

Why we need epidemiologic studies of polycystic ovary syndrome in Africa

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Abstract

The primary objective of the Ghana Polycystic Ovary Syndrome Epidemiology and Phenotype (Ghana-PEP) study will be to assess the relevance and phenotypic distribution of polycystic ovarian syndrome (PCOS) in a medically unbiased population of reproductive-aged women. In addition, the study will also attempt to identify sociodemographic, environmental, and psychological factors that may play a role in the development of PCOS phenotype. The study aims to recruit 990 randomly selected women aged 18–45 years living in Nsawam, the district capital of the Nsawam-Adoagyiri Municipality, in the Eastern region of Ghana. Participants will complete a questionnaire with the aid of trained personnel, undergo a physical examination, and undergo ultrasonography and biochemical evaluations relevant to PCOS. It is anticipated that the study will provide the population prevalence and phenotypes, and distribution of PCOS.

KEYWORDS: Ghana; PCOS; Phenotypes; Polycystic ovarian syndrome; Prevalence

Polycystic ovarian syndrome (PCOS) is a common endocrine–metabolic disorder. Although it is most clinically apparent among women of reproductive age, PCOS can be symptomatic in pre-adolescent and menopausal women, and potentially even in men.¹ Typically, the syndrome is characterized by chronic oligo-anovulation, biochemical and/or clinical hyperandrogenism, and polycystic ovarian morphology (PCOM). In addition to hyperandrogenic dermatologic symptoms (acne, alopecia, and hirsutism), PCOS is associated with impaired reproduction and obstetric outcomes.²

Women with PCOS seem to be more frequently obese than their non-affected counterparts, although the degree of this association is weak when medically unbiased populations are studied.^{3,4} PCOS

is also associated with an increased risk of endometrial and possibly ovarian carcinoma. Mood disturbances and psychosexual dysfunction are more frequent in PCOS. Lastly, most women with PCOS, regardless of body mass, have variable degrees of chronic subacute inflammation and insulin resistance, which are associated with an increased risk of type 2 diabetes mellitus, dyslipidemia, and vascular disorders including cerebrovascular incidents and possibly even cardiovascular disease.^{1,2}

As a syndrome, PCOS is defined by a collection of signs and symptoms after the exclusion of related or mimicking disorders. In 1990, the relatively strict US National Institutes of Health (NIH) criterion categorized two phenotypes of PCOS: phenotype A, comprising oligo-anovulation, hyperandrogenism, and PCOM; and phenotype B,

comprising oligo-anovulation and hyperandrogenism.⁵ Subsequently, the 2006 Androgen Excess and PCOS (AE-PCOS) Society diagnostic criterion included phenotype C, comprising hyperandrogenism and PCOM, in addition to A and B,⁶ while the 2003 Rotterdam criterion of the European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) additionally included phenotype D (oligo-anovulation and PCOM).^{7,8} Phenotypically, the Rotterdam 2003 and AE-PCOS Society 2006 definitions are effectively expansions of the NIH 1990 criterion. In 2012, a consensus workshop sponsored by the NIH recommended use of the Rotterdam 2003 criterion to identify the broadest number of affected individuals, coupled with the need to define the specific phenotype of affected individuals (i.e. as phenotypes A–D).⁹ Of note, the phenotypic presentation of PCOS shows ethnic diversity.¹⁰

There is strong evidence that the features of PCOS identified among clinically referred patients are more severe than the phenotypes of PCOS identified in studies of medically unbiased (unselected) populations. For example, Ezeh et al.³ compared two cohorts from the same geographic area, the first consisting of individuals with PCOS seeking medical care and the second comprising individuals with PCOS identified during a routine pre-employment health assessment.³ They reported that the referred (medically biased) individuals more frequently showed the more complete PCOS phenotype (phenotype A), were more hirsute, had higher serum androgen levels, and were more obese as compared with individuals identified in the unselected cohort. A similar conclusion was reached in a study of Spanish women screened during blood donation.¹¹ At least in part, this bias is determined by the negative impact of PCOS features, particularly obesity and hirsutism, on quality of life^{12–14} and ability to access medical care.³ A meta-analysis of studies on PCOS has provided further evidence of referral bias for the PCOS phenotype.⁴ Consequently, to gain the most accurate understanding of the prevalence of PCOS, epidemiologic studies of unselected or unbiased populations must be undertaken.

Polycystic ovarian syndrome seems to be a complex prehistoric genetic trait, possibly dating back 50 000 years or longer.¹⁵ Thus, despite its clear reproductive disadvantages, the disorder has apparently persisted for tens of thousands of years. Various potential benefits of PCOS among ancestral women have been considered to account for this paradox, including metabolic, immune, and musculoskeletal benefits, patterns of child-rearing and mothering, reproductive longevity, and in utero or childhood survival advantages, which might have had a significant role in our hunter-gatherer past.¹⁵ In reality, however, there is little evidence to indicate that the persistence of PCOS is due to direct positive selection. Instead, the evolution of PCOS has probably been driven by non-adaptive mechanisms, including genetic drift and population balance.^{15–17} Among other approaches, insight into the origins of PCOS may emerge through the epidemiologic study of different populations around the globe, particularly populations whose diet, fertility, and disease load resemble those of ancestral humans.

