BRITISH MEDICAL JOURNAL

British Medical Journal

Volume 2, No.5, September 2022

Internet address: http://ejournals.id/index.php/bmj
E-mail: info@ejournals.id
Published by British Medical Journal
Issued Bimonthly
3 knoll drive. London. N14 5LU United Kingdom
+44 7542 987055

Chief editor
Dr. Fiona Egea

Requirements for the authors.

The manuscript authors must provide reliable results of the work done, as well as anobjective judgment on the significance of the study. The data underlying the work shouldbe presented accurately, without errors. The work should contain enough details andbibliographic references for possible reproduction. False or knowingly erroneous statementsare perceived as unethical behavior and unacceptable.

Authors should make sure that the original work is submitted and, if other authors'works or claims are used, provide appropriate bibliographic references or citations. Plagiarismcan exist in many forms - from representing someone else's work as copyright to copying orparaphrasing significant parts of another's work without attribution, as well as claimingone's rights to the results of another's research. Plagiarism in all forms constitutes unethicalacts and is unacceptable. Responsibility for plagiarism is entirely on the shoulders of theauthors.

Significant errors in published works. If the author detects significant errors or inaccuraciesin the publication, the author must inform the editor of the journal or the publisher aboutthis and interact with them in order to remove the publication as soon as possible or correcterrors. If the editor or publisher has received information from a third party that thepublication contains significant errors, the author must withdraw the work or correct theerrors as soon as possible.

OPEN ACCESS

Copyright © 2022 by British Medical Journal

CHIEF EDITOR

Dr. Fiona Egea

EDITORIAL BOARD

J. Shapiro, MD

S. Shea, MD

M. Sherman, MB BCh PhD, FRCP(C)

H. Shortliffe, MD, PhD, FACMI

D.S. Siegel, MD, MPH

M.D. Siegel, MD, MPH, FCCP

S.Sipila, PhD

P.Slocum, DO

A. Soll, MD

ELSEVIER SSRN Universal Impact Factor

UDK-633.8: 618.15-002.1-08-092.9

MOLECULAR GENETIC PREDICTORS OF METABOLIC AND FOLLICULOGENESIS DISORDERS IN PREDICTING OUTCOMES OF ASSISTED REPRODUCTIVE TECHNOLOGY PROGRAMS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

Muzaffarova M.H
Ikhtiyarova G.A
Oripova F. Sh
Bukhara State Medical Institute named after Abu Ali ibn Sino.
Bukhara, Uzbekistan.

Resume In the modern literature, indications for unloading the upper urinary tract in pregnant women with obstructive lesions with the choice of the optimal method of kidney drainage, especially against the background of gestational complications, are insufficiently covered.

Goal. Achievement of prognostic criteria for the outcomes of ART programs in women with infertility in PCOS based on molecular genetic predictors of folliculogenesis disorders.

Keywords: genetic predictors, polycystic ovaries, assisted reproductive technologies

Materials and methods. Based on the above, we present the data of our own studies on the assessment of the state, ultrasound of the pelvic organs (folliculometry with CHAF counting), hormonal studies (AMH, E, FSH, LH, St.testosterone), steroid hormone genes (CYP17A1-rs743572, CYP19A1-rs247015) based on the analysis of laboratory parameters.

The results of the study. As a result of evaluating the effectiveness of predicting polymorphism (AUC) of the CYP17A1 rs743572 gene, statistically significant indicators such as sensitivity (SE) and specificity (SP) were identified as independent markers.

Relevance. Polycystic ovary syndrome is a heterogeneous syndrome characterized by hypersecretion of luteinizing hormone (LH), ovarian hyperandrogenism, polycystic ovaries, hyperinsulinemia due to insulin resistance and decreased fertility. Variable phenotypic expression of reproductive and metabolic abnormalities in patients with PCOS leads to differences in the ability of oocytes to develop, defined as the ability of oocytes to complete meiosis and undergo fertilization, embryogenesis and full-term development. Some women with PCOS undergoing ovarian stimulation for in vitro fertilization (IVF) have normal embryo development and normal pregnancy outcome, while others have impaired oocyte development. Women with PCOS who are also overweight are particularly vulnerable and suffer from low fertilization of eggs and the inability to implant embryos into their own uterus or the uterus of other women [1,2,3]. PCOS is characterized by endocrinological disorders; therefore, polymorphisms in genes encoding sex hormones or regulators of their activity have been investigated [4,5,6]. The follicle-stimulating hormone receptor (FSHR) gene contains two important single nucleotide polymorphisms (SNPs) in exon 10, which are in nonequilibrium coupling and replace two amino acids at positions A307T and N680S.

