# PREVALENCE OF POLYCYSTIC OVARY SYNDROME IN A POPULATION OF WOMEN OF REPRODUCTIVE AGE USING ROTTERDAM 2003 CRITERIA (LITERATURE REVIEW)

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## ABSTRACT

*Polycystic ovary syndrome (PCOS) is considered a common endocrine disorder among women of reproductive age, and the associated health risks persist throughout life. At the same time, there is a wide range of variations in the incidence of the syndrome (4–21 %), which in turn is explained by the influence of the study population characteristics, including ethnicity and race, as well as the applied diagnostic criteria.*
***The aim of the study.*** *To systematize the available data on the prevalence of polycystic ovary syndrome using the Rotterdam 2003 criteria in a population of women of reproductive age.*
***Materials and methods.*** *The search for information was carried out using Internet resources (PubMed, EMBASE, Google Scholar, eLibrary). Literature sources for the period 1990–2023 were analyzed. As a result, the article presents current data on the prevalence of PCOS using the Rotterdam 2003 definitions, the features of the PCOS incidence in hospital and non-selective (medically unbiased) populations, as well as in various ethnic groups. The review also discusses current guidelines for conducting studies on the PCOS prevalence.*
***Conclusion.*** *The latest guidelines on the diagnosis and management of patients with PCOS, published in 2018, propose to consider the provisions adopted in Rotterdam as the basis for the diagnosis of the syndrome; at the same time, the need to take into account racial and age characteristics is noted.*

***Key words:*** *PCOS, prevalence, ethnicity, population, Rotterdam criteria, women of reproductive age*

# РАСПРОСТРАНЁННОСТЬ СИНДРОМА ПОЛИКИСТОЗНЫХ ЯИЧНИКОВ В ПОПУЛЯЦИИ ЖЕНЩИН РЕПРОДУКТИВНОГО ВОЗРАСТА ПРИ ИСПОЛЬЗОВАНИИ КРИТЕРИЕВ ROTTERDAM 2003 (ОБЗОР ЛИТЕРАТУРЫ)

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## РЕЗЮМЕ

*Синдром поликистозных яичников (СПКЯ) считается распространённым эндокринным заболеванием среди женщин репродуктивного возраста, а связанные с ним риски для здоровья сохраняются в течение жизни. В то же время отмечается широкий диапазон вариаций частоты встречаемости синдрома (4–21 %), что в свою очередь объясняется влиянием характеристик исследуемой популяции, в том числе этнической и расовой принадлежностью, а также применяемыми диагностическими критериями.*

***Цель исследования.*** *Систематизировать имеющиеся данные о распространённости синдрома поликистозных яичников при использовании критериев Rotterdam 2003 в популяции женщин репродуктивного возраста.*

***Материалы и методы.*** *Поиск информации проводился с использованием интернет-ресурсов (PubMed, EMBASE, Google Scholar, eLibrary). Проанализированы литературные источники за период 1990–2023 гг. В результате в рукописи представлены современные данные о распространённости СПКЯ при применении дефиниций Rotterdam 2003, особенности частоты встречаемости синдрома в госпитальных и неселективных (медицински непредвзятых) популяциях, а также в различных этнических группах. В обзоре также обсуждаются современные рекомендации по проведению исследований по распространённости СПКЯ.*

***Заключение.*** *В последнем руководстве по диагностике и ведению пациентов с СПКЯ, опубликованном в 2018 г., предлагается рассматривать положения, принятые в Роттердаме, как базовые относительно диагностики синдрома; при этом отмечается необходимость учитывать расовые и возрастные особенности.*

***Ключевые слова:*** *СПКЯ, распространённость, этника, популяция, критерии Rotterdam, женщины репродуктивного возраста*

## INTRODUCTION

Polycystic ovary syndrome (PCOS) is considered a common endocrine disorder among women of reproductive age, and the associated health risks persist throughout life. Even postmenopausal women with PCOS may exhibit hyperandrogenism and insulin resistance [1–3]. In recent years, the prevalence of PCOS has been increasing [4], which may be due to improved methods of diagnosing the disease. At the same time, there is a wide range of variations in the incidence of the syndrome (4–21 %) [5–7], which in turn is explained by the influence of the study population characteristics, including ethnicity and race, as well as the applied diagnostic criteria. Nevertheless, it is estimated that up to 105 million women of childbearing age suffer from PCOS worldwide [8].