Overall, the available data suggest that well-controlled epidemiologic studies of unselected (medically unbiased) populations are critically needed worldwide. First, such studies will help to define the

true prevalence and phenotype of the disorder in the region studied. Second, they will allow investigators to assess the impact of differences in race and/or ethnicity, environment, socioeconomics, and diet and nutrition on the development, complications, phenotype, and prevalence of PCOS. Third, they are essential for determining the relationship between genotype and phenotype, potentially fostering an improved understanding of the molecular mechanisms underlying the disorder. Fourth, well conducted epidemiologic studies may provide clues to the evolutionary history of the disorder, which in turn could potentially assist identification of the core elements of PCOS. Last, they will lead to a better assessment of the public health and economic implications of PCOS in a region, and facilitate the development of an informed, cogent, and effective public health and prevention policy.

The earliest epidemiologic study to evaluate PCOS was carried out in 1998 by Azziz and colleagues,¹⁸ who assessed reproductive-aged women undergoing pre-employment physical examinations at a university in the southern United States. Based on the NIH 1990 criteria, the study observed a prevalence of PCOS of 4%, which varied little by race (black or white).¹⁸ Subsequent studies have verified and expanded this assessment. To date, the reported prevalence of PCOS varies from 5% to 20%, depending on factors such as which diagnostic criterion is used, how the study population is identified, the methods used to define each phenotypic feature, and the completeness of the phenotypic assessment and recruitment process of the populations. For example, a recent meta-analysis found that the reported prevalence of PCOS based on the diagnostic criteria of the 1990 NIH, 2003 Rotterdam, and 2006 AE-PCOS Society was 6% (95% confidence interval [CI] 5%–8%; 18 trials), 10% (95% CI 8%–13%; 15 trials), and 10% (95% CI 7%–13%; 10 trials), respectively.¹⁹

However, most if not all studies of PCOS prevalence are from populations in North America, Europe, the Middle East, southern Asia, and Australia (Fig. 1).⁵ In fact, there are no significant data from South America, Russia (i.e., northern Asia), the island countries of Oceania (Melanesia, Micronesia, and Polynesia), or Africa. Also notable is the paucity of studies among black women, with few exceptions.^{18, 20}

An assessment of studies in Africa highlights the lack of research among black women in Sub-Saharan Africa, where there have been no large-scale epidemiologic studies of PCOS and only a very few studies of the PCOS phenotype.^{21–25} This is particularly alarming given the need to improve women's health in the region²⁶ and the great need to address health disparities globally.²⁷ Furthermore, PCOS among black women may be associated with additional or more severe morbidities, such as uterine leiomyomata, as compared with white women.²⁸ The negative impact that PCOS has on fertility is particularly harmful for African women in low socioeconomic settings. Many are affected by psychosocial effects such as anxiety and depression, stress, intimate partner violence, and divorce.^{29, 30}

It is clear that additional research is needed to address the gap in studies of this highly prevalent and morbid disorder. To begin to address this deficit, the Ghana Polycystic Ovary Syndrome Epidemiology and Phenotype (Ghana-PEP) study is undertaking a large community-based assessment of PCOS in the Nsawam municipality of Ghana. The study has been approved by the Noguchi Memorial Institute for



FIGURE 1 Map showing the location of PCOS prevalence studies conducted worldwide through 2015. Red dots indicate individual study centers; green circles indicate regions of the world where the epidemiology of PCOS remains unknown or understudied.

Medical Research, University Of Ghana, Institutional Review Board (CPN 064/16-17), and Ghana Health Service Ethics Review Committee (GHS-ERC-11-03-2016).

The primary endpoint of the Ghana-PEP study will be the prevalence and phenotypic distribution of PCOS in a medically unbiased population of reproductive-aged women; secondary endpoints include the frequency of other common health disorders of women (overweightness and obesity, uterine leiomyomata, glucose intolerance, and thyroid dysfunction, among others).³¹ The study will be the first of its kind in Africa and will provide data not only for Ghana, but also for the broader Sub-Saharan African region. The study is a collaboration between researchers at the University of Ghana Schools of Public Health, Medicine and Dentistry, and Noguchi Memorial Institute for Medical Research, and researchers based in the USA.

The study plans to recruit and assess 990 randomly selected women aged 18–45 years living in Nsawam, the district capital of the Nsawam–Adoagyiri municipality, in the eastern region of Ghana. The women will complete a questionnaire with the aid of trained personnel, undergo a physical examination, and ultrasonography and biochemical evaluations. One of the strengths of the study is that it will be community-based rather than clinic-based, thereby avoiding the bias that characterizes clinic-based studies. In addition to the primary and secondary endpoints noted above, the Ghana-PEP study will attempt to identify sociodemographic, environmental, and psychologic factors that might be involved in the development of PCOS phenotype.

Understanding better the prevalence and phenotypes of PCOS in Sub-Saharan Africa will help to build local capacity in PCOS and reproductive endocrine research. It is anticipated that these data will facilitate the development of locally tailored early screening strategies and tools, which may lead to earlier diagnosis and management of affected individuals and potentially a reduction in the long-term sequelae of PCOS in the region. The study will also facilitate the development of education materials tailored to both local healthcare providers and the population in general. Furthermore,

this information will help to document the public health and economic burden of PCOS in the region, and to foster the establishment of sound public health policies to help to address this common and morbid syndrome.

CONFLICTS OF INTEREST

RA is a consultant to Ansh Labs, Fractyl, Medtronics, and Longitude Capital, and is on the advisory board of Global PET Imaging. RMKA is the Editor of the International Journal of Gynecology and Obstetrics. The authors have no other conflicts of interest.

AUTHOR CONTRIBUTIONS

ETM contributed to the design of the study and to writing the manuscript. CG, BS, MN, EB, DL, and WW contributed to the design and planning of the study, and to writing the manuscript. RMKA contributed to the design and planning of the study, and to writing and revising the manuscript. RA contributed to designing, planning, and conducting the study, and to writing and revising the manuscript. All authors read and approved the final manuscript.

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