might be a good predictor for hyperuricemia in women with PCOS. It has been reported that NC is a potential predictor of hyperuricemia in the general population(19, 20). However, to the best of our knowledge, there are currently limited studies focused on assessing the association between NC and hyperuricemia in women with PCOS. Thus, we conducted a retrospective study to examine whether NC was a good predictor for hyperuricemia and to determine the optimal cutoff points of NC for hyperuricemia in PCOS.

Patients And Methods

Participants

This was a cross-sectional study that enrolled 229 PCOS females aged between 20 and 40 years from January 2018 to December 2019 at the reproductive center of the First Affiliated Hospital of Wenzhou Medical University. The exclusion criteria were as follows: 1) patients with other causes of hyperandrogenemia, including congenital adrenal hyperplasia, androgen-secreting neoplasms, and Cushing's syndrome; 2) patients with any medical intervention or diseases that could alter the neck circumference, including neck surgery, neck malformation, thyroid dysfunction, thyromegaly, and regular oral glucocorticoid treatment; and 3) patients with incomplete information for anthropometric parameters or laboratory examination. Finally, 190 (83.0%) patients were included for further analysis. This study was approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University. Written informed consent for the whole procedure was obtained from each patient. The study protocol conforms to the ethical guidelines of the Declaration of Helsinki as reflected in the a prior approval by the institution's human research committee.

Definitions

Polycystic ovary syndrome was diagnosed according to the Rotterdam definition, in which two of the following three criteria should be met: 1) oligomenorrhoea or amenorrhea (less than eight menstrual cycles in 12 months, or if the menstrual interval was more than 35 days); 2) biochemical or clinical hyperandrogenism (such as hirsutism and acne); and 3) characteristic image of polycystic ovaries (at least one ovary containing 12 or more peripheral follicles measuring 2–9 mm in diameter and/or ovarian volume of at least 10 mL) on transvaginal or abdominal ultrasound(21). Hyperuricemia was defined as an SUA level of at least 357 $\mu\text{mol/L}$ (22).

Anthropometric and laboratory measurements

The anthropometric measurements included BMI, NC, WC, HC and blood pressure. BMI was calculated as the body weight in kilograms divided by the body height in meters squared(23). Neck circumference was measured using a flexible tape, with the subject remaining standing, head held erect, at the level of the thyroid cartilage(24). WC was measured at the midpoint between the lowest rib and the iliac crest, and HC was measured at the greater trochanter(25). Blood pressure was measured with an electronic sphygmomanometer in the sitting position after 10 min of rest. Fasting blood samples were collected after an overnight fast of at least 8 hours during the 2nd to 5th day of the menstrual cycle to measure hormonal and metabolic parameters. All biochemical measurements were tested in the central laboratory of the First Affiliated Hospital of Wenzhou Medical University. Serum LH, FSH, E2 and testosterone were measured using an autoimmunoassay analyzer [Unicel Dxl 800, Beckman Coulter, USA]. Fasting plasma glucose, total cholesterol (TC), serum triglycerides (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were quantified by an autoanalyzer [AU 5800, Beckman, USA].

Statistical analysis

Statistical analyses were performed using SPSS version 23.0 software (IBM Corporation), and receiver operating characteristic (ROC) analyses were conducted using MedCalc Application version 19.7.2 software. Data are presented as the median (interquartile range) or as the mean $\pm$ standard deviation for continuous variables. Skewness and kurtosis tests for normality were performed and found that the level of basal LH, basal FSH, LH/FSH ratio, basal E2, AMH, FINS, HOMA-IR, HOMA- β , TG, and uric acid did not follow normal distributions. Variables with skewed distributions were logarithmically transformed before statistical analysis. Differences between the two groups were analyzed by using Student's t test for normally distributed continuous variables and the Kruskal-Wallis test for those with skewed distributions. Multivariable linear regression was used to explore the association of NC with serum uric acid level (log-transformed) in different models with adjustment for potential confounders. Binary logistic regression analysis was used to calculate the odds ratios (OR) and 95% confidence interval (CI) of NC for hyperuricemia. For both logistic regression analyses and multivariable linear regression, no variables were adjusted in model 1. Adjusted variables in model 2 included age, SBP, and DBP. In model 3, TG (log-transformed), HDL, FINS (log-transformed), HOMA-IR (log-transformed), HOMA- β (log-transformed) and eGRF (log-transformed) were further adjusted. The interactions of NC with BMI, WC and HC were tested using binary logistic regression. Patients enrolled were stratified into quartiles according to their NC and

