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Prevalence of polyendocrine metabolic ovarian syndrome in adolescents and its association with metabolic syndrome

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Prevalence of polyendocrine metabolic ovarian syndrome in adolescents and its association with metabolic syndrome

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ABSTRACT

INTRODUCTION: Polycystic ovarian syndrome (PCOS), currently known as polyendocrine metabolic ovarian syndrome (PMOS), is the most common endocrine problem in young women, characterized by a varied complex of metabolic and endocrine abnormalities. PMOS in adolescents is further distinguished by menstrual irregularities and hyperandrogenism which can manifest clinically and biochemically**.**

OBJECTIVE: To determine the prevalence of PMOS among adolescents in Malaysia, and to investigate its association with metabolic syndrome and other cardiometabolic risk factors.

MATERIAL & METHODS: This is a cross-sectional study involving adolescent girls attending public secondary schools in Peninsular Malaysia, as part of the Malaysian Health and Adolescents Longitudinal Research Study (MyHeART), using the Pediatric Endocrine Society 2015 (PES 2015) criteria, which was current at time of data collection. Data collected includes questionnaires, hirsutism self-assessment, clinical and blood parameters.

RESULTS: A total of 615 adolescent girls with mean age of 16.0 ± 0.2 years, and mean age of menarche 12.0 ± 1.2 years were included. The prevalence of PMOS among the sample population was 3.7% (n=23). One in five (21.7%) adolescents with PMOS have metabolic syndrome. Adolescents with PMOS were 11 times more likely to develop metabolic syndrome compared to non-PMOS [OR 11.3 (95% CI 3.6-35.4, p<0.001)]. They were also more likely to have central obesity [OR 5.94 (95% CI 2.6-13.9, p<0.001)], hyperinsulinaemia [OR 4.56 (95% CI 1.9-10.9, p<0.001)] and insulin resistance [OR 4.11 (95% CI 1.6-10.5, p<0.001)] compared to the non-PMOS group.

CONCLUSION: The prevalence of PMOS among adolescent girls in Malaysia is comparable to that of other countries. Adolescent girls with PMOS are more likely to have metabolic syndrome, being overweight or obese, and having insulin resistance.

Keywords: Adolescent girls, PCOS, PMOS, metabolic syndrome, insulin resistance, cardiometabolic risks

INTRODUCTION

Polycystic ovarian syndrome (PCOS), currently known as polyendocrine metabolic ovarian syndrome (PMOS) (1), is the most common endocrine problem in young women, characterised by a complex of metabolic and endocrine abnormalities. Hallmarks of PMOS in adolescents are menstrual irregularities and hyperandrogenism, which manifests clinically and biochemically. (2, 3) The prevalence rates of PMOS of all ages in general can reach up to 12.7%, (4) and prevalence using the widely used Rotterdam criteria is 9.8% to 11.04%. (5, 6) This is likely an overdiagnosis as it includes polycystic ovarian morphology, which can be a normal pubertal development. Another study in Australia demonstrated a high prevalence of PMOS, however, with much lower prevalence rates using the Androgen Excess Society and NIH criteria, respectively. (7)

Three international conferences developed the diagnostic criteria to diagnose PMOS in adults **(Appendix 1)**, with no specific criteria proposed for the diagnosis of PMOS in the adolescent population, causing diagnostic difficulties due to overlapping of normal pubertal features. At the time this study was conducted, PES 2015 was the first to suggest specific criteria to be used for the diagnosis of PMOS in adolescents, including an unexplained combination of abnormal uterine bleeding patterns that persist for 1-2 years and hyperandrogenism (clinically and/or biochemically). (8)

As there is no available data on prevalence of PMOS among Malaysian adolescents, this study was suggested and included as part of the Malaysian Health and Adolescents Longitudinal Research Study (MyHeART), a prospective longitudinal cohort study on risk factors for chronic non-communicable diseases among adolescents in Malaysia. (9) The MyHeART study among 13 years old students had shown that 10% of the Malaysian school-going adolescents have high BMI, and from this cohort, 2.6% were found to have metabolic

syndrome. This study aims to determine the prevalence of PMOS among adolescents in Malaysia using the criteria from the Pediatric Endocrine Society (PES) 2015, (8) and to investigate the association between PMOS and metabolic syndrome, as well as with other cardiometabolic risk factors. This study was designed and conducted in 2016, when the PES 2015 criteria represented the most current adolescent-specific diagnostic framework available, which has since evolved to the most updated 2025 consensus of adolescent-specific recommendations of the 2023 International Evidence-Based Guideline for PCOS. (3, 10)

This is the first community-based study of its kind in Malaysia and Southeast Asia, and as part of the MyHeART longitudinal cohort, this dataset offers a baseline against which the evolving understanding of adolescent PCOS/PMOS can be measured in the future follow-up analyses.

