Review Article

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Impact of Ethnicity on the Presentation of Hyperandrogenism in Polycystic Ovarian Syndrome: A Review

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a common endocrinopathy affecting women of reproductive age. Diagnosis of PCOS is widely based on the 2003 Rotterdam criteria: Oligo-anovulation, hyperandrogenism and polycystic ovaries on ultrasound. However, clinical hyperandrogenism which is commonly used as a diagnostic criterion for PCOS is not particularly prevalent amongst certain ethnic groups. This review article explores the diverse manifestation of hyperandrogenism in different ethnicities and the difficulties of accurately diagnosing PCOS, with a focus on Malaysian patients.

Keywords: Polycystic ovary syndrome, ethnicity, hyperandrogenism, hirsutism.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common endocrinopathy amongst women in their reproductive ages. It is a complex disorder, with multiple phenotypes and heterogenous manifestations which suggest an interplay between genetic vulnerability and environmental conditions.[1]

In 1990, the National Institute of Health (NIH) in the United States concluded the first diagnostic criteria for PCOS which included both clinical or biochemical hyperandrogenism and chronic anovulation. These criteria served as the standard for both clinical physicians and researchers alike for over a decade.[2]

Subsequently, the 2003 Rotterdam criteria established in Rotterdam, Holland expanded on the NIH diagnostic criteria. The Rotterdam diagnostic criteria have since then received international recognition and are now used globally in the diagnosis of PCOS.[2]

The most prominently used criteria in the Malaysian setting is modified 2003 Rotterdam criteria as mentioned.

- Ovulatory dysfunction with irregular or absent menstrual cycles. This is clinically reflected by a menstrual cycle of <21 days or >45 days for women between 1-3 years post-menarche, or a cycle of <21 days or >35 days for women from 3 years post-menarche to menopause.
- Clinical or biochemical hyperandrogenism which is the focus of this article.
- Polycystic ovaries which are defined as more than twelve follicles per ovary (2-9 mm) and/or increased ovarian volume (more than 10 cm^3 in either ovary).[3,4]

Diagnosis of PCOS is made with the fulfilment of two of the above three features. Moreover, other endocrine disorders such as congenital adrenal hyperplasia, androgen secreting tumors, thyroid disease must be excluded.[3]

The 2006 Androgen Excess-PCOS (AE-PCOS) society cited hyperandrogenism as the fundamental criteria in PCOS, where ovarian dysfunction characterized by

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either oligo-anovulation or polycystic ovaries defined the complete syndrome.[5]

In 2012, the NIH Office for Disease Prevention -Sponsored Evidence-Based Methodology Workshop on Polycystic Ovary Syndrome proposed 2 major suggestions regarding the diagnostic criteria of PCOS. First was to completely rename the disorder to better reflect the complexity of this condition leading to its reproductive implications. Despite this recommendation, no specific name was suggested. Secondly, the major change was to use the 2003 Rotterdam diagnostic criteria, with the addition of identifying subphenotypes.[6]

Most recently, the 2018 International PCOS Guidelines collectively endorsed the Rotterdam diagnostic criteria to diagnose PCOS with certain recommendations. For adults, should a patient have both hyperandrogenism and oligo-anovulation, an ultrasound is not required for diagnosis. Another recommendation was that more stringent guidelines were required for adolescents. It is to be noted that due to the relative recentness of this guideline, not many studies have used this set of criterion.[7]

By contrast, in the Japanese diagnostic criteria of PCOS, developed by the Japanese Society for Obstetrics and Gynecology (JSOG), either the measurement of high luteinizing hormone (LH) with normal follicle-stimulating hormone (FSH) or the presence of hyperandrogenemia can be used to replace the criteria of hyperandrogenism. There was little emphasis on hyperandrogenism as fewer patients presented with this feature in the Japanese population. This suggests the ethnic variations in the expression of PCOS.[8]

Based on the Rotterdam criteria, there is a wide range of the reported prevalence of PCOS amongst various ethnic groups, from 2% to 20%. This leads us to the question of whether the said criteria can be used accurately to aid diagnosis for all ethnicities, given its diverse clinical presentation.[8]

Furthermore, Amsterdam ESHRE/ASRM-sponsored third PCOS Consensus Workshop Group reinforced the idea that the possible causes of differing clinical features of PCOS are ethnic origin, cultural or social practices as well as geographical location. Thus, daily clinical encounters should identify these likely contributors of clinical manifestations. However, all the diagnostic criteria did not have a specific definition for clinical hyperandrogenism such as a cutoff point for the modified Ferriman-Gallwey (mFG) score expressly based on ethnicity.[9]

According to a 2019 cross-sectional study by Dashti, the prevalence of PCOS in the Malaysian population was 12.6%, based on the 2003 Rotterdam criteria.[10]

Elaborating on this, the 3 major ethnicities in Malaysia are the Malays, the Chinese and the Indians. However, hyperandrogenism which is one of the key diagnostic criteria for PCOS is not particularly prevalent amongst the Chinese and Malay patients. This report explores the diverse manifestations of hyperandrogenism in various ethnic groups and the difficulties of accurately diagnosing PCOS amongst different ethnicities, specifically in Malaysia.