The criteria presented by the European Society of Human Reproduction and Embryology (ESHRE) in 2003 are the most frequently used in research and clinical practice. In Rotterdam (Rotterdam 2003) [8], according to which the presence of at least two of the following three signs is required to establish the diagnosis of PCOS: clinical or biochemical hyperandrogenism (HA); oligo/amenorrhea (OA); polycystic ovarian morphology (PCOM) according to ultrasound, – after the exclusion of PCOS-simulating states. These conditions include, first of all, congenital adrenal hyperplasia (CAH), thyroid dysfunction, hyperprolactinemia [1, 9]. A large contribution to the development of diagnostic criteria was made by a group of experts from the National Institutes of Health (NIH) in 2012 [10]. The improvement consisted in maintaining the broad inclusive diagnostic criteria of Rotterdam 2003 while differentiating the syndrome into phenotypes. The proposed phenotypes included the following manifestations: 1) hyperandrogenism + ovulatory dysfunction; 2) hyperandrogenism + polycystic ovarian structure by ultrasound; 3) ovulatory dysfunction + polycystic ovarian structure by ultrasound; 4) androgen excess + ovulatory dysfunction + polycystic ovarian structure by ultrasound [11].

In 2018, there was another revision of the International Recommendations for the Diagnosis and Treatment of PCOS [1], where new provisions were proposed. The main change was the possibility to take into account elevated levels of androstenedione (A4) and dehydroepiandrosterone sulfate (DHEA-S) in the diagnostic process if the values of free or total testosterone are within the reference values. In addition, a new "cut-off point" for the number of follicles per ovary was determined due to the fact that the progress of equipment has increased the sensitivity of ultrasound [1] in relation to the diagnosis of PCOS.

## THE AIM

To systematize the available data on the prevalence of polycystic ovary syndrome using the Rotterdam 2003 criteria in a population of women of reproductive age.

## MATERIALS AND METHODS

The search for information was carried out using Internet resources (PubMed, EMBASE, Google Scholar, eLibrary). Literature sources for the period 1990–2023 were analyzed. As a result, the article presents current data on the prevalence of PCOS using the Rotterdam 2003 definitions, the features of the PCOS incidence in hospital and non-selective (medically unbiased) populations, as well as in various ethnic groups.

There are 6 published systematic reviews and meta-analyses summarizing comparative studies of PCOS prevalence using the Rotterdam 2003 definitions [8].

For example, a meta-analysis involving a total of 19,226 Iranian women aged 10 to 45 years showed that, according to the Rotterdam 2003 criteria, PCOS was diagnosed in 19.5 % of cases [12]. In another study, 24 articles were analyzed, which presented the overall prevalence of the syndrome – 10 % [5, 7] in accordance with the Rotterdam 2003 definitions. In addition, the study revealed a high incidence of isolated hirsutism, HA, OA and PCOM – 13 %, 11 %, 15 % and 28 % respectively. The authors focus on the heterogeneity of research, and therefore, consider it necessary to strengthen the standardization of methods to improve the comparability of the prevalence of PCOS worldwide.

In 2018, M.A. Skiba et al. analyzed 21 studies of the incidence of PCOS over the period from 1990 to 2018 [13]. In this review, the authors presented a unified definition of PCOS prevalence based on the NIH and Rotterdam 2003 criteria and confirmed the statistical significance of the differences when using these criteria ($p < 0.0001$). On the contrary, when comparing the data obtained using the diagnostic classifications Rott and AES (Androgen Excess Society), there were no differences in the incidence of the syndrome ($p = 0.201$). The authors suggested that the higher prevalence of PCOS reported in studies using the latest diagnostic approaches was due to the inclusion of the ultrasound diagnostic criterion. Moreover, differences in estimates of PCOS prevalence could be explained by the lack of standardization of criterion values, the diversity of clinical phenotypes and the study groups.