METHODOLOGY

Study design

This was a 2016 cross-sectional study which followed a stratified sampling design based on the MyHeART study. (9) Only female students were invited to participate in this study. Written information about the study and consent forms were distributed to the participants and their parents/guardians. Those with signed written informed consent and assent were then allowed to participate in this study.

Recruitment for the study was conducted from 25 March 2016 to 24 May 2016. A total of 1035 participants were recruited from all participating schools, of which 681 participants were girls approximately 16 years old from different ethnicities. Participants who did not complete the questionnaires, refused to participate in blood taking, or had missing blood samples and menarche less than 2 years prior to the study were excluded (n=66). A final study sample of 615 adolescent girls was recruited and analysed **(Figure 1).**

Participants were asked to fast for at least ten hours before the study. A total of 15 ml of fasting blood was withdrawn from each participant. Blood samples were sent to a certified International Standardization for Organization (ISO) hospital pathology lab for analysis (analysed for fasting glucose, fasting insulin, fasting lipid profile, and free testosterone level). The samples were temporarily stored at four degrees Celsius in a cool box immediately after the blood had been withdrawn to preserve levels of markers that are sensitive to degradation due to an increase in temperatures. All samples were processed in the field laboratories. Samples were spun and stored as serum, divided into several aliquots of 0.5 ml serum.

Ethical consideration

Approval for the study was obtained from the Ethical Committee, University Malaya Medical Centre (UMMC) (*Approval number MEC 896.34*). Written informed consent was obtained from the parent or guardian, and all participating adolescents were also required to sign an assent form. All testing was performed in accordance with the approved guidelines.

Questionnaire, anthropometric measurement, and physical examination

Participants and parental questionnaires

Two self-administered questionnaires were used: a Parental Questionnaire and a Participant Questionnaire. These questionnaires were from MyHeART study adapted from the Young Hearts study, an adolescent cohort study conducted in Northern Ireland (11) adjusted to suit the local population.

The parental questionnaires gathered information on the participant's birth, health, and lifestyle as a child, the parents' socioeconomic status, and lifestyle, as well as personal and family history of non-communicable diseases (NCDs) and menstrual problems.

The participant questionnaires collected information on demographics and menstrual histories (age at menarche, cycle pattern regularity, hormone treatment prescribed, and family history of menstrual disorders) based on The Parker Sneddon MDOT (Menstrual Disorder of Teenagers Questionnaire). (12) This includes the presence of acne, although no specific grading system was applied.

The questionnaire also covered questions on body hair (hirsutism or hair thinning) and weight problems. The participants were asked to self-report the degree of hirsutism based on the Modified Ferriman-Gallwey score, which showed different degrees of body hair over nine regions (upper lip, chin, chest, upper and lower abdomen, upper arms, and thighs) (Appendix 2). (13) A total score of less than 8 is considered normal, a score of 8 to 15 indicates mild hirsutism, and a score greater than 15 indicates moderate-to-severe hirsutism.

Awareness of sexual and reproductive health issues, history of taking contraceptive pills, family history of menstrual problems was also part of the assessment.

These questionnaires were translated into Bahasa Melayu (the Malaysian national language). Self-administered parental questionnaires were completed by parents at home and submitted. The adolescents completed their questionnaires at school (on the study day) under the supervision of the research team. Missing information was later obtained by telephone interview.

Height was measured without socks and shoes using a calibrated vertical stadiometer (Seca Portable 217, Seca, UK) and was recorded to the nearest 0.1 cm. Weight was measured with light clothing, using a digital electronic weighing scale (Seca 813, Seca, UK) and was recorded to the nearest decimal fraction of a kilogram (0.1 kg). Both waist circumference (WC) and hip circumference (HC) were respectively measured with a non-elastic Seca measuring tape to the nearest millimetre.