HYPERANDROGENISM

Based on the diagnostic criteria of PCOS mentioned above, hyperandrogenism can be evaluated either clinically or biochemically.

Physiologically, 97-98% of testosterone are bound to sex hormone binding globulins (SHBG) and are biologically inactive. The remaining 2-3% circulating freely in the bloodstream are biologically active. Thus, in order to have accurate measurement of biologically active testosterone, the calculation of free androgen index (FAI) with the determination of SHBG is needed. However, there is an absence of universally calibrated standards in laboratories to measure serum testosterone. Furthermore, the concentration of testosterone fluctuates throughout the day. These controversies put biochemical hyperandrogenism in the lower sensitivity and lower accuracy range.[8]

Clinical hyperandrogenism can present with hirsutism, acne and/or androgenetic alopecia. Among these three clinical presentations, hirsutism is found to be more strongly associated with hyperandrogenism than androgenetic alopecia or acne.[11]

However, this literary review focuses on both hirsutism and acne, with the exception of androgenic alopecia as it appears to be a poor marker for androgen excess and has received limited study.[12,13]

Hirsutism is defined as the evidence of excessive terminal hair in women especially at androgen-sensitive areas. The prevalence of hirsutism is nearly 10% in most of the populations.[14]

In women with PCOS, dihydrotestosterone, which is a potent metabolite of testosterone, converts vellus hairs to terminal hairs in androgen-sensitive areas such

as upper lip, chin, upper and lower abdomen, upper and lower back, chest, upper arms and thighs.[11]

The conversion of testosterone to the active metabolite dihydrotestosterone requires the enzyme 5 alpha reductase. This enzyme activity might differ due to genetic or ethnicity variation.[15]

Modified Ferriman-Gallwey (mFG) visual scoring system was developed to clinically assess the severity of hirsutism. A rate of zero to four will be given to each of the nine androgen-sensitive body areas. Zero signifies the absence of hair whereas a score of four represents the extensive growth of terminal hair. This will make up a total mFG score of 0 to 36. Initially, a score of eight or above was defined as having clinical hirsutism.[16]

However, this cut off point was based on the evaluation of 60 Caucasian women, which might not be representative to the other ethnicities.[17]

The modified scoring systems have already recognized the importance of ethnicity in evaluating a patient with hirsutism. Unfortunately, there is no actual integration of ethnicity variation into the modified updated scoring system.[17]

The AE-PCOS Society also suggested the necessity to develop cut off values specific to each ethnicity in order to accurately define hirsutism in women with PCOS.[16]

Acne is defined as inflammation of the sebaceous gland of the skin. The 5 alpha reductase enzyme acts to convert testosterone to a more potent androgen, dihydrotestosterone (DHT). These androgens act to cause excessive sebum production which blocks the gland, allowing for subsequent bacterial colonization. There have been controversial results regarding the association of acne severity with the plasma androgen levels which could be due to differences in the local concentration of androgens or level of androgen receptors in the skin.[12]

Furthermore, the incidence and severity of elevated androgen levels could also be associated with eating habits, working and living environment.[18]

The severity of acne is evaluated subjectively, according to the number, distribution and type of lesion. There are many proposed grading systems for the acne lesions such as the Acne Severity Index, Global Acne Grading System and the Consensus Conference on Acne Classification. However, there is no well quantified or global scoring system for acne in PCOS patients.[12]

Ethnicity Variation on Prevalence of PCOS

The prevalence of PCOS is dependent on the diagnostic criteria used and the population. Thirteen studies on the prevalence of PCOS were reviewed in this report and is depicted by Figure 1. The diagnostic criteria used were the 1990 NIH, 2003 Rotterdam and the 2006 AE-PCOS criteria.

