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Research on History of PCOS (Polycystic Ovarian Syndrome) *Marz Akyas Khusyatur Rahim*)

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Abstract-

Background: The research is about the literature of history of Polycystic Ovarian Syndrome. PCOS is commonest endocrine disorder. It describes a combination of Clinical and biochemical features. The incidence varies between 0.5 to 4%. It is prevalent in young reproductive age group (20-30%). It is clinically defined as a syndrome manifested by amenorrhea, hirsutism and obesity associated with enlarged polycystic ovaries. PCOS is diagnosed on the basis of a combination of clinical or biochemical evidence of hyperandrogenism, amenorrhea or oligomenorrhoea and the ultrasound appearance of polycystic ovaries. Approximately half of patients with PCOS are obese and abnormalities in insulin dynamics are common as in metabolic syndrome. Symptoms generally begin shortly after menarche and are slowly progressive. The patient complains of increasing obesity (abdominal–50%), menstrual abnormalities (70%) in the form of oligomenorrhoea, amenorrhea and sterility. Presence of hirsutism and acne are the important features. Typically, the ovaries are enlarged. Presence of multiple (> 12) follicular cysts measuring about 2-9 mm in diameter are found crowded around the cortex. Objective: To study the history of PCOS

Key words: PCOS, History

INTRODUCTION

Nicholas Malebranche put forth a theory known as theory of encasement. According to this theory ovaries has many ova's/ eggs from birth. The ova's/ eggs are present in the ovaries of *Hazrat Hawa (AS)* and every descended women after *Hazrat Hawa (AS)* possess one egg less in her ovary. According to him after 200 million generations there will be no ova/ egg left in the ovaries of female which ultimately leads to end of human life. ¹

Ancient Chinese (3000 B.C) were fully aware about the ovary, but they were not aware about the mechanism of reproduction. According to them (*Tsin*) male gamete enters into (*Tse Kong*) female gamete and meet the vesicles which were present in the ovary. According to them vesicles were the ova.¹

In the Egyptian papyri (Kahun 2000- 1800 B.C, Edwin Smith 1700 B.C and Ebers 1553- 1550 B.C) there is description regarding the antiquity of PCOS, an examination of later ancient medical records provides clues.²

Buqrat (**Hippocrates 460- 377 BC**), he mentioned that one women had many children, suddenly became widow, she experienced secondary amenorrhea for a long period of time. During this period, features of male appeared, like appearance of hair on the whole body, beard appeared, voice became hoarse and then she died. He mentioned the another women who had same features, Hippocrates tried a lot to regulate her menstruation but all in vain and she died. Further he mentioned that when the color of menstrual blood is not uniform, does not come on expected date then body needs *Tanqiya*. A.5.6 A Unani physician mentioned a women whose husband was live stay away from her, she had secondary amenorrhea, beard appeared and then she died.

In Unani System of medicine, health is depend on four *Khilt* (humours) i.e. *Dam* (Sanguine), *Balgham* (Phlegm), *Safra* (Bile) and *Sawda*' (Black bile). Abnormality or disturbance in the quantity and quality of these four humours results in the disease. It is mentioned that the features of this syndrome occurs due to excessive viscous or cold humour (*Barid Khilt*) i.e., *Balgham*. 3,4,5,8,9

Arastu (Aristotle 384 – 322 BC) mentioned in his book *Generation of Animals* that *Rahim* (uterus) is an animal inside the living being. He also told that uterus is attracted towards fragrance and repelled towards foul smell.¹

Jalinus (Galen 129-200 AD) said that development of male features in female occur due to the change in the temperament of the female. He mentioned if female's temperament transfer into male's temperament then amenorrhea occur and this transformation occur in those females who resemble with the male. ^{4,5,6} He mentioned it occur in those females who had many children, these features are due to complications of amenorrhea. Unani Physicians have mentioned a lot of affected women like this who had these features, either they had some complications or they died.³