Medically trained personnel, either paediatricians or paediatric medical officers, manually measured the blood pressure and pulse rate of the participants, using a stethoscope and a mercury sphygmomanometer. Three readings of blood pressure were taken with two-minutes interval between each reading, and the mean of the three readings were obtained. Participants

were also examined for the presence of acanthosis nigricans (a clinical sign of insulin resistance) using Burke scale quantification for Acanthosis Nigricans (Stage 1-4). (14)

Operational Definitions

Polyendocrine Metabolic Ovarian Syndrome (PMOS) (8, 15)

Unexplained combination of abnormal uterine bleeding or irregular menses pattern and hyperandrogenism (clinical and/or biochemical hyperandrogenaemia) of more than 2 years. For this study, the diagnosis of PMOS was based on the PES 2015 diagnostic framework, which was current at the time of data collection. (8)

Abnormal Uterine Bleeding/Irregular Menses Pattern

Irregular menses is defined as irregular and inconsistent menstrual blood flow in a woman or infrequent menstrual cycles of less than 21 days or more than 45 days after the second-year post-menarche. (8)

Clinical hyperandrogenism

Moderate to severe hirsutism, assessed by Ferriman-Gallwey score of more than 15 over 9 body parts (8, 15, 16)

Biochemical hyperandrogenaemia

Free testosterone (FT) level >2.57 pg/mL. (17) Normal reference values for FT were determined by the ISO-certified clinical laboratory of Pantai Medical Lab, which uses LC-MS/MS assays.

Body mass index

Calculated as weight in kilograms divided by the square of height in meters using the IOTF criteria (18) of <18.5 kg/m^2 for underweight, 18.5-24.9 kg/m^2 for normal weight, 25-29.9 kg/m^2 for overweight, and >30 kg/m^2 for obese.

Metabolic syndrome based on IDF criteria **(19)**

Central obesity (defined as waist circumference ≥80 cm) plus any two of the following four factors:

i) triglycerides ≥1.7 mmol/L,

ii) high-density lipoprotein cholesterol (HDL-C) <1.29 mmol/L,

iii) systolic blood pressure ≥130 mmHg, diastolic blood pressure ≥85 mmHg,

iv) fasting plasma glucose (FPG) ≥5.6 mmol/L

Other cardiometabolic risk factors (20-22)

i) Raised total cholesterol ≥5.2 mmol/L,

ii) Low-density lipoprotein cholesterol (LDL-C) ≥3.4 mmol/L

iii) Fasting level of insulin ≥15 μU/ml for hyperinsulinaemia

Insulin resistance was assessed by calculating HOMA-IR using the formula: [fasting glucose (mmol/L) x fasting insulin (μU/mL)] / 22.5, taking a value of >3.8 as insulin resistance. (23)

Analysis Methodology

Data were analysed at time of data collection using the Statistical Package for the Social Sciences software (version 20.0, IBM SPSS Statistics) and Excel. Prevalence of PMOS and corresponding adjusted odds ratio (adjusted to the rural and urban population), 95% confidence intervals (CI) and p-values were calculated. The differences between the mean values of the two groups (PMOS vs non-PMOS) were compared. The p-value <0.05 was accepted as statistically significant.

RESULTS

A total of 615 adolescent girls (out of 681) who fulfilled the inclusion and exclusion criteria were analysed. **(Figure 2).** The mean age of the participants was 16.0 ± 0.2 years, and the mean age of menarche was 12.0 ± 1.2 years.

Prevalence of PMOS

From a total of 615 participants, 549 (89.3%) had regular menses and 66 (10.7%) had a history of irregular menses. Of those with a history consistent with irregular menses, 23 (34.8%) fulfilled the criteria of PMOS, bringing the prevalence of PMOS among these adolescent girls to 3.7% (23 out of 615 girls).

[Table 1]

[Table 2]

[Table 3]

Association of PMOS with overweight and obesity parameters

Among those 23 adolescents with PMOS, one (4.3%) was underweight, eight (34.8%) were normal weight, four (17.4%) were overweight, and ten (43.8%) were obese. Adolescents with PMOS showed significantly higher waist circumference and prevalence of central obesity than non-PCOS **(Table 1 and 2)**. Adolescents with PMOS were 6 times more likely to have central obesity compared to non-PCOS (OR 5.94, 95% CI 2.6-13.9, p<0.001) **(Table 2)**.

Association of PMOS with metabolic syndrome and other cardiometabolic risk factors

The prevalence of metabolic syndrome based on IDF criteria in this population (n=615) was 3.3% (n=20). The prevalence of metabolic syndrome among those with PMOS was higher

(21.7%) than among the non-PMOS (2.5%). Those with PMOS were about 11 times more likely to develop metabolic syndrome [OR 11.3 (95% CI 3.6-35.4, p < 0.001)] **(Table 2)**.

Adolescents with PMOS showed significantly higher TG, LDL-C, and raised blood pressure. There were no significant differences in fasting blood glucose, HDL-C, and total cholesterol **(Table 1)**.

Table 2 showed adolescents with PMOS were more likely to have hyperinsulinaemia [OR 4.56 (95% CI 1.9-10.9, p<0.001)] and insulin resistance [OR 4.11 (95% CI 1.6-10.5, p<0.001)] compared to non-PMOS adolescents.