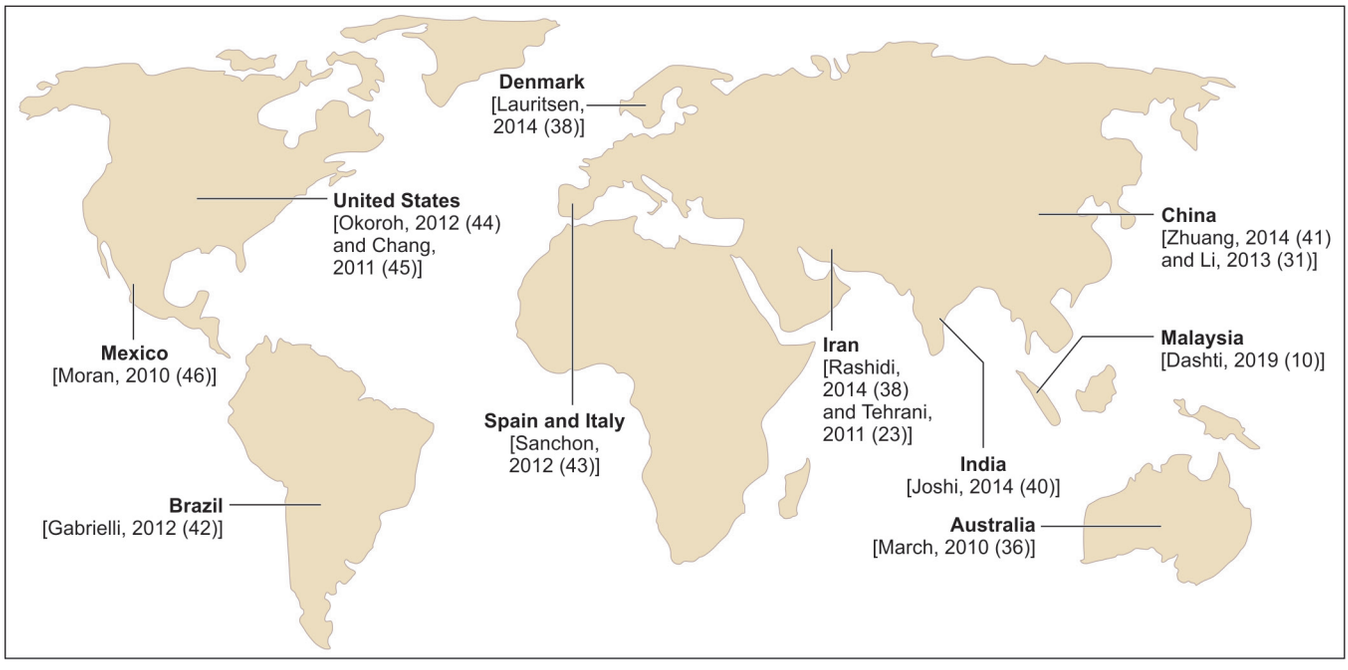

Fig. 1: Studies on prevalence of PCOS illustrated by region
iStock. (2013, October 6). World Map Earth Global Continents World [Clip Art]. Pixabay. https://pixabay.com/vectors/world-map-earth-global-continents-146505/

MALAYSIA, ROTTERDAM CRITERIA

A 2019 cross-sectional study in Malaysia involving 675 females revealed a prevalence rate of PCOS of 12.6% based on the 2003 Rotterdam criteria. However, as this study involved only females working at University Putra Malaysia, it is not reflective of the general population. Moreover, the ethnicities of the participants were not indicated in the study. As such, it cannot delineate the specific prevalence of the major ethnic groups in Malaysia.[10]

PREVALENCE OF PCOS IN OTHER COUNTRIES

Figure 2 illustrates the prevalence of PCOS according to various ethnic groups and diagnostic criteria in the form of a bar chart. Table 1 provides additional information with regards to the sample size and limitations of each study.

Amongst all the reviewed studies which used more than one diagnostic criteria, the usage of the Rotterdam criteria produced the highest prevalence, which is likely due to having a broader diagnostic criterion. It can also be seen that the prevalence of PCOS varies widely amongst different ethnicities and geographical regions. Take for example, the 2 studies from China. China is a large country with a huge population with multiple tribes and ethnicities and the regions of China are geographically different which may have contributed to the discrepancies in reported prevalence. Therefore, we can conclude there could be a need for a review of the diagnostic criteria to make it more specific and sensitive towards different ethnic groups and regions.

ETHNICITY VARIATION AND HIRSUTISM

Hirsutism is one of the most prominent features of clinical hyperandrogenism resulting from excess