It has been reported that A307T located in the extracellular domain of FSHR, the site responsible for high-affinity hormone binding [7,8], it affects hormone transfer and signal transmission. Phosphorylation of Ser and Thr residues in the intracellular regions of FSHR can affect dissociation with adenylate cyclase. As a result, a change in amino acids associated with the corresponding SNPs may affect posttranslational modifications

of the FSHR protein, hence the function of the receptor, including the effectiveness of FSH [9, 10]. Several genetic studies have studied the relationship between the polymorphism of the FSHR gene and PCOS.

Goal. Achievement of prognostic criteria for the outcomes of ART programs in women with infertility in PCOS based on molecular genetic predictors of folliculogenesis disorders.

Materials and methods. The results of the research 743572, CYP19A1-rs247015) based on laboratory analysis 125 women were examined to solve the tasks set in the work: 1 group of 45 women with primary PCOS and infertility; 2 group of 46 women with infertility and PCOS in preparation for ART; 3 group of 26 conditionally healthy women.

A genetic study of the polymorphism of the CYP17A1 (rs743572) and CYP19A1(rs2470152) genes was performed in all 106 patients of the observed baseline group. The control group consists of 52 healthy volunteers who have no history of predisposition to PCOS. At the same time, 106 patients were also divided into 2 groups. In one of them there were patients with metabolic syndrome (n=60) (MS+), in the second group there were patients with PCOS without metabolic syndrome (n=46).

Results. In patients with PCOS AA, the homozygote or wild type of the allelic genotype of the gene SUR17A1 was 36.8%, AG heterozygous genotype in 48.1% of patients, GG homozygous mutant genotype was found in 15.1% of patients.

In our study, polymorphism of the homozygous normal or wild AA genotype of the CYP17A1 gene was observed in 45.0% of MS+ patients, compared with the MS group of the CYP17A1 gene genotype was observed in 45.0% of MS+ patients, compared with the MS group where this percentage was 26.1%, in the third observation group this percentage was 40.4%. In addition, among MS+ patients with PCOS, the mutant homozygote of the GG genotype of the CYP17A1 gene polymorphism was low and amounted to 11.7% in the first group, 19.6% in the second group and 13.5% in the control group. Also, the difference in the occurrence of heterozygous genotype (AG genotype) in the first and second groups was 9%, and in this case the patients of the second group (54.3%) prevailed, the difference between the indicators of the first and control group was only 3.2%. The G allele was determined in 40% of patients of the first group and 43% of patients of the second group (Table 1). When we compared the level of occurrence of polymorphism of the CYP17A1 gene with the control group, it was found that normal - "wild" AA genotypes with a smaller difference were more common in the control group, while the genotypes of heterozygous AA and mutant GG slightly prevailed in the group of patients with PCOS (OR=1.06; 95% CI 0.55-2.10; $p<0.8$ for heterozygous genotype and OR=1.14; 95% CI 0.44-2.98; $P<0.8$ for homozygous genotype).

Table 1

Results of comparison of the polymorphism of the SUR17A1 gene between PCOS patients and healthy people

Alleles and genotypes	Number of alleles and genotypes examined				Хи2	P	RR	95%CI	OR	95% CI
	Main group (n=106)		Control group (n=52)							
	N	%	N	%						
A	129	60,8	66	63,0	0,2	p < 0,7	0,96	0,82 - 1,128	0,9	0,551-1,45
G	83	39,2	38	37,0	0,2	p < 0,7	1,0	0,88 - 1,213	1,1	0,68-1,815
A/ A	39	36,8	21	40,4	0,2	p < 0,7	0,9	0,75 - 1,196	0,86	0,435-1,69
A/G	51	48,1	24	46,1	0,05	p < 0,8	1,06	0,85 - 1,328	1,1	0

Interestingly, when we divided patients with PCOS into two groups with the presence of metobolic syndrome disease, we found that in the MS+ group, the wild variant (AA genotype) of the CYP17A1 gene is even greater than in the control group (45.0% and 40.4%, respectively), the heterozygous variant (AG genotype) is almost equal (43.3 and 46.1%, respectively), and the mutant variant was more common in the control group. Therefore, we concluded that the importance of the development of PCOS in MS+ patients with the mutant form of the genotype - GG does not matter (хи2=0,08; OR = 0,85; 95% CI: 0,27 - 2,60; p=0,77).