stratified into low, medium and high groups according to the tertiles of BMI, WC and HC. Receiver operating characteristic (ROC) curves were used to compare the predictive ability of NC, BMI, WC and HC for hyperuricemia by calculating the area under the curve (AUC). The Youden index, defined as sensitivity + specificity – 1, was calculated to identify the optimal cutoff points. The sensitivity and specificity of NC, BMI, WC and HC as well as positive and negative predictive values were calculated for each cutoff point in the sample. All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant.

Results

Baseline characteristics in women with PCOS

The baseline characteristics categorized by the existence of hyperuricemia in women with PCOS are presented in Table 1. The prevalence of hyperuricemia in women with PCOS was 24.74%. Age was matched between the two groups. Compared with women with PCOS without hyperuricemia, women with PCOS with hyperuricemia had significantly greater BMI, NC, WC, HC, SBP, DBP, fasting insulin, HOMA-IR, HOMA- β , TG and serum uric acid levels and lower HDL levels (all $P < 0.05$). There were no significant differences between the two groups in basal hormone levels (LH, FSH, E2, T, AMH), LH/FSH ratio, FBG, TC, LDL or eGFR.

Table 1
Baseline characteristics of women with PCOS

Variables	HUA	Non-HUA	Pvalue
Number	47	143	-
Age (year)	30.02 ± 3.79	29.58 ± 3.94	0.50
BMI (kg/m ²)	26.10 ± 3.20	22.99 ± 2.92	< 0.001
NC (cm)	34.57 ± 2.22	32.12 ± 2.15	< 0.001
WC (cm)	86.06 ± 8.16	78.45 ± 8.71	< 0.001
HC (cm)	98.11 ± 6.69	91.95 ± 6.34	< 0.001
SBP (mmHg)	122.70 ± 10.62	110.42 ± 12.40	< 0.001
DBP (mmHg)	79.57 ± 8.58	73.50 ± 8.50	< 0.001
Basal LH (IU/L)	5.90 (4.05–9.11)	6.42 (4.27–9.39)	0.54
Basal FSH (IU/L)	6.70 (5.64–7.51)	6.73 (5.67–7.93)	0.48
LH/FSH ratio	0.98 (0.69–1.37)	0.92 (0.63–1.39)	0.94
Basal E2 (pmol/L)	188.00 (121.00-233.00)	159.00 (120.50-219.25)	0.34
Basal T (nmol/L)	2.06 ± 0.63	1.87 ± 0.75	0.13
AMH (ng/mL)	7.81 (4.60–11.20)	7.09 (5.53–9.27)	0.58
FBG (mmol/L)	5.56 ± 1.33	5.25 ± 1.08	0.11
FINS (mIU/L)	14.74 (12.24–22.01)	9.85 (6.79–12.81)	< 0.001
HOMA-IR	3.39 (2.95–5.87)	2.18 (1.55–3.06)	< 0.001
HOMA-β	197.60 (113.49-281.96)	133.11 (86.09-179.54)	0.01
TC (mmol/L)	5.01 ± 1.01	4.85 ± 0.94	0.33
TG (mmol/L)	1.98 (1.07–2.48)	1.20 (0.81–1.74)	< 0.001
HDL (mmol/L)	1.15 ± 0.26	1.38 ± 0.32	< 0.001
LDL (mmol/L)	2.98 ± 0.85	2.75 ± 0.79	0.10
Uric acid (μmol/L)	402.00 (376.00-435.00)	282.00 (250.00-307.00)	< 0.001