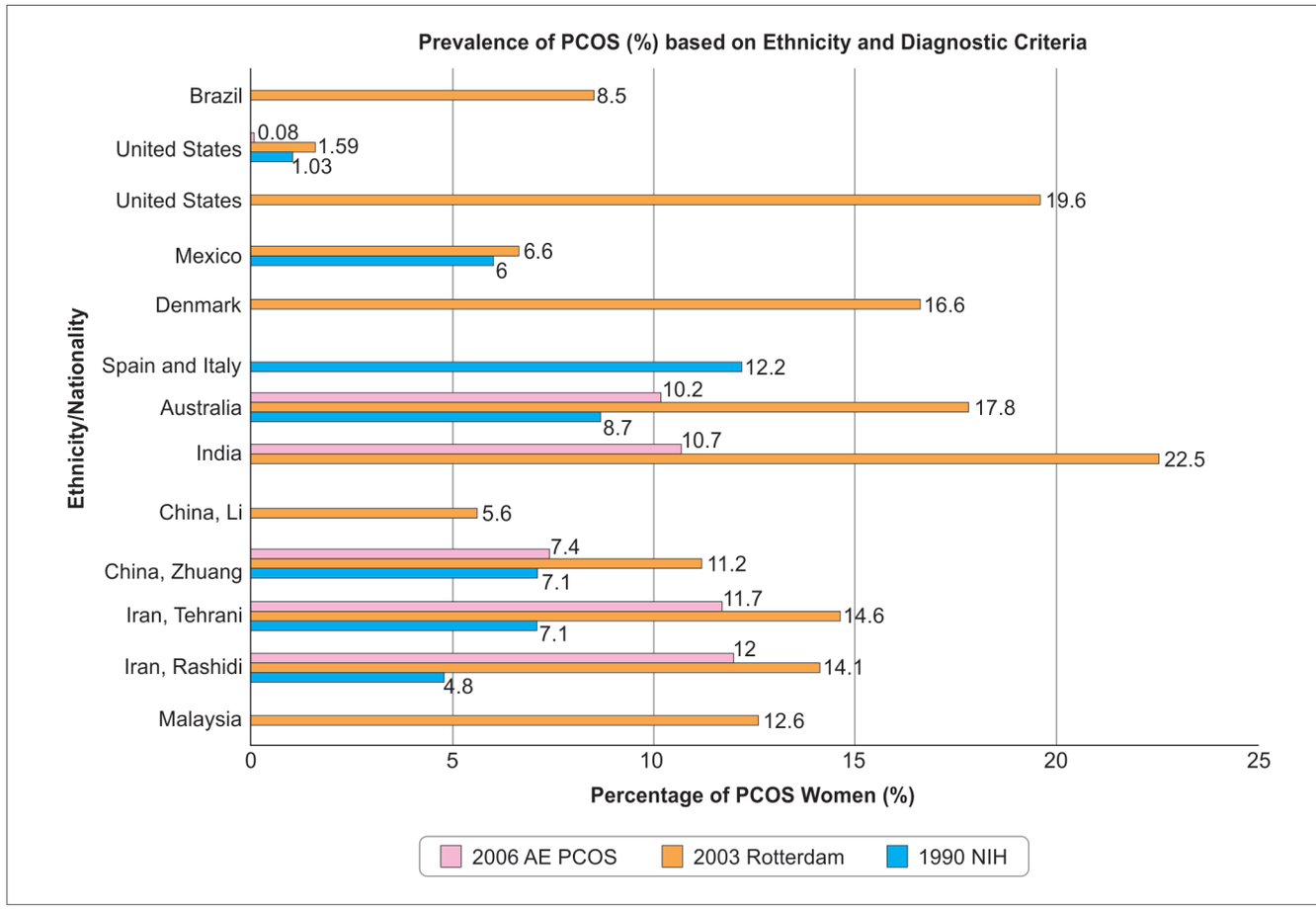

Fig. 2: Prevalence of PCOS (%) based on ethnicity and diagnostic criteria in various countries

Table 1

Sample size and limitations of various studies withe reference to prevalence of PCOS among various ethnicities across the world

Author, year	*Ethnicity/ Nationality*	*Prevalence of PCOS(%)*			*Sample size*	*Method of study*	*Comments/limitations*
		1990 NIH	*2003 Rotterdam*	*2006 AE-PCOS*			
Dashti, 2019[10]	Malaysia	N/A	12.6	N/A	675	Cross sectional	Selection bias: All the participants were university employees
Lauritsen, 2014[38]	Denmark	N/A	16.6	N/A	447	Prospective cross sectional	Selection bias: All the participants were health care workers and there was exclusion of hormonal contraceptive users
Rashidi, 2014[39]	Iran	4.8	14.1	12	602	Epidemiological study	Sample taken from community in Southwest of Iran, which may not be reflective of the general population of Iran
Joshi, 2014[40]	Indian	N/A	22.5	10.7	600	Cross sectional	Selection bias: Only young females aged 15-24 years. Represents only one socioeconomic background, may not accurately reflect the general population
Zhuang, 2014[41]	Han Chinese	7.1	11.2	7.4	1645	Cross sectional	The sample size used is wider than reproductive age range (12-45 years)
Li, 2013[31]	Han Chinese	N/A	5.6	N/A	15924	Large-scale epidemiological study	Deviation in age distribution (19-45 years)
Gabrielli, 2012[42]	Brazil	N/A	8.5	N/A	859	Cross sectional	Self-reporting of hirsutism and acne using questionnaire is less sensitive as compared to medical examination/ consultation
Sanchon et al, 2012[43]	Spain, Italy	12.2	N/A	N/A	592	?Cohort study/ cross sectional	Multicenter prevalence survey Use of blood donors as sample size No control sampling for fasting/time/phase of menstrual cycle
Okoroh, 2012[44]	United States	1.03	1.59	0.08	12,171, 830	Retrospective study	Lack of info of race and ethnicity, prevalence estimate may be low due to retrospective design

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Author, year	*Ethnicity/ Nationality*	*Prevalence of PCOS(%)*			*Sample size*	*Method of study*	*Comments/limitations*
		1990 NIH	*2003 Rotterdam*	*2006 AE-PCOS*			
Chang, 2011[45]	United States	N/A	19.6	N/A	697	Cross sectional	
Tehrani, 2011[23]	Iran	7.10	14.60	11.70	929	Cross-sectional study	Unselected population (general population with and without PCOS)
March, 2010[36]	Australia	8.7	17.8	10.2	728	Retrospective cohort	Restricted age range of 27-34 years, it is noted that a prevalence estimate should be generated to account for a larger age range. Lack of information with regards to race and ethnic group
Moran, 2010[46]	Mexico	6.0	6.6	N/A	150	Prospective cross sectional	Small sample size

androgens along with androgen sensitivity. The differing prevalence of hirsutism between ethnicities may be explained by the genetic variations of the 5 alpha reductase enzyme activity which converts testosterone to the highly potent dihydrotestosterone.[15]

The results of 19 studies from 2010 to 2019 showing the mean mFG score and percentage of clinical hirsutism of participants from different ethnicities are summarized in Table 2.