As a result of evaluating the effectiveness of predicting polymorphism (AUC) of the CYP17A1 rs743572 gene, statistically significant indicators such as sensitivity (SE) and specificity (SP) were identified as independent markers. In patients of the main group, the prediction efficiency of rs743572 mutant allele A of the CYP17A1 gene was AUC=0.51 (SE=0.63; SP=0.39; OR=1.09; 95% CI=0.75-1.59; p=0.48). Sensitivity, specificity and prognostic efficacy of wild alleles are as follows in the group of patients with PCOS who do not suffer from metobolic syndrome: AUC=0.55; SE=0.63; SP=0.47; OR=1.49; 95% CI=0.91-2.44; p=0.64. In the group with metobolic syndrome, respectively, AUC=0.48; SE=0.63; SP=0.33; OR=0.85; 95% CI=0.53-1.37; p=0.66 (AUC is evaluated with the following criteria: AUC=0.9-1.0 - excellent quality; AUC=0.8-0.9 - high quality; AUC=0.7-0.8- good quality; AUC=0.6-0.7- average quality; AUC=0.5-0.6- poor (unsatisfactory) qualit.

Table 2.Evaluation of the effectiveness of predicting polymorphism of the CYP19A1_1 gene in the pathogenesis of PCOS by homozygous genotype AA.

Factor	Group	SE	SP	AUC	OR	95%CI	p
A /A	Main group // Control group	0,36	0,83	0,6	2,67	1,42 - 5,03	0,44
	PCOS with metabolic syndrome // Control group	0,37	0,83	0,6	2,77	1,35 - 5,68	0,31
	PCOS without metabolic syndrome // Control group	0,35	0,83	0,59	2,55	1,17 - 5,55	0,26

With such an image, according to our results, we decided to determine some important parameters of the population in the conditions of the Bukhara region. In accordance with this concept, it means that there will be a lot of problems, based on the methods of proven medicine, informative factors of risk of developing besplodye.

In the results of the investigation, we will decide on the prognosis of the current situation and problems, which will lead to the establishment of the current situation and increase the results of the treatment measures.

Used literature.

1.Балтер Р.Б. и др. Бесплодный брак : учебное пособие для студентов педиатрического и медикопрофилактического факультетов. - Самара, 2015.

2.Васюхина А.А., Целкович Л.С. Иммуногистохимические особенности эндометрия женщин с трубноперитонеальным бесплодием // Аспирантский вестник Поволжья. - 2016. - № 1- 2. - С. 13-16.

3.Дейнека Н.В., Целкович Л.С., Иванова Т.В. и др. Психологическая реабилитация женщин, страдающих бесплодием // Перинатальная медицина: от прегравидарной подготовки к здоровому материнству и крепкой семье.

4. Ихтиярова Г.А., Матризаева Г.Ж., Исматова М.М. "Гинекологияда ?амширалик иши "2018

5.Ихтиярова Г.А., Аслонова М.Ж., Курбанова З.Ш., Калиматова Д.М. Перспективы диагностики эндометриоза с учетом роли генетических факторов в патогенезе заболевания. РМЖ. Мать и дитя. 2021;1:12-16. DOI: 10.32364/2618-8430-2021-4-1-12-16.

6.Takhmina K. Zavkibekova et al/ Differential markers for the diagnosis of recurrent benign ovarian tumors in women of reproductive and premenopausal age// International Journal of Pharmaceutical Research | Jan - Mar 2021 | Vol 13 | Issue 1.

7.Amato A.A., de Assis Rocha Neves F. Idealized PPARy-based therapies: lessons from bench and bedside. PPAR Res. 2012; 2012: 978687.

8.Balter RB and others. Infertile marriage: a textbook for students of pediatric and medical-prophylactic faculties. - Samara, 2015.

9.Cakal E., Ozkaya M., Engin-Ustun Y., Ustun Y.Serum lipocalin-2 as an insulin resistance marker in patients with polycystic ovary syndrome. J. Endocrinol. Invest. 2011; 34 (2): 97-100.

10.Deineka N.V., Tselkovich L.S., Ivanova T.V. and others. Psychological rehabilitation of women suffering from infertility // Perinatal medicine: from pregravid preparation to healthy motherhood and a strong family.

ELSEVIER SSRN Universal Impact Factor