Note: Variables are expressed as mean ± standard deviation or median (interquartile range). HUA = hyperuricemia; BMI = body mass index; NC = neck circumference; WC = waist circumference; HC = hip circumference; SBP = systolic pressure; DBP = diastolic pressure; LH = luteinizing hormone; FSH = follicle stimulating hormone; T = testosterone; AMH = anti-mullerian hormone; FBG = fasting plasma glucose; FINS = fasting insulin; HOMA-IR = homeostasis model assessment of insulin resistance; HOMA-β = homeostasis model assessment of β cell function; TC = total cholesterol; TG = triglycerides; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

Variables	HUA	Non-HUA	Pvalue
eGFR (mL/min/1.73m ²)	123.51 ± 6.90	125.22 ± 8.74	0.18
Note: Variables are expressed as mean ± standard deviation or median (interquartile range). HUA = hyperuricemia; BMI = body mass index; NC = neck circumference; WC = waist circumference; HC = hip circumference; SBP = systolic pressure; DBP = diastolic pressure; LH = luteinizing hormone; FSH = follicle stimulating hormone; T = testosterone; AMH = anti-mullerian hormone; FBG = fasting plasma glucose; FINS = fasting insulin; HOMA-IR = homeostasis model assessment of insulin resistance; HOMA-β = homeostasis model assessment of β cell function; TC = total cholesterol; TG = triglycerides; HDL = high-density lipoprotein; LDL = low-density lipoprotein.			

Associations of NC with serum uric acid and hyperuricemia

Multivariable linear regression analysis was performed to explore the associations between NC and serum uric acid levels (Table 2). In unadjusted model 1, NC was significantly associated with the level of uric acid, and the standardized coefficient was 0.51 ($P < .001$). In model 2 (adjustment for age, SBP, and DBP) and model 3 (further adjustment for log TG, HDL, log FINS, log HOMA-IR, log HOMA-β and log eGFR), NC was still significantly associated with the level of uric acid, and the standardized coefficients were 0.45 ($P < 0.001$) and 0.34 ($P = 0.004$), respectively.

Table 2

Association of neck circumference with serum uric acid level and hyperuricemia in women with polycystic ovary syndrome

Variables	Linear regression on Log (serum uric acid level)		Logistic regression on the hyperuricemia		
	Standardized coefficient	P value	OR	95% CI	P value
Model 1, NC	0.51	< 0.001	1.62	1.36–1.93	< 0.001
Model 2, NC	0.45	< 0.001	1.48	1.23–1.77	< 0.001
Model 3, NC	0.34	0.004	1.58	1.11–2.25	0.01
Note: Model 1 was unadjusted. Model 2 was adjusted for age, SBP, and DBP. Model 3 was further adjusted for TG (log-transformmed), HDL, FINS (log-transformmed), HOMA-IR (log-transformmed), HOMA-β (log-transformmed) and eGFR (log-transformmed). NC = neck circumference; SBP = systolic pressure; DBP = diastolic pressure; TC = total cholesterol; TG = triglycerides; HDL = high-density lipoprotein; LDL = low-density lipoprotein; FINSBG = fasting insulin plasma glucose; HOMA-IR = homeostasis model assessment of insulin resistance; HOMA-β = homeostasis model assessment of β cell function; eGFR = estimated glomerular filtration rate; CI = confidence interval; OR = odds ratio.					

In addition, binary logistic regression analysis was also conducted to further identify the correlation between NC and hyperuricemia (Table 2). In model 1 without any adjustment, the OR (95% CI) was 1.62

(1.36–1.93; $P < 0.001$). In model 2 and model 3, with the same adjustment as those in multivariate linear regression analysis, the correlation between NC and hyperuricemia was still statistically significant, and the ORs (95% CI) were 1.48 (1.23–1.78; $P < 0.001$) and 1.58 (1.11–2.25; $P = 0.01$), respectively.