In 2021, Chinese scientists [14] assessed the prevalence of polycystic ovary syndrome in Chinese women based on an analysis of 69 studies. A total of 154,599 participants were included, of which 12,845 women were diagnosed with PCOS. The prevalence of PCOS was 10.01 % (95 % confidence interval (95% CI): 8.31–11.89 %). The authors note a lower incidence of PCOS among Chinese women compared, for example, with the prevalence of the disease among women in the Middle East (16 %) [15] and associate such variability with both racial characteristics and optimization of approaches to diagnosing the syndrome. In addition, the heterogeneity of the occurrence of PCOS in China was noted, depending on the affiliation of the surveyed audience to a certain economic zone. The analysis of the subgroups showed that the incidence of the syndrome in different regions was as follows: 13.35 % in the West, 7.82 % in the East, 14.24 % in the cen-

ter and 8.68 % in the North-East. At the same time, a meta-analysis of Indian scientists in 2022, including 11 studies, found the overall prevalence of PCOS among Indian women at 11.33 %.

A meta-analysis of F. Chiaffarino et al. (2022) noted the same prevalence of PCOS in European countries and the United States using the same criteria for diagnosing the syndrome [16]. As a result, the overall prevalence of the disease, according to the Rotterdam 2003 definitions, was about 19.5 % in the absence of significant heterogeneity by geographical region [16]. However, differences in the prevalence of PCOS phenotypes were noted: the incidence of phenotype A was higher, and phenotype C is lower in the USA compared to European countries (Table 1).

A. Yasmin et al. in their systematic review of 2022, after analyzing 118 studies, they noted the presence of variations in the clinical manifestations of PCOS depending on geographical regions among different ethnic groups [18]. So, in one of the largest studies of the prevalence of PCOS among the American population living in different geographical territories, the prevalence of the syndrome in the southern regions was 47.5 % higher than in the rest of the country [19].

It is believed that the prevalence of PCOS differs significantly in non-selective and hospital populations. Recent studies show that PCOS is usually characteristic of patients with acne, hirsutism, oligoanulation, obesity and infertility. So, 12 % of PCOS prevalence was reported among women with hirsutism [13], 82 % in patients with clinically pronounced androgen excess [20]. It is important to note that a significant proportion of women with clinical hyperandrogenism had the classic phenotype of the syndrome [21].

S.E. Allen et al. analyzed the frequency of hyperandrogenism and PCOS among women with oligoanulation [20]. The authors demonstrated that the prevalence of PCOS in the group of patients with a long history of oligoovulation reached 38 % vs. 5 % in the cohort of wo-

men with episodes of ovulatory dysfunction. In general, up to 40 % of nulliparous women with a menstrual cycle of 45 days or more were identified as patients with PCOS [20–23]. The Australian authors noted that the incidence of polycystic ovarian structure according to ultrasound data among 100 female partners of infertile men reached 23 %, while 12 % of women were diagnosed with three of the three criteria of the disease in accordance with Rotterdam 2003 [24]. Moreover, in a cross-sectional study conducted at the University infertility Clinic, PCOS was identified in 46 % of infertile women as one of the main causes of infertility [25]. There is some evidence that the prevalence of the syndrome in infertile women depends on race. For example, it is significantly higher among South Asians compared to Caucasians (44.2 % vs. 11.5 %; relative risk (RR) – 6.1; 95 % CI: 2.2–16.7) [26]. Similar results were demonstrated by Russian researchers when studying the causes of infertility in women of Caucasian and Asian ethnicity living in Eastern Siberia. The peculiarity of the group of women in the Caucasian population was also the high incidence of PCOS compared to the Asian population (33 (22.92 %) cases vs. 9 (8.65 %) cases) [27–31].