Based on the reviewed studies, the top 3 highest mFG scores were from Glintborg in Denmark, with the studied Middle East population score at 16 ± 6, followed by Turkish population studied by Hacivelioglu at 11.6 ± 8.3 and finally back to Glintborg's Caucasian population at 11 ± 4. All these studies had adequate sample sizes of 784, 133 and 190 respectively.[12,15]

Conversely, the lowest mFG score was 1.49 ± 2.24 based on a 2019 study involving 479 Vietnamese women.[19]

This is followed by another 2019 cross-sectional study from Singapore with 321 Chinese (n = 228) and non-Chinese (n = 93) participants of which revealed a mFG score of 1.6 ± 2.4.[20]

However, it is noted for that we do not know the ethnicity of the non-Chinese participants, whether they are Malay, Indian or other races which are typical from the Singaporean demographic.

From this, it is observed that the Middle Eastern and Caucasian population had significantly higher mFG scores than the Vietnamese and Singaporean population. The difference between the mean mFG scores supports the association of varying clinical hyperandrogenism with different ethnicities.

Studies from the Philippines, Korea, Taiwan, Sri Lanka, Iran and Thailand were reviewed. With a cut-off mFG score of ≥7, 17.9% of 28 Filipino women were hirsute with a mean mFG score of 4.3 ± 3.0. However, this study is limited by its small sample size.[21]

60% of 40 Korean women and 19% of 627 Taiwanese women were found to have hirsutism based on a cut-off mFG score of ≥6.[13,22]

Similarly, the small sample size of 40 Korean women makes it difficult for the results to reflect the general Korean population. Based on a mFG cut-off of ≥8, 79.7% of Sri Lankans, 22.4% of Iranians and 15.6% of Thai women were clinically hirsute.[23-25]

Interestingly, studies based in Western countries comparing mFG scores of Caucasians and Asians revealed similar numbers. A 2013 cross-sectional study based in the United States by Wang and colleagues

Table 2

Mean mFG score and clinical hirsutism (%) of different ethnicities and countries

Author, year	*Country*	*Ethnicity*	*Mean mFG score*	*Clinical hirsutism (%)*	*Cutoff mFG*	*Sample size*	*Criteria*	*Method of study*	*Limitations/comments*
Dashti, 2019[10]	Malaysia	Malaysian	N/A	26.5	≥6	85	2003 Rotterdam	Cross-sectional study	Selection bias: All the participants were university employees
Cao, 2019[19]	Vietnam	Vietnamese	1.49 ± 2.24	34.4	≥5	479	2003 Rotterdam	Prospective Cross sectional	First study that characterizes the manifestations of PCOS amongst the Vietnamese population
Ilagan, 2019[21]	Philippines	Filipino	4.3 ± 3.0	17.9	≥7	28	2003 Rotterdam	Prospective cross sectional	Small sample size. Study was performed at one center. Suggestion: Perform at multiple centers to validate results to better reflect the Filipino population
Lim, 2019[20]	Singapore	Singaporean	1.6 ± 2.4	N/A	≥5	321	2003 Rotterdam	Cross sectional	The ethnicity of the participants was mostly Chinese (n= 228) with the remainder being Non-Chinese (n=93). It is unknown if non-Chinese included Malays, Indians or others The results of mean mFG score were based on the total sample size (n=321) of PCOS patients
Zhao, 2018[18]	China	Uygur	2.12 ± 0.35	N/A	N/A	82	2003 Rotterdam	Cross-sectional study	Small sample size
		Han Chinese	2.35 ± 0.24	N/A	N/A	100			
Engmann, 2017[33]	United States	Non-Hispanic White	N/A	86.8	≥8	476	2003 Rotterdam	Prospective Multicenter, double blind controlled clinical trial (PPCOS II)	Study population was young and generally fit. The results may not be reflective of older PCOS women. Self-reporting of ethnicity.
		Non-Hispanic Blacks		82.7		98			
		Hispanic		93.8		128			

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Author, year	*Country*	*Ethnicity*	*Mean mFG score*	*Clinical hirsutism (%)*	*Cutoff mFG*	*Sample size*	*Criteria*	*Method of study*	*Limitations/comments*
Mani, 2015[27]	United Kingdom	Caucasian	N/A	77.4	N/A	929	2003 Rotterdam	Cross sectional, retrospective data analysis	Ethnicities were broadly divided into 2 groups that is Caucasian (white British, White Irish, White) and South Asians (Pakistan, Indian, Bangladeshi) which does not give a homogenous participant group. Missing data due to long period of data collection Selection bias: recruitment of participants based on referral to specialty clinic
		South Asian	N/A	88.5	N/A	381			
Hong, 2015[13]	Korea	Korean	7.4	60	≥6	40	2003 Rotterdam	Cross sectional	Small sample size
Hacivelioglu, 2013[12]	Turkey	Turkish	11.6 ± 8.3	56	≥8	133	2003 Rotterdam	Retrospective cohort	No control data for comparison
Li, 2013[31]	China	Han Chinese	2.7 ± 3.7	N/A	≥6	833	2003 Rotterdam	Large scale epidemiological study	Deviation in age distribution
Wang, 2013[26]	United States	Asian	N/A	46.4	≥8	28	2003 Rotterdam	Cross sectional	Participants were recruited from a single multidisciplinary PCOS clinic. Heterogenous ethnicity of participants Small sample size
		Caucasian	N/A	48.8	≥8	121			
Guo, 2012[32]	China	Han Chinese	3.6 ± 4.9	20.8	≥6	547	2003 Rotterdam	Cross sectional	No *a priori* alignment prior to data collection Selection bias: Exclusion of ovulatory PCOS women No control data
	Netherlands	Caucasian	5.2 ± 5.4	10.2	≥8	427			