Irregular Menses and Hyperandrogenism

Among those with PMOS, (n=23), 14 (60.9%) presented with irregular menses and elevated free testosterone, 8 (34.8%) had irregular menses and hyperandrogenism, while only 1 (4.3%) presented with all three features.

Participants with PMOS had a significantly higher prevalence of elevated free testosterone and clinical hyperandrogenism than those without PMOS **(Table 3),** with no significant difference in the prevalence of acne and alopecia. They were also more likely to have higher levels of free testosterone and moderate to severe hirsutism **(Table 1).**

Family history of menstrual disorders and PMOS

There was a higher prevalence of a positive family history of menstrual problems in the PMOS group compared to a non-PMOS group, 30.4% vs 17.7%. Those with a positive family history were more likely to develop PMOS [OR 2.98 (95% CI 1.25-7.07, p=0.013)] **(Table 2)**.

DISCUSSION

Prevalence of PMOS among adolescents

This cross-sectional study involved a large number of female adolescents in the community who were >2 years post-menarche, recruited under the MyHeART longitudinal study. To our knowledge, at the time this study was conducted, this was the first community study to report PMOS using PES 2015 criteria.

Out of 615 adolescents recruited in this study, only 3.7% fulfilled the criteria of PMOS, which is lower than reported in a meta-analysis looking into diagnosis in adolescents using the Rotterdam 2003 criteria (11.32%). (24) This is expected, because compared to the two-of-three threshold used in Rotterdam's criteria, PES 2015 strictly requires both hyperandrogenism and irregular menses, and entirely excludes polymorphic ovarian morphology. A study by Akgül et al. in 2018 further supported this, which shows in a group of adolescents diagnosed with PMOS using Rotterdam's criteria, only 65.4% fulfill the PES 2015 criteria. (25)

PMOS, Obesity and Adiposity

In this study, about two-thirds of adolescents with PMOS are either overweight or obese. This aligns with another population-based study of adolescents aged 15 to 19 in United States. (26) On the other hand, our study also documented a case of underweight PMOS, which is comparable to other study showing that prevalence of PMOS among underweight is very low. (27)

It is well known that PMOS has a strong correlation with high BMI. (28, 29) From our study, adolescents with PMOS are 6 times more likely to have high BMI (>25 kg/m^2). They were also more likely to have central obesity and higher blood pressure, which is consistent with the study by Rahmanpour et al. (30) Additionally, abdominal obesity is common in PMOS and is associated with greater metabolic dysfunction among adolescents with PMOS. The relationship between adiposity and PMOS in adolescence seems to be bidirectional, in which PMOS prevalence rises with adiposity, (31) while obesity worsens reproductive and metabolic outcomes of PMOS, (26) with higher BMI as an independent predictor of persistent irregular menses. (32, 33) Obesity also modulates the development and course of PMOS, and a high BMI predicts persistent irregular menses. (32, 34)

PMOS, Metabolic Syndrome and Cardiometabolic Risk

It is essential to acknowledge that PMOS has a well-established relationship with metabolic syndrome and other cardiovascular risk factors such as obesity and insulin resistance. (35, 36) The prevalence of metabolic syndrome among adolescents with PMOS is significantly higher compared to those without PMOS, and adolescents with PMOS are at substantially higher risk of getting metabolic syndrome compared to those without PMOS. (37)

The prevalence of metabolic syndrome in our adolescents with PMOS was 21.7%, which is within the wide range of 4.9% to 43.6% from previous studies. (38) Current study prevalence is much lower than in India (60.8%), (39) USA (37%) (40) and Iran (33.3%) (30) but higher than Australia (3.3 %). (41) A meta-analysis found adolescents with PMOS are approximately three times more likely to develop metabolic syndrome than those without PMOS, lower compared to the 11-fold risk in our study. (42) This can be attributed to our smaller overall PMOS prevalence, causing limitations in statistical power for association analysis. Although

obesity might be a better predictor of metabolic dysfunction than PMOS status, androgen excess may also increase the risk for metabolic syndrome independent of obesity.

