

POLYCYSTIC OVARIAN SYNDROME FROM GREEKO-ARAB TO THE PRESENT: A REVIEW**Dr. Abiha A. Khan^{1*}, Dr. Wajeeha Begum² and Dr. Suboohi Mustafa³**¹Lecturer, Dept of Obstetrics and Gynecology AKTC, AMU Aligarh.²HoD, Reader Dept of Obstetrics and Gynecology NIUM, Bangalore.³Senior Lecturer Dept of Obstetrics and Gynecology AKTC AMU Aligarh.***Corresponding Author: Dr. Abiha A. Khan**

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ABSTRACT

This review paper revisited the times when clinical presentation was the only means to diagnose the disease. Eminent scholars from centuries have given similar description of the disease. Since the advent of ultrasound & biochemical assays, numerous parameters have been proposed to define polycystic ovaries. This has helped the definition to evolve from masculine features, amenorrhea and infertility to hormonal imbalance and grave metabolic derangements. Currently, polycystic ovarian syndrome is described as a heterogenous condition with features of menstrual cycle disturbance, hyper-androgenism, obesity and insulin resistance. With the recent advances in the discovery of pathology approach to the management is also changing. From the use of ovarian wedge resection to ovarian drilling and insulin sensitizing agents, the clinicians are trying to overcome this enigma. However, the disease is a constant dilemma. Further, researches in the alternative system of medicine are also increasing and have proved fruitful in managing the syndrome. The details are discussed in the paper.

KEYWORDS: PCOS, Metabolic, Hyper-androgenism, Amenorrhea, Greekoarab.**INTRODUCTION**

Much has changed over the past 80 years in the way we understand, diagnose, and treat PCOS. It is the most common endocrine disorder among women of reproductive age and affects approximately 4 to 12%.^[1] The clinical manifestations of PCOS include menstrual irregularities, signs of androgen excess (alopecia, acne, hirsutism), and obesity. Fortunately or unfortunately, no single diagnostic criterion (such as hyperandrogenism or polycystic ovaries) is sufficient for clinical diagnosis. This disease till date remains a mystery and has evolved over the years from reproductive to a metabolic disorder. Evidence from the ancient literature suggested that the disease was a known entity. This paper is an attempt to find the first description of the disease and how it has evolved over the time.^[2]

GREEKO-ARAB (400 TO 1500 BC)

This was the time when we had no sensitive laboratory markers and sonography machines to diagnose the disease. A time when clinical presentation was the only means to rule out the cause and to prognose the fate. With the advent of modern methods, diagnosis of the disease has reached to organ and even to the cellular level. Hence, the discovery of roentgenogram identified the annoying cluster of symptoms like amenorrhea,

infertility, hirsutism and polycystic ovaries a name called polycystic ovarian syndrome. The background of this disease when reviewed was found to be very interesting and can be correlated with the modern findings and recent development in the evolution of this disease.

Historically, in the greeko arab era the syndrome was not mentioned as such in the classical literature. However, under the headings of amenorrhea (*ihitbas al tamth*), infertility (*uqr*) and obesity (*samane mufarrat*) clinical experiences with in depth discussion on the cases have been stated. Following are the evidences which give us an idea that the disease was a well known entity in the ancient times.^[3]

Hippocrates (460BC-377BC) the pioneer of medicine, for the first time described a woman whose menstruation was less than 3 days or was meager; to be robust. He mentioned that these women have a healthy complexion with a masculine appearance. He concluded that these women neither are concerned to carry children nor do they become pregnant. According to Soranus of Ephesus (98-138AD) who was a greek gynecologist, obstetrician and paediatrician, sometimes it is natural not to menstruate at all provided that the body of the female resembles with masculine features. He observed clinically and mentioned in his writings that majority of

those not menstruating are rather robust (like mannish) and sterile. Claudius Galen (129-200AD) also observed similar changes in some amenorrheic patients. He described that if a woman progresses to develop man like features associated with amenorrhea then no medical therapy is of help to refrain the same. He summarized that this condition is frequently encountered in women who have morphological resemblance to man like features and possess less musculature.