Sushurata (5th century AD) mentioned that the shape of uterus resemble with the shape of Rohu fish (Labeo rohita Ham.) with narrower towards mouth and wider inside. ¹⁰ In the classical texts of Ayurveda, giving birth to a healthy offspring is depend on four basic factors i.e. Ritu, Kshetra, Ambu and Beeja. ^{11,12} Abnormality or disturbance in anatomy and physiology of above factors may result in Vandhya i.e. sterility. ¹²

Rabban Tabari (770-850 AD) stated in his book *Firdaus al-Hikmat* that amenorrhea is caused due to excess in *Hararat* (heat) and *Yabusat* (dryness). During this period if epistaxis occur then there is no harm to the amenorrheic patients. This is because evacuation is done from another side of the body. The another cause of PCOS is obesity.¹³

Sabit Ibn Qurrah Hirani (836-903 A.D) mentioned that those drugs that are emmenagogue decreases the Mani (female germ cell).⁶ He also told about the age of menarche that is 10 - 14 years of age and the age of menopause that is about 35-60 years of age. He also mentioned the duration of flow is minimum two days and maximum is seven days.⁶

Muhammad Ibn Zakariya Razi (Rhazes 860- 925 AD) stated in his book *Kitab al-Hawi* that combination of features conjoined with menstrual irregularities (amenorrhea, oligomenorrhoea) including acne, hirsutism, hoarseness of voice and obesity (which are the symptoms present in the Polycystic ovarian syndrome).^{3, 14}

Ali Ibn Abbas Majusi (Abbas 930- 994 AD) mentioned about the duration between two menstrual cycles should be twenty days to two months. If the duration is more than two months, it is abnormal cessation of menstruation i.e., secondary amenorrhea. Further he said that menarche age ranges from 10 - 14 years of age, ^{4,5} but it has been mentioned that in cold region it starts late and in hot region it starts early. ¹⁵ Menopausal age ranges from 36–60 years of age. The menstruation does not occur in *Khansha Females i.e.*, Transgender. He also said about the duration of flow the minimum duration of bleeding phase is two days and the maximum duration of bleeding phase is seven days and when there is more than seven days it is *Ghair Tabai* (abnormal). ^{4,5} When the menstrual bleeding is unduly scanty or complete absent for more than two months. It is known as *Ihtibas al - tamth* (secondary amenorrhea). ^{4,5}

Abul Qasim Zahrawi (Abulcasis 936-1036 AD) submitted an evidence about PCOS that

Barudat and Ratubat leads to oligomenorrhoea, secondary amenorrhea and sterility. 16

Abu Sahl Masihi (10th centuary A.D) said that when *Ihtibas al-tamth* is due to *Nakseer* (epistaxis) or blood comes from anal canal, then do wet cupping on calf muscles and *Imala* (transfer) the blood to lower side of body and use *Mudirr* drugs (emmenagogue) for this purpose.³ If blood comes through nose or through rectum then there is no harm to the amenorrheic patient,^{4,5} because evacuation is done from the other side of body.

Ehran a Unani physician said, if patient is suffering from nose bleeding or bleeding per rectum and simultaneously oligomenorrhoea occurs, it is not considered as any problem, ⁶ because at that time evacuation is going on from another side of body.

Ibn Sina (Avicenna 980- 1037 AD) mentioned in his book Al-Qanun fi'l Tibb, that the clinical features like amenorrhea, oligomenorrhoea, hoarseness of voice, hirsutism and other male features appear on the body of female and their kind hearted and humbleness disappears. It is because of the menstrual blood which flow through uterus but is not eliminated from body it returns to the body, when this happens again and again, it leads to many diseases like Ikhtinaq -al Rahim (hysteria), Sayalan al-Rahim (leucorrhea), Uqr (sterility), Amraz-i-Hadm (digestive disorders) like Du'f al-Hadm (delayed digestion), Suqut Ishtiha (anorexia), Fasad al-Ishtiha (perverted appetite), Ghathayan (nausea), Amraz Rass like Suraa (epilepsy), Suda' (headache), Malinkholiya (melancholia) and Falij (Hemiplegia), Amraz Sader like Diq al-Nafas (asthma), Amraz Kabid (liver disorders) like Istesqa (ascites), Awram Ahsha' (inflammation of viscera's), color of skin changes, difficulty in micturition, backache, neck pain, patient become restless. The female resembles with the male, there is excessive hair on her body and her voice become hoarse. 4.5