Besides metabolic syndrome, other components of cardiovascular disease risk factors deserve similar focus. The present study showed adolescents with PMOS are more likely to have central obesity, raised blood pressure and high triglycerides but not lower HDL-C, high cholesterol and impaired fasting glucose than adolescents without PMOS. Hyperinsulinaemia and insulin resistance also showed a strong positive correlation with PMOS, from HOMA-IR results and the presence of acanthosis nigricans. Hence, the risks of impaired glucose tolerance and type 2 diabetes are also increased in adolescents with PMOS. An important finding in this study is the relatively high number of PMOS adolescents with hyperinsulinaemia and insulin resistance compared to other studies. (43, 44) This finding is not just simply a byproduct of higher BMI, but a very real effect of PMOS, even in adolescent with relatively lean PMOS. (31)

A retrospective hospital-based study by Akgul and Bonny on adolescents with PMOS and metabolic syndrome using different PMOS criteria (including PES criteria) demonstrated that the prevalence of metabolic syndrome was the highest when PES criteria were used. (45) Consequently, the study showed the importance of using PES criteria to diagnose PMOS in adolescents with its stricter and more refined definitions, accounting for metabolic conditions (in contrast with Rotterdam and NIH criteria).

Not surprisingly, we also note that adolescents with PMOS were more likely to have a positive family history of menstrual disorders compared to non-PMOS group. This is consistent with other studies that have shown that the risk factor of PMOS included family history of menstrual disorders. (46, 47)

Irregular Menses and Hyperandrogenism

Of these adolescents with PMOS, about two-thirds presented with irregular menses and elevated testosterone, one-third with irregular menses and hirsutism, and a small portion (4.3%) had all three features.

Adolescents with PMOS had higher testosterone and hirsutism scores compared to the non-PMOS group. In our study, about two-thirds (65.2%) of adolescents with PMOS had elevated free testosterone levels, and 2 out of 5 had moderate to severe hirsutism. In contrast, a study by Rossi et al had showed 90% of the PMOS group had elevated testosterone while 87.5% had hirsutism. (28) This difference can possibly be attributed to a higher cut-off value for hirsutism score in our study (Modified F-G score >15 instead of >8). However, the modified F-G score >15 cutoff used in this study raised the possibility of underdetection of clinically significant hirsutism. While Malaysian-specific modified F-G scores are yet to be established, Asian populations have generally been found to cluster around a lower modified F-G cutoff of 4 to 5. (48)

Both PMOS and non-PMOS groups showed no significant difference in the occurrence of acne and alopecia. A high percentage of adolescents with PMOS presented with acne: a typical presentation of normal pubertal change. The severity of acne was not graded accordingly and was self-reported information. This may affect the result of the study, as acne without hirsutism may not be clinically important, (49) while severe acne not responding to treatment has a higher association with hyperandrogenism. Presence of acne and alopecia in our study was higher, at 87% and 17.4%, respectively, compared to a similar study by Orsino et al. at 32% and 10%. (50)

Limitations of study

This study exhibited few strengths. First, this study exhibits robust sampling, where anthropometric measurements were taken by trained personnel, with blood pressure taken thrice to eliminate the white-coat effect. This study also excludes physiologic anovulation by limiting the definition of irregular menses to only those more than two years post-menarche. Biochemical hyperandrogenism was assessed via LC-MS/MS free testosterone using ISO-certified equipment, reducing risk of error in this study.

The study had identified several limitations. This includes self-reported physical assessment (hirsutism scoring) not verified by the medical professionals, which could lead to an element of bias. This study could not be generalised to all adolescent girls in Malaysia, as most of the participants were Malays, not representing the three main ethnic groups (Malays, Chinese, and Indians).

The small number of adolescents with PMOS in our study resulted in a wide confidence interval and limited precision in the effect estimate. A larger cohort group is needed to estimate the effect better. The cross-sectional nature of this study as well is unable to establish a temporal or causal relationship between the variables.

This study was also done based on PES 2015 criteria, which have evolved ever since. However, this study provides baseline data that can be referred and compared to once a newer study using the latest criteria is performed in Malaysia.

Future directions

Most participants in this study were not aware of PMOS and its impact on adolescent health. More education to raise awareness of this disease among our adolescents is warranted. It is

352 imperative to screen the adolescents presenting with irregular menses or vice versa
353 (presenting with metabolic syndrome) for PMOS as well. Adolescents who presented with
354 hirsutism or severe acne may also need further evaluation or treatment, as well as
355 psychological assessment due to the nature of the problem, as hirsutism and severe acne may
356 affect the adolescents' well-being. Healthcare professionals should also have a high index of
357 suspicion of PMOS in their patients if any first-degree family members have any menstrual
358 disorders, due to the high association of PMOS with a positive family history.

359 Many efforts have been initiated to promote a healthy lifestyle during early adolescence.
360 These include school-based programs aiming at combating non-communicable diseases
361 among Malaysian adolescents such as MyBFF@school, which was proven to reduce
362 percentage body fat and skeletal muscle mass after at least six months of continuous
363 involvement. (51) A more holistic approach to preventive measures should be taken,
364 especially when teenagers have reached menarche for more than 2 years.