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Author, year	*Country*	*Ethnicity*	*Mean mFG score*	*Clinical hirsutism (%)*	*Cutoff mFG*	*Sample size*	*Criteria*	*Method of study*	*Limitations/comments*
Ishak, 2012[28]	Malaysia	Malay	N/A	60.6	N/A	99	2003 Rotterdam	Cross sectional	Cut off mFG was not stated Small sample size Participants were recruited from north-east Peninsula Malaysia, which is not reflective of the larger population
Mandrelle, 2012[29]	India	South Indian	N/A	28.3	≥8	120	2003 Rotterdam	Prospective cross sectional	No control group of non-PCOS women
Tehrani, 2011[23]	Iran	Iran	N/A	22.40	≥8	929	Rotterdam/NIH/AES	Cross-sectional study	Unselected population (general population with and without PCOS)
Wijeyaratne, 2011[24]	Sri Lanka	Sri Lankan	N/A	79.7	≥8	469	2003 Rotterdam	Cross sectional	Selection bias: Participants were recruited from specialist referral clinic
Glintborg, 2010[15]	Denmark	Caucasian	11 ± 4	N/A	N/A	784	2003 Rotterdam	Retrospective trans-sectional	Single center study
		Middle East	16 ± 6	N/A	N/A	190			
Wongwananuruk, 2010[25]	Thailand	Thai	22	15.6	≥8	250	2003 Rotterdam	Cross sectional	Performed at a single center
Yang, 2010[22]	Taiwan	Taiwan	2.33 ± 1.17	19	≥6	627	2003 Rotterdam	Cross sectional	Subjects recruited from single reproductive clinic in Taipei, does not reflect the general population.

showed 46.4% of Asians and 48.8% of Caucasians were clinically hirsute.[26]

Similarly, another study from the United Kingdom concluded 88.5% of South Asians and 77.4% Caucasians had hirsutism.[27]

Although population-based studies in Asia show lower mFG scores in PCOS women, these studies seem to show that Asian women living in Western countries are more similar to Caucasian women than their counterparts in Asia. This could be due to geographical and environmental influences such as diet which can potentially be a confounding factor.[26]

In Malaysia, the 3 major ethnic groups are Malays, Chinese and Indians. Unfortunately, there is a lack of data with regards to PCOS and its association with ethnicities in Malaysia. Dashti and colleagues conducted a cross-sectional study on 85 Malaysians with a cutoff mFG of ≥6 which revealed 26.5% of participants that were clinically hirsute. However, there was no clear delineation amongst the individual races of the 85 participants which makes it difficult for us to make clear cut associations between hirsutism and the specific ethnicity.[10]

In 2012, Ishak et al.'s study concluded 60.6% of 99 Malays are hirsute. However, this may not be reflective of the general Malay population of Malaysia because participants were recruited only from North-East Peninsula Malaysia which creates a selection bias.[28]

Most Indians in Malaysia can draw their origins from South India. A 2012 prospective cross-sectional study from India revealed 28.3% out of 120 South Indian participants had clinical hirsutism when the cut-off mFG value was ≥8.[29]

The majority of the Malaysian Chinese population are Han Chinese.[30]

As such, studies by Zhao, Li and Guo from China that assessed the Han Chinese group were reviewed. In all these studies, the mean mFG score for 100, 833 and 547 women with PCOS were 2.35 ± 0.24, 2.7 ± 3.7 and 3.6 ± 4.9 respectively.[18,31,32]

Both studies by Li and Guo used a mFG cutoff score of 6 while cutoff score used by Zhao is not known.[18,31,32]

The prevalence of hirsutism differs according to ethnicities. There is a lower prevalence of hirsutism in the Chinese population as compared to Malays and Indians, with the Chinese population having a smaller cutoff mFG score as well. However, the data assessed for both the Chinese and Indian ethnic groups were not collected from the Malaysian population. Moving forward, local studies with participants from the major ethnicities of Malaysia should be conducted to yield a more specific cut off mFG value for each ethnicity in order to aid the diagnosis of PCOS.