Interactions of NC with other anthropometric measurements in relation to serum uric acid level

The quartile ranges of NC were < 31.0 cm ($n = 61$), 31.0 cm to < 32.5 cm ($n = 34$), 32.5 cm to < 34 cm ($n = 50$), and ≥ 34 cm ($n = 45$). The tertile ranges of BMI were < 22.02 kg/m², 22.02 kg/m² to < 25.08 kg/m², and ≥ 25.08 kg/m². The tertile ranges of WC were < 76 cm, 76 cm to < 85 cm, and ≥ 85 cm. The tertile ranges of HC were < 90 cm, 90 cm to < 96 cm, and ≥ 96 cm. There were significant interactions of NC with BMI, WC and HC (P for interaction < 0.001) in relation to serum uric acid level (Fig. 1). The associations between NC and serum uric acid level were more evident in those with medium BMI (22.02 kg/m² $\leq$ BMI < 25.08 kg/m², P for trend = 0.002), low WC (WC < 85 cm, P for trend = 0.001) or medium HC (90 cm $\leq$ HC < 96 cm, P for trend < 0.001).

The predictive ability of NC for hyperuricemia

Receiver operating characteristic (ROC) analysis was used to determine the predictive ability of NC, BMI, WC and HC for hyperuricemia. The areas under the curve (AUCs) for NC, BMI, WC and HC in predicting hyperuricemia are depicted in Fig. 2. The AUC (95% CI) for NC was 0.79 (0.73–0.85; $P < 0.001$), which was comparatively larger than that for BMI, WC, and HC, with AUROCs (95% CI) of 0.77 (0.70–0.82; $P < 0.001$), 0.75 (0.68–0.81; $P < 0.001$), and 0.76 (0.69–0.82; $P < 0.001$), respectively. However, no significant differences were found in the AUCs among these models (Supplementary Table 1). The different cutoff points, sensitivities, specificities, positive and negative predictive values of NC, BMI, WC and HC are shown in Supplementary Table 2. The optimal cutoff points of NC, BMI, WC and HC in predicting hyperuricemia were 32.0 cm (Youden index = 0.48), 25.56 kg/m² (Youden index = 0.46), 82.0 cm (Youden index = 0.42) and 94 cm (Youden index = 0.42), respectively. The sensitivity (SE), positive predictive value (PPV), and negative predictive value (NPV) of NC were 87.23%, 43.16% and 93.68%, respectively, which were comparatively higher than those of BMI (SE: 63.83%; PPV: 53.58%; NPV: 87.31%), WC (SE: 70.21%; PPV: 44.60%; NPV: 87.93%) and HC (SE: 74.47%; PPV: 43.21%; NPV: 88.99%).

Discussion

In the current study, we demonstrated that neck circumference was positively associated with serum uric acid levels and was also significantly correlated with hyperuricemia in women with PCOS. We also observed significant interactions between BMI, WC and HC with NC in relation to serum uric acid concentrations in women with PCOS. Additionally, ROC analysis demonstrated that NC had a higher negative predictive value for hyperuricemia in women with PCOS than BMI, WC, and HC. To the best of our knowledge, this is the first study to demonstrate such a correlation between neck circumference and hyperuricemia in PCOS women.

Hyperuricemia is characterized by an abnormal increase in serum uric acid levels in the human body due to aberrant purine metabolism, abnormal renal secretion and reabsorption(26, 27). Studies have demonstrated that elevated serum uric acid levels are associated with increased risks of hypertension, type 2 diabetes and cardiovascular diseases(28–30), which has received increasing attention as a major public health problem(31). Our previous study showed that the prevalence of hyperuricemia in the PCOS population was 25.48%(8), which is almost threefold higher than that of women in the general population(32). In the present study, the results are in line with our previous findings that showed that 24.74% of PCOS patients were diagnosed with hyperuricemia. Therefore, it is of great importance to find a simple detection method for early recognition of high-risk populations during symptomless periods. Our previous study also found that 58.75% of women with PCOS and obesity had hyperuricemia, which was nearly threefold higher than that in women with PCOS and a normal BMI, which indicated that accumulated fat was positively associated with a high risk of hyperuricemia(8).