365 This study showed the importance of comprehensive health education and intervention as part
366 of school curriculum. Early access to health education by students can be done in formal
367 classrooms (as part of the academic syllabus) or extracurricular settings (outside the
368 classroom) under a larger, more general framework of menstrual and metabolic health.
369 Community health professionals, with direct access to parents and students, need to better
370 equip themselves with knowledge on PMOS (through online education, distance learning
371 modules, apps) to enable them to play a more substantial role in increasing the awareness.

372 **Conclusion**

373 In conclusion, the prevalence of PMOS among adolescents in this community study is rather
374 low compared to previous community studies, as a result of using a more comprehensive and

stringent criteria by the Pediatric Endocrine Society (PES). Consistent with comparable studies, PMOS in adolescents has a high association with central obesity, insulin resistance, metabolic syndrome, and various cardiometabolic risks, indicating that the issue is beyond ovarian dysfunction, encompassing wider endocrine and metabolic disorders, justifying the conceptual shift to polyendocrine metabolic ovarian syndrome (PMOS).

List of Abbrevation

F-G – Ferriman-Gallwey Score

FPG – Fasting Plasma Glucose

FT – Free Testosterone

HC – Hip circumference

HDL-C – High Density Lipoprotein Cholesterol

HOMA-IR – Homeostatic Model Assessment for Insulin Resistance

IDF – International Diabetes Federation

LDL-C – Low Density Lipoprotein Cholesterol

MDOT - Menstrual Disorder of Teenagers Questionnaire

MyHeART – Malaysian Health and Adolescents Longitudinal Research Study

PCOS – Polycystic Ovarian Syndrome

PMOS – Polyendocrine Metabolic Ovarian Syndrome

PES – Paediatric Endocrine Society

WC – Waist Circumference

Implications and Contribution

This study is part of the first adolescent longitudinal study that was conducted in Malaysia. It was also the first in Southeast Asia with a total number of participants greater than 600 in a community-setup (school-based) study.

Declarations

Ethical Consideration

Approval for the study was obtained from the Ethical Committee, University Malaya Medical Centre (UMMC) (*Approval number MEC 896.34*).

Consent for Publication

Written informed consent was obtained from the parent or guardian, and all participating adolescents were also required to sign an assent form. Informed consent for publication was also obtained from the parent and guardian in the same consent and assent form.

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 Interest

Authors declare no conflict of interest.

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Table 1

Differences in physical characteristics and metabolic profiles between PMOS and non-PMOS groups

Variable	PMOS n=23	Non-PMOS n=592	p-value
Age (years)	16.05 ± 0.2	16.03 ± 0.2	0.4802
BMI (kg/m^2)	28.8 ± 6.3	21.9 ± 5.0	<0.001
Waist Circumference (cm)	86.6 ± 13.3	70.8 ± 10.3	<0.001
Waist-hip Ratio	0.9 ± 0.1	0.8 ± 0.1	<0.001
Systolic Blood Pressure (mmHg)	115.6 ± 16.1	106.7 ± 11.7	<0.001
Diastolic Blood Pressure (mmHg)	73.6 ± 11.2	65.5 ± 9.3	<0.001
Hirsutism score	13.9 ± 3.9	11.2 ± 3.6	<0.001
Insulin level (μU/mL)	19.6 ± 17.6	10 ± 6.1	<0.001
FPG (mmol/L)	4.9 ± 0.7	4.8 ± 0.7	0.502
HOMA-IR	4.3 ± 4	2.1 ± 1.5	<0.001
HDL-C (mmol/L)	1.4 ± 0.3	1.5 ± 0.3	0.117
TG (mmol/L)	1.1 ± 1	0.8 ± 0.4	0.001
LDL-C (mmol/L)	3.0 ± 1	2.8 ± 0.7	0.048
Cholesterol (mmol/L)	4.9 ± 1.1	4.7 ± 0.8	0.247
Free Testosterone (pg/mL)	3.2 ± 2	1.1 ± 1.1	<0.001

Note. FPG: Fasting plasma glucose; HDL-C: high-density lipoprotein-cholesterol; TG: Triglyceride; LDL- C: low-density lipoprotein-cholesterol

603 **Table 2**

604 *Analysis of metabolic syndrome and other cardiovascular risk factors between adolescents*
605 *with PMOS and non-PMOS*
606