ETHNICITY VARIATION AND ACNE

Table 3 summarizes the percentages of PCOS women of different ethnicities presenting with acne. The diagnostic criteria used for all the studies in Table 3 was 2003 Rotterdam criteria. A 2019 Vietnamese study by Cao and colleagues involving 479 women revealed that 23.8% of Vietnamese women had acne. However, the grading system for acne was not stated.[19]

In the United states, a 2017 cross-sectional study involved non-Hispanic white (NHW), Non-Hispanic Black (NHB) and Hispanics revealed 35.2%, 25.5% and 64.1% of the participants had acne respectively. This study used a cut-off acne score of >5 based on the number of acne lesions which were assessed by trained study personnel.[33]

Mani and colleagues conducted a cross-sectional study in the United Kingdom which revealed 23.9% of Caucasian and 16.8% of Asian PCOS patients had acne as part of their PCOS presentation.[27]

In 2013, Wang concluded that 46.4% and 73.9% of Caucasian and Asian patients suffered from acne. However, the sample size for Asians was very small at 28 participants.[26]

A cross-sectional study performed in 2011 by Tehrani involving 929 Iranians with PCOS was found to have the lowest prevalence of the presentation of acne at 3.5%.[23]

Ninety five percent out of 40 Korean participants in a 2014 cross-sectional study have acne which was recorded by two independent, blinded physicians counting the lesions. Comparing the acne characteristics, it is revealed that acne lesions were found most often on the face, chest and back. The severity of the lesions was highest in the face as compared to other regions.[13]

In Turkey, 23% out of 133 PCOS participants had acne, which was scored by the Global Acne Grading System (GAGS) which is not commonly used in PCOS patients.[12]

Yang and colleagues recorded that 38% of 627 Taiwanese patients presented with acne lesions.[22]

39.2% of 469 Sri Lankan participants were revealed to have acne as part of the PCOS manifestations. Similar to

Table 3

Presentation of acne in different ethnic groups

Author, year	*Country*	*Ethnicity*	*Acne (%)*	*Sample size*	*Criteria*	*Method of study*	*Limitations/comments*
Dashti, 2019[10]	Malaysia	Malaysian	21.7	85	2003 Rotterdam	Cross-sectional study	Selection bias: All the participants were university employees Occurrence of acne was recorded using Consensus Conference on Acne Classification
Cao, 2019[19]	Vietnam	Vietnamese	23.8	479	2003 Rotterdam	Cross-sectional study	Grading system for acne was not stated
Engmann, 2017[33]	United States	Non-Hispanic White	35.2	475	2003 Rotterdam	Prospective Multicenter, double blind controlled clinical trial (PPCOS II)	Cut off: Acne Score >5 based on both inflammatory and non-inflammatory lesions which was assessed by trained study personnel
		Non-Hispanic Blacks	25.5	98			
		Hispanic	64.1	128			
Mani, 2015[27]	United Kingdom	Caucasian	23.9	929	2003 Rotterdam	Cross sectional	Missing data Unknown how acne is assessed
		South Asian	16.8	381	2003 Rotterdam		
Hong, 2015[13]	Korea	Korean	95	40	2003 Rotterdam	Cross sectional	Small sample size Acne occurrence was recorded by two independent, blinded physicians counting the lesions
Hacivelioglu, 2013[12]	Turkey	Turkish	23	133	2003 Rotterdam	Retrospective cohort study	No control group for comparative purposes Classification of acne: Global Acne Grading System
Wang, 2013[26]	United States	Asian	73.9	28	2003 Rotterdam	Cross sectional	Acne evaluated by dermatologist Heterogenous ethnicities in Asian groups
		Caucasian	46.4	121			

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Author, year	*Country*	*Ethnicity*	*Acne (%)*	*Sample size*	*Criteria*	*Method of study*	*Limitations/comments*
Guo, 2012[32]	China	Han Chinese	40.8	547	2003 Rotterdam	Cross sectional	
	Netherlands	Caucasians	19.8	427			
Ishak, 2012[28]	Malaysia	Malay	41.4	99	2003 Rotterdam	Cross sectional	
Mandrelle, 2012[29]	India	South Indian	9.2	120	2003 Rotterdam	Cross sectional	Acne was recorded by sites of distribution and severity
Wijeyaratne, 2011[24]	Sri Lanka	Sri Lankan	39.2	469	2003 Rotterdam	Cross sectional	
Tehrani, 2011[23]	Iran	Irans	3.50%	929	NIH/2003 Rotterdam/ AES	Cross sectional	Unselected population (general population with and without PCOS)
Yang, 2010[22]	Taiwan	Taiwan	38.0	627	2003 Rotterdam	Cross sectional	Acne was defined as lesions on the face, chest and back for >6 months

Hong and colleagues' study, the common sites of acne were the face (36.9%), chest (12.8%) and back (8.5%).[24]

There is a glaring difference between different ethnicities that present with acne as a cutaneous manifestation of hyperandrogenism. As an illustration, 95% of Koreans with PCOS presented with acne while only 3.5% of Iranians had a similar presentation.[13,23]

In Malaysia, a 2019 study revealed 21.7% of the 85 participants had acne which was graded based on the Consensus Conference on Acne Classification. There is, however, the probability of a selection bias as all the participants were university employees. Additionally, the study did not categorize and analyze the data based on ethnicity.[10]

A 2012 study by Ishak and colleagues revealed that 41.4% out of 99 Malays from North East Peninsula Malaysia had acne.[28]

No data was found regarding the Chinese and Indian ethnic groups in Malaysia. As such, studies from China and South India were taken for review. 40.8% of 547 Han Chinese patients presented with acne while 9.2% of 120 South Indians were recorded to have acne.[29,32]

Given that the data for the Chinese and Indian ethnic groups were not obtained locally, it may not be a true representative of these ethnic groups in Malaysia given that there are significant differences in the climate and dietary lifestyles between Malaysia and countries from which the data was obtained from.