As a reliable anthropometric index of upper-body subcutaneous fat, neck circumference has the advantages of convenience and standardized measurement and has been widely applied in the screening of abnormal fat distribution(33). It has been well acknowledged that NC is positively associated with the risk of obstructive sleep apnea(34), insulin resistance(35), type 2 diabetes and metabolic syndrome(36) in the general population. For women with PCOS, studies have shown that NC was positively correlated with visceral fat and could be adopted as an innovative tool for assessing body adiposity distribution(37, 38). Several studies have suggested that body fat accumulated in the upper body segment may contribute to hyperuricemia(12, 39). Each additional 5 mm increase in NC was associated with a 17% higher likelihood of having hyperuricemia in women(20). In the current study, we also found a positive association between NC and the level of uric acid. Further adjustment for age and other confounders still found a positive association between NC and hyperuricemia, suggesting that neck circumference was an independent predictive marker of hyperuricemia in PCOS patients. We also observed significant interactions between BMI, WC and HC with NC in relation to serum uric acid concentrations in women with PCOS. Interestingly, the associations between NC and serum uric acid level were more evident in those with medium BMI ($22.02 \text{ kg/m}^2 \leq \text{BMI} < 25.08 \text{ kg/m}^2$), low WC ($\text{WC} < 85 \text{ cm}$) or medium HC ($90 \text{ cm} \leq \text{HC} < 96 \text{ cm}$), which suggests that NC as an indicator for upper-body subcutaneous fat is a pathogenic and independent fat depot that confers additional risks for hyperuricemia. In addition, our results showed that the area under the curve of NC in predicting hyperuricemia appeared comparatively larger than that of BMI, WC and HC. NC has good sensitivity and negative predictive value for the identification of hyperuricemia, which could avoid unnecessary medical intervention in some ways.

Several potential mechanisms account for the high prevalence of hyperuricemia in women with PCOS and larger NCs. First, recent compelling evidence indicates that in women with PCOS, NC is a good predictor for insulin resistance (IR)(40), which consequently increases the risk of hyperuricemia by reducing the excretion of uric acid through increased proximal tubular sodium reabsorption(26, 41). Second, since an increased prevalence of obstructive sleep apnea has been observed in women with PCOS(42), xanthine oxidase, an enzyme that plays a key role in uric acid synthesis, could be activated

under hypoxic conditions in those patients(43). Third, increasing evidence has shown that more than 60% of free fatty acids (FFAs) are released from upper-body subcutaneous adipose tissue(44). High levels of FFAs exert pathogenic effects on the glomerulus[42] and tubulointerstitium(45), leading to abnormal renal secretion and reabsorption of uric acid(27, 46). In summary, the underlying mechanism of higher uric acid levels in PCOS women with larger NCs lies in more free fatty acid release and higher airway pressure from upper body adiposity tissue, both of which could result in oxidative stress and insulin resistance(20).

This study is the first to assess the effects of NC as a parameter in the prediction of hyperuricemia in women with PCOS by using ROC curves. The strengths of our study lie in the simple and standardized measuring method of neck circumference, as well as the validated and complete metabolic data, which make our findings highly applicable to clinical practice. Moreover, the high Youden index, high sensitivity and high negative predictive value of NC in predicting hyperuricemia enable NC to be a more practical predictor in clinical practice. However, several limitations should be taken into consideration. First, the single-center retrospective design has some limitations with regard to interpreting the causality of associations. Second, due to the limited sample size, we did not classify the phenotypes of PCOS and did not calculate the prevalence of hyperuricemia in each phenotype. Thus, prospectively designed studies and follow-up of reproductive outcomes await further evaluation.

Conclusions

In summary, we found a positive correlation between NC and serum uric acid, and NC has a good predictive ability for hyperuricemia in PCOS women. Neck circumference could be recommended as a comparatively simple, fast, and reliable measuring method in the routine clinical assessment of women with PCOS to screen those at high risk of hyperuricemia.