A clear link has been established between PCOS and obesity [32]. B.O. Yildiz et al. conducted a study of Turkish data on two population-based studies of the prevalence of PCOS and the hospital database of all patients with PCOS who had not received treatment before. In this study, in women with underweight, normal, overweight and obese in Turkey, the prevalence of the syndrome was 8.2 %, 9.8 %, 9.9 % and 9.0 %, respectively. The highest proportion of patients with PCOS (12.4 and 11.5 %) was found in women with a BMI of 35–40 kg/m$^2$ and more than 40 kg/m$^2$, respectively [33]. The incidence of PCOS in 421 obese Chinese patients was quite high (67 %), but it did not correlate with the presence of metabolic syndrome [34].

Databases of public health authorities and resources of health insurance systems were also used to study the prevalence of PCOS. In a cross-sectional study conducted by L. Gabrielli et al., the medical records of 859 Bra-

T A B L E   1

**SYSTEMATIC REVIEWS AND META-ANALYSES OF THE PCOS PREVALENCE USING THE ROTTERDAM 2003 DIAGNOSTIC CRITERIA**

| Authors | Year | Design (as suggested by the authors) | Rotterdam 2003, % [95% CI] |
|---|---|---|---|
| Jalilian A. et al. [12] | 2015 | Meta-analysis | 19.5 [2.24–8.14] |
| Bozdag G. et al. [5] | 2016 | Systematic review and meta-analysis | 10 [8–13] |
| Skiba M.A. et al. [13] | 2018 | Systematic review and meta-analysis | 12 [10–15] |
| Wu Q. et al. [14] | 2021 | Meta-analysis | 10.01 [8.3–11.8] |
| Bharali M.D. et al. [17] | 2022 | Systematic review and meta-analysis | 11.33 [7.69–15.59] |
| Chiaffarino F. et al. [16] | 2022 | Systematic review and meta-analysis | 19.5 [17.3–21.6] |

zilian women undergoing cervical cancer screening in primary health care facilities were analyzed [35]. It was found that according to the Rotterdam 2003 criteria, the prevalence of PCOS is 8.5 %.

Limited epidemiological data were obtained from secondary analysis of databases and registries of non-PCOS studies. In 2010, C. Moran et al. reported a lower estimate of the prevalence of PCOS in Mexican female volunteers – 6.6 % (Rotterdam 2003) [36]. Among 827 women participating in a cross-sectional study of relatives of patients with cardiovascular diseases in the Dallas study (2000–2002), PCOS, according to the Rotterdam 2003 criteria [8], was diagnosed in 19.6 % of the examined [37].

Undoubtedly, the above studies are important and valuable. Nevertheless, the results of PCOS assessment in specialized medical institutions are definitely at risk of bias due to the characteristics of the sample of participants [38]. Therefore, non-selective (medically objective) studies are more representative and therefore preferable for epidemiological studies. These cases, identified in preclinical conditions, allow scientists to establish population "control" and determine the prevalence of PCOS.

Population-based research is the "gold standard" for estimating prevalence, but the method has its limitations. When conducting such experiments, different approaches are used to recruit participants. For example, they use a random sample from families, communities, and age groups. In Sri Lanka in 2008, V. Kumarapeli et al. conducted a cross-population study to identify the prevalence of PCOS and its phenotypes [39]. The authors compiled a questionnaire and offered it to the interviewers to fill out in order to identify probable cases of PCOS, and then sent the probable cases to experts for further analysis. With previously identified cases, the overall prevalence according to the Rotterdam 2003 diagnostic criteria was 6.3 % [39]. Later, in a retrospective study of a certain age group conducted in 2010, W.A. March et al. demonstrated that the prevalence rates of PCOS in accordance with the Rotterdam 2003 definitions and AES were twice as high as those obtained using the NIH criteria. Significantly 68–69 % of PCOS patients identified in this study had not been diagnosed with polycystic fibrosis before.