Variable	All n (%)	PMOS n (%)	Non-PMOS n (%)	Odds Ratio	95% CI	p-value
Central obesity*	104 (16.9)	12 (52.2)	92 (15.5)	5.94	2.6-13.9	<0.001
TG >1.7 mmol/L	26 (4.2)	4 (17.4)	22 (3.7)	5.77	1.8-18.7	0.007
HDL-C <1.29 mmol/L	104 (16.9)	6 (26.1)	98 (16.6)	1.84	0.7-4.8	0.33
Raised Systolic BP > 130 mmHg	28 (4.6)	4 (17.4)	19 (3.2)	4.22	1.3-13.4	0.027
Raised Diastolic BP >85 mmHg	20 (3.2)	5 (21.7)	15 (2.5)	9.49	3.1-29.3	<0.001
FBG >5.6 mmol/L	13 (2.1)	2 (8.7)	11 (1.9)	5.32	1.1-25.3	0.105
Hyperinsulinaemia [a]	102 (16.6)	11 (47.8)	91 (15.4)	4.56	1.9-10.9	<0.001
Insulin resistant (HOMA-IR [b])	59 (9.6)	7 (30.4)	52 (8.8)	4.11	1.6-10.5	0.004
Acanthosis nigricans	125 (20.3)	15 (65.2)	110 (18.6)	8.51	3.5-20.7	<0.001
Total Cholesterol >5.2 mmol/L	11 (1.8)	3 (13.0)	8 (1.4)	9.88	2.4-40.3	0.003
LDL-C >3.4 mmol/L	118 (19.2)	8 (34.8)	110 (18.6)	2.21	0.9-5.3	0.121
Metabolic syndrome **	20 (3.3)	5 (21.7)	15 (2.5)	11.3	3.6-35.4	<0.001
Family history of menstrual problems	112 (18.2)	7 (30.4)	105 (17.7)	2.98	1.25-7.07	0.013
Central obesity*	104 (16.9)	12 (52.2)	92 (15.5)	5.94	2.6-13.9	<0.001
TG >1.7 mmol/L	26 (4.2)	4 (17.4)	22 (3.7)	5.77	1.8-18.7	0.007

Note. FBG: Fasting blood glucose; HDL-C: high-density lipoprotein-cholesterol; TG: Triglyceride; LDL-C: low-density lipoprotein-cholesterol

*Waist circumference >80cm

CV: cardiovascular, [a]Insulin >15 μU/L, [b]HOMA (IR) >3.8 (mol × μU/l^2), LDL-C: low-density lipoprotein-cholesterol

**Central obesity + 2 out of 4 other parameters to meet diagnosis

[c] Odds ratio (OR) adjusted to urban and rural adolescent population

Table 3

Analysis of hyperandrogenaemia and clinical hyperandrogenism in PMOS and non-PMOS group

Hyperandrogenism	PMOS n (%)	Non-PMOS n (%)	Odds Ratio (OR)	Confidence Interval (CI)	p-value
Elevated testosterone [a]	15 (65.2)	45 (7.6)	18.85	7.49-47.45	<0.001
Mod-severe hirsutism [b]	9 (39.1)	68 (11.5)	5.04	2.09-12.18	<0.001
Acne	20 (87)	457 (77.2)	0.48	0.21-0.89	0.036
Alopecia	4 (17.4)	100 (16.9)	0.98	0.32-2.97	0.974

Note. *[a] Free testosterone > 2.57 pg/mL, [b] Modified Ferriman-Galway score >15, [C] Odds ratio (OR) adjusted to urban and rural adolescent population*