Younus, a Unani physician said that disturbance in menstruation occur due to *Da'uf Kabid* (Weakness of liver).⁶

Isma'il Jurjani (1041 -1136 AD) mentioned that persistence of amenorrhea for long duration results in hirsutism, hoarseness of voice and other masculine features.¹⁷

Ibn Rushd (Averroes 1126- 1198 A.D) has been mentioned that the syndrome occurs due to *Galba Balgham* i.e., due to change in quantity and quality of *Khilt Balgham*.¹⁴

Moises Maimonides (1135-1204 A.D), the medieval physician mentioned that there are some women whose skin is dry and hard and their nature resembles with the nature of a man. ²

Abd al – Latif Baghdadi (1163- 1231 AD) mentioned in his book *Kitab al Mukhtarat fit Tibb*, that the function of uterus is very important and Muqaddas (holy and sacred). It is the living organ inside a living being which has ability to give birth to the young ones. He mentioned that amenorrhea lead to many diseases. It is caused by defect in the power of evacuation. When amenorrhea occur masculine features appear like hair on whole body, beard and hoarseness of voice, particularly in those females who were multiparous and then secondary amenorrhea occur. He also mentioned about the duration between two cycles should be 23 days to two months. The menstrual cycle should be started from 10 - 14 years of age, but it may be delayed in cold region and occurs early in hot region. ¹⁵

Najib al - din Samarqandi (13th century A.D) mentioned that sometimes the cause of amenorrhea is Barudat (coldness) due to which the viscosity of blood increases. It occurs mostly in cold region and by cold water.¹⁸

Coitre 1573, a student of Fallopus given the name corpus luteum to body which remains in the ovary after ovulation.¹

Fallopus 1600 AD an anatomist, discovered a tube that connects *Rahim* (uterus) with *Baiza Daan* (ovaries). This tube is known as fallopian tube naming after the same scientist.¹

De Graffe 1672, a Dutch scientist not only discovered ovum but also mentioned the process of ovulation.¹

Vallisneri 1721, an Italian scientist, described a married women having no child with shiny ovaries having a white surface and with the size of pigeon eggs. ¹⁹

Akbar Arzani (1722 AD) mentioned that *Rahim* (uterus) is a neuromuscular organ that is why it is also known as *Asbani*. There are a pair of *Khusya* (ovaries) nearby the uterus. They are smaller than male *Khusya* (testes). ²⁰

Bischoff 1844, first time described the relation between ovulation and menstruation.¹

Ajmal Khan (1868-1927 AD) mentioned that menstrual blood is *Fuzla* (waste mater), if it remains in the body it will leads to many complications. ²¹

Lawson Tait 1879, presented the need for the treatment of symptomatic cystic degeneration of the ovaries. 19

Von Kahlden 1902, published a review on the pathological and clinical implications of these ovaries.¹⁹

John A. McGlinn 1915, suggested puncturing those cysts which are upon the surface rather than restoring to ovarian resection. ¹⁹ **Stein and Leventhal 1935**, originally described Polycystic ovarian syndrome as a syndrome manifested by amenorrhea, hirsutism and obesity associated with enlarged polycystic ovaries, ²² that is why it is sometimes known as Stein and Leventhal syndrome, after the two physicians who first described it. ²³

1990, a consensus workshop sponsored by the National Institute of health suggested that a female has PCOS if she has oligo ovulation, signs of androgen excess (clinical or biochemical) and exclusion of other disorders that can result in menstrual irregularity

and hyperandrogenism.19

In 2003, Rotterdam ESHRE/ASRM (European Society for Human Reproduction and Embryology/ American Society for Reproductive Medicine) consensus meeting a refined definition of the PCOS was agreed: namely the presence of two out of the following three criteria: Oligo- and/or anovulation; Hyperandrogenism (clinical and/or biochemical); Polycystic ovaries.^{24,25} This consensus meeting a refined definition of the PCOS was agreed, encompassing a description of the morphology of the polycystic ovary. According to available literature, the criteria fulfilling sufficient specificity and sensitivity to define the poly cystic ovary (PCO) are the presence of 12 or more follicles measuring 2- 9mm in diameter and increased ovarian volume (>10 cm³).²⁴