In a population-based study involving women of reproductive age living in randomly selected areas of Iran, the prevalence of PCOS, depending on diagnostic criteria, was 7.1–14.6 % [40]. These figures are consistent with the previously announced frequency of PCOS detection in Iranian women referred for mandatory premarital screening: the indicator was 7–15.2 % with various diagnostic criteria [41]. In 2014, in Iran, H. Rashidi et al. conducted an epidemiological study estimating the prevalence of PCOS at 14.1 % in accordance with the Rotterdam approach [42]. However, in 2013 in China, a large-scale study among ethnic communities showed a much lower prevalence of PCOS in accordance with the Rotterdam 2003 criteria, which was 5.6 % [43]. At the same time in 2014, J. Zhuang et al. noted that the prevalence of PCOS in Chinese women aged 12 to 44 years varied from 7.1 to 11.2 %, depending on the diagnostic criteria used [44].

The population model identifies PCOS in non-selective groups of the population who need medical examination for non-medical reasons: annual medical examination at work, before applying for a job, etc. For example, the prevalence of PCOS among employees of a public institution in Turkey, according to the Rotterdam 2003 criteria, reached 19.9 % [45].

Another model of objective epidemiological research uses population groups undergoing medical examination for non-productive medical reasons. In 2008. X. Chen et al. analyzed 915 Chinese women of reproductive age during the annual survey. This representative epidemiological study revealed a 2.4 % prevalence of PCOS in accordance with the Rotterdam 2003 criteria [46].

An analysis of healthy volunteers and medical staff may be useful, but its quality is lower due to a systematic selection error. Among women of reproductive age working at the University of Copenhagen Hospital, the overall prevalence of PCOS was 16.6 % according to the Rotterdam 2003 criteria. However, the researchers noted that the frequency of PCOS detection decreased significantly when the subjects were divided by age categories: from 33.3 % in women under 30 years of age to 10.2 % in women over 35 years of age ($p < 0.001$). The authors suggest that the studied population (healthcare practitioners) and the exclusion of women taking hormonal contraceptives (HC) could have caused a systematic selection error [47].

Obviously, we can argue that ethnicity and race influence the heterogeneity of the prevalence and clinical manifestations of PCOS. Thus, PCOS is less common in East Asians than in Caucasians, so the Asian phenotype of PCOS attracts the attention of researchers [52]. The incidence of PCOS (according to NIH 1990 criteria) in black and white women is comparable and amounts to 8.0 and 4.8 %, respectively [53]. T. Ding et al. (2017) [15] using various criteria analyzed the prevalence of PCOS by ethnicity in a systematic review and meta-analysis in 13 studies. They found the lowest prevalence of PCOS (5.6 % (95% CI: 4.4–7.3 %) according to Rotterdam 2003 criteria) among the Chinese group. This review showed how important it is to develop ethnicity-sensitive recommendations to prevent under- or overdiagnosis of PCOS [15]. Relatively recently, H.J. Kim et al. reported the impact of race and ethnicity on the standardization of PCOS diagnosis [15, 54].

To improve the quality and comparability of PCOS prevalence studies, AES has announced the release of practical recommendations for the development and conduct of epidemiological and phenotypic studies of PCOS [55]. The published document describes the main recommendations for the study plan, it also provides some recommendations on the selection of the study population, diagnostic criteria, type of observational study, as well as primary and secondary endpoints. According to the recommendations, it is important to use generalized population groups, broad diagnostic criteria and high sensitivity methods in assessing the individual characteristics of PCOS in the study of its prevalence. It is also important and strongly recommended to give a precise definition of what is "normal" for the study population. It is noteworthy that the rec-