Abbreviations

PCOS: Polycystic ovary syndrome

NC: Neck circumference

BMI: Body mass index

WC: Waist circumference

HC: Hip circumference

SBP: Systolic pressure

DBP: Diastolic blood pressure

LH: Luteinizing hormone

FSH: Follicle stimulating hormone

T: Testosterone

AMH: Anti-mullerian hormone

FBG: Fasting plasma glucose

FINS: Fasting insulin

HOMA-IR: Homeostasis model assessment of insulin resistance

HOMA-β: Homeostasis model assessment of β cell function

TC: Total cholesterol

TG: Triglycerides

HDL: High-density lipoprotein

LDL: Low-density lipoprotein

eGFR: estimated glomerular filtration rate

CI: Confidence interval

OR: Odds ratio

AUC: Area under the curve

SE: Sensitivity

SP: Specificity

PPV: Positive predictive value

NPV: negative predictive value

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University. (Reference number: 2021R011).

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

H.Y. Y. and C. L. drafted and finished the manuscript equally. C.C. J. participated in the collection of data and literature. R. Y. participated in the statistical analysis. L.S. M. and L. D. designed and revised the manuscript. All authors read and approved the final manuscript.

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References

1. Louwers YV, Laven JSE. Characteristics of polycystic ovary syndrome throughout life. *Ther Adv Reprod Health*. 2020;14:2633494120911038.
2. Wolf WM, Wattick RA, Kinkade ON, Olfert MD. Geographical Prevalence of Polycystic Ovary Syndrome as Determined by Region and Race/Ethnicity. *Int J Environ Res Public Health*. 2018;15(11).
3. 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.
4. Cooney LG, Dokras A. Beyond fertility: polycystic ovary syndrome and long-term health. *Fertil Steril*. 2018;110(5):794-809.
5. Wawrzekiewicz-Jałowicka A, Kowalczyk K, Trybek P, Jarosz T, Radosz P, Setlak M, et al. In Search of New Therapeutics-Molecular Aspects of the PCOS Pathophysiology: Genetics, Hormones, Metabolism and Beyond. *Int J Mol Sci*. 2020;21(19).

6. Szczuko M, Zapalowska-Chwyc M, Drozd R. A Low Glycemic Index Decreases Inflammation by Increasing the Concentration of Uric Acid and the Activity of Glutathione Peroxidase (GPx3) in Patients with Polycystic Ovary Syndrome (PCOS). *Molecules*. 2019;24(8).
7. Hu J, Xu W, Yang H, Mu L. Uric acid participating in female reproductive disorders: a review. *Reprod Biol Endocrinol*. 2021;19(1):65.
8. Mu L, Pan J, Yang L, Chen Q, Chen Y, Teng Y, et al. Association between the prevalence of hyperuricemia and reproductive hormones in polycystic ovary syndrome. *Reprod Biol Endocrinol*. 2018;16(1):104.
9. Bellos I, Pergialiotis V, Loutradis D, Daskalakis G. The prognostic role of serum uric acid levels in preeclampsia: A meta-analysis. *J Clin Hypertens (Greenwich)*. 2020;22(5):826-34.
10. Laughon SK, Catov J, Provins T, Roberts JM, Gandley RE. Elevated first-trimester uric acid concentrations are associated with the development of gestational diabetes. *Am J Obstet Gynecol*. 2009;201(4):402.e1-5.
11. Luo J, Hendryx M, Laddu D, Phillips LS, Chlebowski R, LeBlanc ES, et al. Racial and Ethnic Differences in Anthropometric Measures as Risk Factors for Diabetes. *Diabetes Care*. 2019;42(1):126-33.
12. Ali N, Perveen R, Rahman S, Mahmood S, Rahman S, Islam S, et al. Prevalence of hyperuricemia and the relationship between serum uric acid and obesity: A study on Bangladeshi adults. *PLoS One*. 2018;13(11):e0206850.
13. Ni Q, Lu X, Chen C, Du H, Zhang R. Risk factors for the development of hyperuricemia: A STROBE-compliant cross-sectional and longitudinal study. *Medicine (Baltimore)*. 2019;98(42):e17597.
14. Kuwabara M, Kuwabara R, Niwa K, Hisatome I, Smits G, Roncal-Jimenez CA, et al. Different Risk for Hypertension, Diabetes, Dyslipidemia, and Hyperuricemia According to Level of Body Mass Index in Japanese and American Subjects. *Nutrients*. 2018;10(8).
15. Miyagami T, Yokokawa H, Fujibayashi K, Gunji T, Sasabe N, Okumura M, et al. The waist circumference-adjusted associations between hyperuricemia and other lifestyle-related diseases. *Diabetol Metab Syndr*. 2017;9:11.
16. Park DY, Kim YS, Ryu SH, Jin YS. The association between sedentary behavior, physical activity and hyperuricemia. *Vasc Health Risk Manag*. 2019;15:291-9.
17. Han QX, Zhang D, Zhao YL, Liu L, Li J, Zhang F, et al. Risk Factors For Hyperuricemia In Chinese Centenarians And Near-Centenarians. *Clin Interv Aging*. 2019;14:2239-47.
18. Di Bella S, Cesareo R, De Cristofaro P, Palermo A, Sanson G, Roman-Pognuz E, et al. Neck circumference as reliable predictor of mechanical ventilation support in adult inpatients with COVID-19: A multicentric prospective evaluation. *Diabetes Metab Res Rev*. 2021;37(1):e3354.
19. An P, Chen K, Wang A, Jin X, Chen Y, Gu W, et al. Neck circumference is an independent risk factor for hyperuricemia within 3 years in women: a longitudinal study. *Clin Rheumatol*. 2020;39(12):3757-67.
20. Shen X, Wu S, Xu R, Wu Y, Li J, Cui L, et al. Neck circumference is associated with hyperuricemia: a cross-sectional study. *Clin Rheumatol*. 2019;38(9):2373-81.

21. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertil Steril*. 2004;81(1):19-25.
22. So A, Thorens B. Uric acid transport and disease. *J Clin Invest*. 2010;120(6):1791-9.
23. Flegal KM. Body-mass index and all-cause mortality. *Lancet*. 2017;389(10086):2284-5.
24. Preis SR, Massaro JM, Hoffmann U, D'Agostino RB, Sr., Levy D, Robins SJ, et al. Neck circumference as a novel measure of cardiometabolic risk: the Framingham Heart study. *J Clin Endocrinol Metab*. 2010;95(8):3701-10.
25. Ross R, Neeland IJ, Yamashita S, Shai I, Seidell J, Magni P, et al. Waist circumference as a vital sign in clinical practice: a Consensus Statement from the IAS and ICCR Working Group on Visceral Obesity. *Nat Rev Endocrinol*. 2020;16(3):177-89.
26. Cappuccio FP, Strazzullo P, Farinaro E, Trevisan M. Uric acid metabolism and tubular sodium handling. Results from a population-based study. *Jama*. 1993;270(3):354-9.
27. Mandal AK, Mount DB. The molecular physiology of uric acid homeostasis. *Annu Rev Physiol*. 2015;77:323-45.
28. De Cosmo S, Viazzi F, Pacilli A, Giorda C, Ceriello A, Gentile S, et al. Serum Uric Acid and Risk of CKD in Type 2 Diabetes. *Clin J Am Soc Nephrol*. 2015;10(11):1921-9.
29. Kuwabara M, Hisatome I, Niwa K, Hara S, Roncal-Jimenez CA, Bjornstad P, et al. Uric Acid Is a Strong Risk Marker for Developing Hypertension From Prehypertension: A 5-Year Japanese Cohort Study. *Hypertension*. 2018;71(1):78-86.
30. Kuwabara M, Kanbay M, Hisatome I. Uric Acid and Hypertension Because of Arterial Stiffness. *Hypertension*. 2018;72(3):582-4.
31. Song P, Wang H, Xia W, Chang X, Wang M, An L. Prevalence and correlates of hyperuricemia in the middle-aged and older adults in China. *Sci Rep*. 2018;8(1):4314.
32. Dehlin M, Jacobsson L, Roddy E. Global epidemiology of gout: prevalence, incidence, treatment patterns and risk factors. *Nat Rev Rheumatol*. 2020;16(7):380-90.
33. Arias Téllez MJ, Acosta FM, Sanchez-Delgado G, Martinez-Tellez B, Muñoz-Hernández V, Martinez-Avila WD, et al. Association of Neck Circumference with Anthropometric Indicators and Body Composition Measured by DXA in Young Spanish Adults. *Nutrients*. 2020;12(2).
34. Szaulińska K, Wichniak A. BMI-NECK: A simple assessment of risk of obstructive sleep apnea in schizophrenia. *J Psychiatr Res*. 2020;125:33-7.
35. Liang J, Teng F, Li Y, Liu X, Zou C, Wang Y, et al. neck circumference and insulin resistance in Chinese adults: the Cardiometabolic Risk in Chinese (CRC) Study. *Diabetes Care*. 2013;36(9):e145-6.
36. Ebrahimi H, Mahmoudi P, Zamani F, Moradi S. Neck circumference and metabolic syndrome: A cross-sectional population-based study. *Prim Care Diabetes*. 2021.
37. Penaforte FR, Japur CC, Diez-Garcia RW, Chiarello PG. Upper trunk fat assessment and its relationship with metabolic and biochemical variables and body fat in polycystic ovary syndrome. *J Hum Nutr Diet*. 2011;24(1):39-46.