2004, it was previously considered as a disorder of adult women. Recent evidence suggests that PCOS is a lifelong syndrome, manifesting since prenatal age. In fact, according to the Rotterdam diagnostic criteria, the prevalence of PCOS in adolescents varies between a minimum of 3% (Hashemipour et al., 2004) and a maximum of 26% (discroll 2003).²⁶

2005, the economic burden of PCOS was significantly huge. Around four billion dollars are spent annually in the United States to screen for the disease and treat its various morbidities, including hirsutism, infertility and diabetes mellitus. The Australian Health System spends more than 800 million dollars every year to account for the disease. ²⁶

2006, Androgen Excess and PCOS Society (AE-PCOS) concluded that PCOS should be based only on two criteria, that is, hyperandrogenism, clinical or biochemical and ovarian dysfunction (OD). According to this criteria, women with chronic anovulation with PCOM but without hyperandrogenism were excluded from PCOS.²⁵

2008, studies also show an elevated number of follicles, primarily pre-antral and small antral follicles, in females with PCOS. A defect in apoptotic processes in some maturing follicles further increases their count in PCOS patients. ²⁶

2009, many hypotheses emerged trying to explain the pathophysiology of PCOS. Initially, excess intrauterine androgen had been thought to be a main culprit in the development of the disease. Yet recently, human studies showed neither an association between excessive prenatal androgen exposures nor the development of PCOS in youth.²⁶

2010, a polymorphic marker in fibrillin 3 gene associated with PCOS, D19S884, has been identified in independent sets of families carrying the disease.²⁶

2011, familial aggregation of PCOS and genomic identification of PCOS-susceptibility loci support the role of genetics in the etiology of this disease. ²⁶ The symptomatic presentation of PCOS usually varies with age, young women mainly complaining of reproductive and psychological problems while older women complaining of metabolic symptoms. ²⁶

2012, due to controversies among diagnostic criteria, in 2012, NIH Consensus (NIH and ESHRE/ASRM) recommended broader Rotterdam/ESHRE/ASRM 2003 criteria with detailed PCOS phenotype of all PCOS. According to which, two out of three criteria (hyperandrogenism, ovulatory dysfunction and PCOM) are needed to diagnose and each case has to classify into a specific phenotype A: hyperandrogenism+

ovulatory dysfunction +PCOM; Phenotype B: hyperandrogenism + ovulatory dysfunction; Phenotype C: hyperandrogenism + PCOM; and Phenotype D: ovulatory dysfunction + PCOM.²⁵

2013, Cross-sectional and prospective longitudinal studies have consistently shown that women suffering from PCOS have a higher risk of developing type II diabetes mellitus or impaired glucose tolerance compared to control populations matched for age and ethnic background.²⁶

2014, normal physiological changes and variations in the volume and size of the ovaries during puberty make ultrasonography findings controversial for the diagnosis of PCOS.²⁶

2015, the prevalence of the disease in children is still considered unknown. Diagnosing PCOS in children and adolescence is challenging because the normal pubertal physiological events tend to mimic the signs and symptoms of PCOS. This overlap between normal puberty and the diagnostic pathological criteria of PCOS may cause an over-diagnosis of PCOS among adolescent girls. A great deal of attention has been given to the metabolic disturbances that accompany PCOS, as well as to the consequences of these disturbances later in life. Today, insulin resistance is considered the main pathogenic factor in the background of increased metabolic disturbances in women with PCOS. Concerning the effects on the embryo, women with PCOS are 2.5 times at a higher risk of giving birth to small for gestational age children in comparison to healthy females and offspring show an increased morbidity and mortality compared to control.²⁶