**T A B L E  2**
**PREVALENCE OF PCOS ACCORDING TO ROTTERDAM 2003 DEFINITIONS IN NON-SELECTIVE POPULATIONS**

| Authors (year) | Country | Study design* | Population | Prevalence,% [95% CI] (if available) |
|---|---|---|---|---|
| Chen X. et al. (2008) [46] | China | Observational study | 915 women aged 20–45 years living in Guangzhou, examined during the annual medical examination | 2.4 % |
| Kumarapeli V. et al. (2008) [39] | Sri Lanka | Cross-sectional study of certain communities | A random sample of 2,915 women aged 15–39 years permanently residing in the Gampaha area | 6.3 % [5.9–6.8] |
| March W.A. et al. (2010) [48] | Australia | A retrospective study of a certain age group | 728 women born in 1973–1975 in one maternity hospital in Adelaide, examined in adulthood, 27–34 years old | 11.9 % |
| Moran C. et al. (2010) [36] | Mexico | A prospective cross-sectional study | 150 female volunteers from Mexico, 20–45 years old, employee of the Hospital of Obstetrics and Gynecology of the Mexican Institute of Social Welfare (Mexico City) | 6.6 % [2.3–10.9] |
| Mehrabian F. et al. (2011) [49] | Iran | Cross-sectional study | 820 women aged 17–34 years selected during mandatory premarital medical examination in Isfahan | 15.2 % |
| Tehrani F.R. et al. (2011) [40] | Iran | The study of certain communities | 1126 women aged 18–45 years, randomly selected from the population of various geographical regions of Iran | 14.6 % [12.3–16.9] |
| Gabrielli L. et al. (2012) [35] | Brazil | Observational | 859 women subject to cervical screening | 8.5 % |
| Yildiz B.O. et al. (2012) [45] | Turkey | Cross-sectional study | 392 women aged 18–45 years, employees of the State Institute in Ankara | 19.9 % |
| Li R. et al. (2013) [43] | China | The study of certain communities | 15,924 women aged 19–45 years from 152 cities and 112 villages in 10 provinces and municipalities of China | 5.6 % |
| Lauritsen M.P. et al. (2014) [47] | Denmark | A prospective cross-sectional study | 447 women (20–40 years old), employees of the University Hospital of Copenhagen. | 16.6 % |
| Rashidi H. et al. (2014) [42] | Iran | The study of certain communities | 646 women aged 18–45 years living in urban areas of three randomly selected cities in Khuzestan province | 14.1 % |
| Zhuang J. et al. (2014) [44] | China | Cross-sectional study of certain communities | 1,645 Chengdu residents aged 12–44 years | 11.2 % |
| Deswal R. et al. (2019) [50] | India | Cross-sectional study, stratification sampling method | 2,248 women aged 16–45 years, urban and rural residents | 4.21 % 5,4 % |
| Ganie M.A. et al. (2020) [51] | Kashmir, India | Cross-sectional study | 962 women aged 15–45 years from educational institutions in Kashmir | 35.3 % |

**Note.**  * – by definition of the authors.

ommendations provide researchers around the world with tools for conducting very high-quality reliable epidemiological studies of PCOS [55].

The latest guidelines on the diagnosis and management of patients with PCOS, published in 2018 [1], propose to consider the provisions adopted in Rotterdam as the basis for the diagnosis of the syndrome [1]; at the same time, the need to take into account racial and age characteristics is noted [1].

## CONCLUSION

Based on the results of the analysis, it can be concluded that the prevalence of PCOS according to the criteria of Rotterdam 2003 in the USA, Spain, Brazil, Mexico, Iran and Asia ranges from 6 % to 19.5 %. According to the Rotterdam 2003 definitions, the prevalence of PCOS in Indian women was the highest (35.3 %), while in Chinese women it was the lowest. The presence of the influence of race or ethnicity on the prevalence of the disease is also confirmed. The differences are often very small, which may be due to the variety of study designs, sampling characteristics, as well as the limitations of classical epidemiological studies of the prevalence of PCOS in a nonselective population.

Further epidemiological studies are needed to better understand PCOS and finalize its diagnostic criteria. The data currently available are insufficient to make definitive conclusions about the exact prevalence of the disease. The known facts about PCOS and its incidence in different geographical regions are not convincing enough to confirm significant differences in the prevalence of the syndrome in different ethnic groups.

### Conflict of interest

The author of this article declares that there is no conflict of interest.

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