38. Rodrigues de Oliveira Penaforte F, Cremonesi Japur C, Díez-García RW, Salles Macedo C, García Chiarello P. The use of body circumferences for the prediction of intra-abdominal fat in obese women with polycystic ovary syndrome. *Nutr Hosp.* 2012;27(5):1662-6.
39. da Silva Cde C, Zambon MP, Vasques AC, Rodrigues AM, Camilo DF, Antonio M, et al. Neck circumference as a new anthropometric indicator for prediction of insulin resistance and components of metabolic syndrome in adolescents: Brazilian Metabolic Syndrome Study. *Rev Paul Pediatr.* 2014;32(2):221-9.
40. Chen Y, Zheng X, Ma D, Zheng S, Han Y, Su W, et al. Neck circumference is a good predictor for insulin resistance in women with polycystic ovary syndrome. *Fertil Steril.* 2021;115(3):753-60.
41. Han T, Lan L, Qu R, Xu Q, Jiang R, Na L, et al. Temporal Relationship Between Hyperuricemia and Insulin Resistance and Its Impact on Future Risk of Hypertension. *Hypertension.* 2017;70(4):703-11.
42. Fogel RB, Malhotra A, Pillar G, Pittman SD, Dunaif A, White DP. Increased prevalence of obstructive sleep apnea syndrome in obese women with polycystic ovary syndrome. *J Clin Endocrinol Metab.* 2001;86(3):1175-80.
43. Shi T, Min M, Sun C, Cheng C, Zhang Y, Liang M, et al. A meta-analysis of the association between gout, serum uric acid level, and obstructive sleep apnea. *Sleep Breath.* 2019;23(4):1047-57.
44. Xue J, Li B, Wang J, Yu S, Wang A, An P, et al. Association between Neck Circumference and the Risk of Decreased Estimated Glomerular Filtration Rate in the General Population of China: A Cross-Sectional Study. *Biomed Res Int.* 2020;2020:3496328.
45. Kamijo A, Kimura K, Sugaya T, Yamanouchi M, Hase H, Kaneko T, et al. Urinary free fatty acids bound to albumin aggravate tubulointerstitial damage. *Kidney Int.* 2002;62(5):1628-37.
46. Johnson RJ, Nakagawa T, Jalal D, Sánchez-Lozada LG, Kang DH, Ritz E. Uric acid and chronic kidney disease: which is chasing which? *Nephrol Dial Transplant.* 2013;28(9):2221-8.

Figures

Figure 1

Interactions of NC with other anthropometric measurements in serum uric acid level Abbreviations: NC = neck circumference; BMI = body mass index; WC = waist circumference; HC = hip circumference.

Figure 2

Receiver operating characteristic curves for the detection of hyperuricemia using NC, BMI, WC and HC
 Abbreviations: NC = neck circumference; BMI = body mass index; WC = waist circumference; HC = hip circumference.

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