2016 Studies have shown that bariatric surgery can play an important role in the management of patients with PCOS and improve fertility. Similarly bariatric surgery has a positive effect on endometrial hyperplasia, making surgically induced weight loss a potentially attractive option for endometrial cancer prevention and treatment. Obesity has an adverse impact on spontaneous pregnancy, assisted reproduction methods and feto-maternal outcomes. After bariatric surgery obese women with subfertility can achieve spontaneous pregnancy.²⁷

2017 A case – control study indicates that the presence of PCOS is associated with an increased risk of psychological burden. ²⁸

2018 The cross- sectional study was conducted with conclusion that metabolic syndrome and insulin resistance syndrome are prevalent disorders among infertile Vietnamese women with PCOS. PCOS is not solely a reproductive problem. Screening and early intervention for MS and IRS based on anthropometric, metabolic and reproductive hormone risk factors should be an integral part of fertility care.²⁹

2019 An observational study with 85.5% prevalence rate of PCOS among obese females, strongly shows that there is an association among the two. Thus increase in BMI causes increased risk of PCOS in females.³⁰

2020 I complete the research on PCOS and concludes that the root cause of the PCOS should be treated in these patients. The root cause may be stress, that disturbs the hypothalamus pituitary ovarian axis (HPO). During stress cortisol, epinephrine and norepinephrine is released increases glucose in the bloodstream to tackle in emergency and stress. This is related with sympathetic nervous system. But for growth of follicle, release of ovum (ovulation) harmony, peace and calmness is all that is required. This is related with parasympathetic nervous system. These two systems are totally opposite to each other. One works in emergency and

second works in rest/peace. The brain and emotions regulate and control the HPO axis and affects the release of hormones ant any level of hypothalamus – pituitary – ovarian axis. So it is believed that if a female is in continuous stress A-RH (Adrenocorticotrophin – releasing hormone) from hypothalamus acts on anterior pituitary to secrete ACTH (adrenocorticotropic hormone). ACTH via blood stream reach to adrenal gland to release hormone (cortisol). With regards to the reproductive system, it is believed that abnormal levels of the pituitary hormone, luteinizing hormone (LH) and high levels of male hormone (androgens) interfere with normal function of ovaries. Androgens from ovary and adrenals may also increase leads to acne, hirsutism. The hormones released by the pituitary and ovary stimulate follicular growth so as effectively coordinate the function of HPO axis and maintain the homeostasis of the reproductive endocrine system. But when there is continuous stress to a female, it will promote the promote the secretions of pituitary and adrenal hormones including the increase the level of LH and LH/FSH which in turn disturbs the monthly cycle results in polycystic change in one or the both ovaries. In PCOS the anterior pituitary release high amount of LH disrupting normal menstrual cycle as a result follicle does not mature, ovum is not released, ovulation does not occur. Some of the immature follicles does not dissolve and remain as fluid filled sacs or cyst.

2021 Neurological study, concludes that PCOS is a common complication in patients with epilepsy. The reason may be the limbic system, a site closely related to epilepsy, has extensive and direct contact with the hypothalamus, so abnormal discharges can cause reproductive endocrine disorders through the HPO axis. Another reason may be complex connection between neurotransmitters and epilepsy and GnRH neurons, abnormal levels of neurotransmitters may also cause reproductive endocrine disorders through the HPO axis.³¹

2022 PCOS is prevalent among obese. Insulin was markedly elevated in PCOS patients. Insulin resistance change the level of luteinizing hormone and sex hormone binding globulins. Hyperprolactinemia is associated with anovulation or oligo ovulation, galactorrhea and hirsutism. In obese PCOS women, prolactin and insulin could be diagnostic markers of PCOS.³²

2023 The correlation between biochemical and clinical hyperandrogenism parameters varied with age in East Asian population. Clinical hyperandrogenism was positively corelated with FAI in younger women with PCOS. The correlation between biochemical and clinical hyperandrogenism was not significant in older women with PCOS.³³

METHODOLOGY

The Clinical trial was conducted in Regional Research Institute of Unani Medicine, Naseem Bagh Campus, University of Kashmir, after taking approval from institutional ethical committee. It starts from dec 2018 to Aug -2019. A total 66 number of patients were taken in this clinical trial, randomly divide into two groups, control group and test group after obtaining written inform consent.

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