DISCUSSION

The difference in severity of hirsutism between each distinct ethnicity suggests a need to adjust mFG cutoff value based on the ethnic population as well as the geographical region. Lower mFG criteria should be applied for East Asian women, possibly a cutoff mFG score between 5-7, based on the data in the reviewed studies. On the other end, Caucasian, Hispanic, Middle Eastern and South Asian women should use a higher cutoff mFG score of ≥8. Large scale epidemiological studies should be conducted to get a specific cut off score for different ethnic groups.[16]

Acne is another sign of clinical hyperandrogenism in PCOS patients which can be the most prevalent cutaneous manifestation, especially in ethnic groups with less dense hair patterns in hirsutism. In the reviewed studies, acne was represented in percentages. However, there is no single standardized system of quantifying the severity of acne which may explain the wide range of acne prevalence rates. Therefore, more objective criteria are needed for the systematic evaluation of acne, with the assessment performed by trained dermatologists.

FITZPATRICK SKIN PHOTOTYPES

On the other hand, setting a cutoff value of total mFG score based on ethnicity to define hirsutism might pose challenges if patients are of mixed ethnicities. In 2018, 18,509 out of 206,253 marriages in Malaysia were inter-ethnic marriages. This makes up to 9% out of total marriages according to the Department of Statistics Malaysia's Marriage and Divorce Statistics report. There is an increasing trend noted compared to 8% of marriages involving those of different ethnic groups in 2017.[34]

Similar trends are happening worldwide including the US and Singapore. Based on the US Census Bureau, there was a growth in interracial marriages from 7.4% to 10.2% in the US from 2000 to 2016. On the other hand, Singapore had an increase from 22.1% to 22.4% of inter-ethnic marriages from 2017 to 2018.[34]

Thus, the cutoff value of mFG score specific to ethnicity might not be applicable to the offspring of interracial marriages.

Considering the possibility of skin color as a factor for mFG cutoff value, three articles were found on the association of skin lightness and the prevalence of hirsutism. In a 2017 study done by Afifi and colleagues, Fitzpatrick skin type (FST) was used to evaluate skin color. The six types of FST are categorized based on skin color and response of skin to sun exposure. Type 1 skin always burns and never tans while type 2 skin usually burns and tan minimally. Type 3 is defined as skin that burns mildly and tans uniformly. FST type 4 burns minimally and always tan well while FST type 5 very rarely burns but very easily tans. Lastly, skin that never burns and never tans is classified as FST type 6.[16]

The study published in 2017 showed a positive association between higher FST and hirsutism especially at the truncal region. The highest mFG scores were reported in patients with FST type 6 and type 5 followed by FST type 4 and 3. PCOS patients with FST type 1 and type 2 had the least prevalence of hirsutism. However, higher FST is not correlated with the mFG scores at upper lip.[16]

This exception aligns with the study published in 2014 by Javorsky and colleagues.[17]

Although the study showed that patients with darker skin tone of cheek, forehead and inner arm had hair growth at upper lip, logistic regression proved that skin lightness was not predictive of hair growth. Nonetheless, this study by Javorsky only evaluated hair growth at the upper lip instead of all nine androgen-sensitive areas.[17]

Another study in 2013 suggested that dark-skinned women had significantly higher mean mFG scores even with a similar number of hair follicles. The study also suggested that the distribution of terminal hair was similar between patients with different tones of skin color.[35]

In a nutshell, the mFG scoring system should not be used rigidly and strictly. Age, FST of patients and the family history should be taken into consideration in modifying the criteria to diagnose hirsutism. As an instance higher mFG cutoff score should be applied if the patient is comparatively young, dark-skinned and has a familial complaint.[35]

METABOLIC CONSEQUENCES OF PCOS

Accurate diagnosis of hirsutism and standardized system of quantifying the severity of acne is vital in order to lower the potential of misdiagnosis in patients. Many women especially those from East Asian countries with PCOS go undiagnosed in the community.[36]

Women with PCOS are known to have higher risks of developing metabolic complications such as metabolic syndrome, obesity, insulin resistance, hypertension and dyslipidemia. These long-term metabolic consequences of PCOS contribute to substantial morbidity and financial burden for patients.

With the existence of specific cut-off mFG scores for hirsutism and a standardized acne scoring system, healthcare providers will be able to diagnose PCOS early and accurately, which allows for early intervention and primary prevention.[32,37]

CONCLUSION

This report highlights the role of ethnicity in influencing the degree of cutaneous manifestation of hyperandrogenism among women with PCOS. Furthermore, ethnic difference in PCOS appeared to be associated with metabolic complications. However, the associations between skin color and hirsutism was not strongly proven.

There is a need for more data from comparative studies before we can accurately diagnose hirsutism and PCOS in a multi-ethnic nation like Malaysia. Unfortunately, the local data in Malaysia is glaringly insufficient.

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Conflict of Interest

None to declare.

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