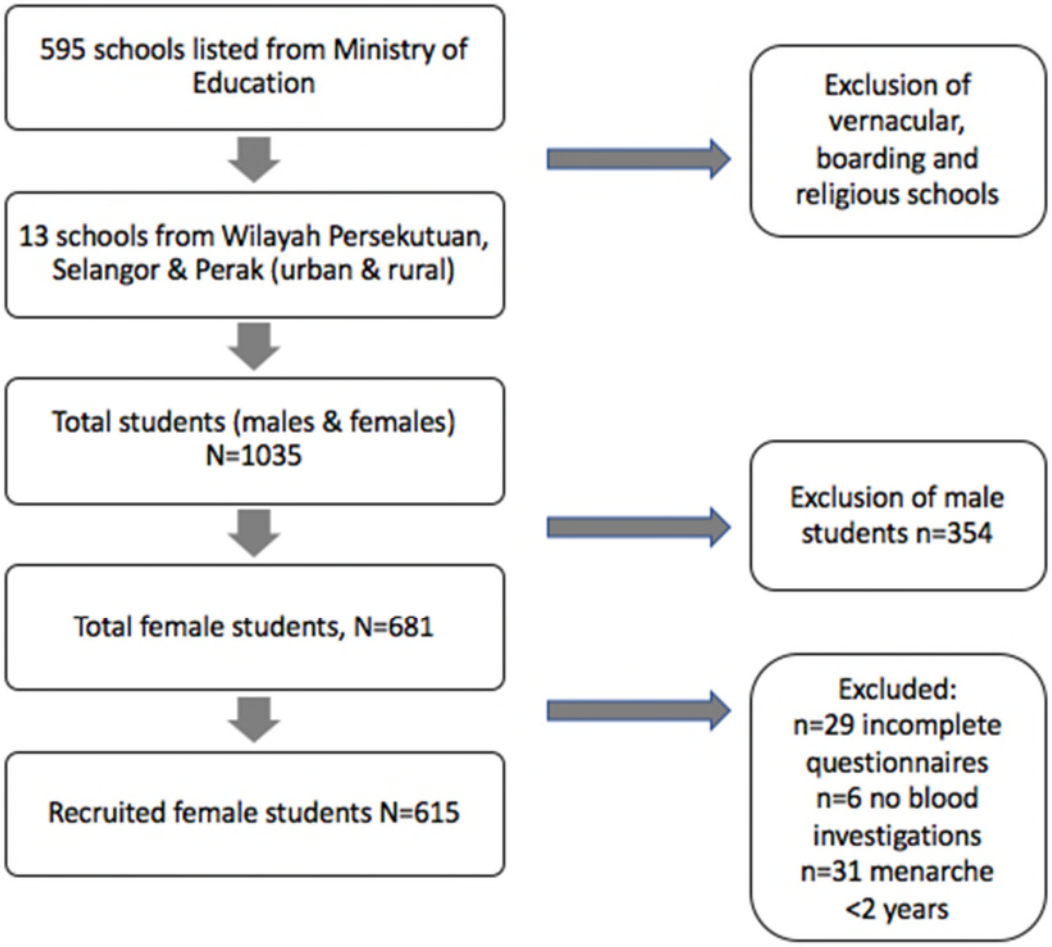

Figure 1 Flow chart of recruited adolescents

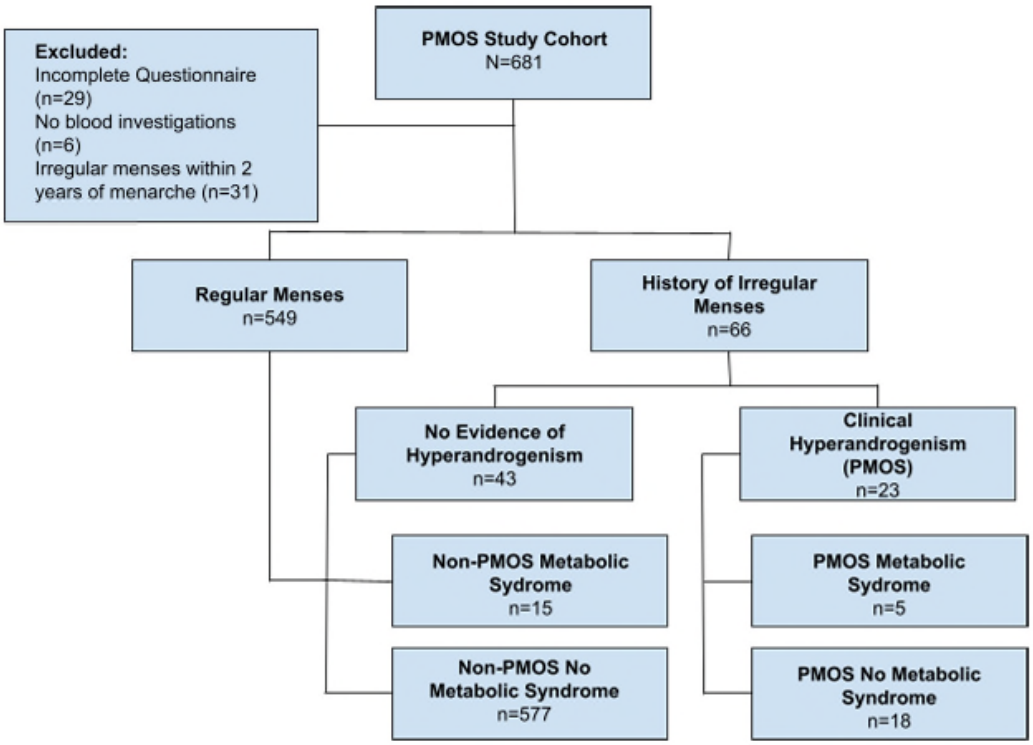

Figure 2 Outflow of results

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- APPENDIX1PMOS.docx
- APPENDIX2PMOS.docx