Among these physician philosophers admiring and challenging was Zakariya Razi (865-925 AD) who in his writings discussed a case of amenorrheic widowed women, with beard and male like hair growth over the chest and hoarseness in voice and with the course of time she died. He concluded that amenorrhea (*ihibas al tamth*) ensue in women with fair complexion and phlegmatic temperament. He also discussed that menstruation may develop due to weakness of the liver. His concept of involvement of liver in causing amenorrhea is similar to the present concept of Insulin Resistance and insulin mediated disease in the secretion of sex hormone binding globulin (SHBG).^[3] Razes concept of involvement of liver in extrauterine causes for amenorrhea was supported by Ali Ibn Abbas Majoosi (930-994AD). He added to the concept that when the temperament of liver alters and becomes cold (*Barid*), it is unable to convert chyme into blood and instead changes to tenacious phlegm. He also added obesity (*samanne mufarrat*) as a cause for absent menstruation due to reduced blood flow and narrowing of blood vessels.^[4] With increasing times more and more eminent scholars provided clinical evidence through description of the cases and confirmed involvement of liver in the disease process. Ibn hubl Baghdadi (1122-1213 AD) and Ibn Rushd (1126-1298 AD) added the concept of humors to this disease. They gave a generalized idea that the diseases of cold and moist nature arise due to imbalance in the quantity or quality of the phlegm.^[5] The most common diseases arising due to it are phlegmatic swellings or fevers.^[6] Hence, by the early medieval times the disease concept has evolved from a mere symptom to humoral imbalance, obesity and liver weakness.

By the end of medieval era, Moises Maimonides a renowned philosopher gave a contradictory description of a woman with disturbed menstrual cyclicality. He mentioned that women whose skin is dry and hard and nature resembles a man concluded that this does not arise from medications, but is caused by heavy menstrual cyclicality.^[3,6] Ambroise Pare (1510-1590AD) a celebrated renaissance surgeon and obstetrician observed a number of females with reduced sexual cyclicality changing in a certain manly nature and called them viragines. The word viragines was described as to stay stout or manly woman and their voice was loud and big like a man and they will be bearded.^[7]

The 18th and the 19th century

For centuries this disease was considered to develop in stout, robust and manly women and the pathology revolved around weakness of liver and humoral imbalance. The 18th and the 19th century claim the first description of anatomy and pathology of the polycystic ovary as well as the features of this condition was made evident during the period via sonography.^[8] In the year 1830 J. Lisfranc described an entity for which Chereau introduced the term sclerotic disease of the ovary or sclerocystic disease in 1844. With the popularity of laparotomy in the 1800s and reports of ovarian microcystic degeneration in sclerotic ovaries with associated abnormal bleeding patterns appeared in the early 1900s.

By now, the term sclerotic and abnormal bleeding pattern was added to the definition of this mysterious disease. During the year 1921, a French pathologist Achard and his associate Theirs, described a striking characteristic of diabetes in a bearded women.^[9] This peculiar finding laid the foundation of Insulin resistance in hirsute females and the disease evolved from reproductive to metabolic.

Further, Irving stein and Michael Leventhal from Chicago also produced with the similar findings of women with amenorrhea and polycystic ovaries. They added that the use of bilateral ovarian wedge resection the menstruation of women can be resumed. Ten years later, after intense studies and research the year 1945, stein defined the syndrome as a cluster of symptoms like oligomenorrhea, hirsutism, infertility and polycystic ovaries. During this period stein and leventhal surgically explored these women and revealed the characteristic feature of the ovaries which were found to enlarge two to four times and were full of tiny fluid filled cysts. The authors claimed that the diagnosis of enlarged polycystic ovaries could be greatly enhanced by the use of pneumoroentgenography, an X-ray procedure that evaluated the female genital tract including the ovaries by using gas insufflation. In the following decades, the disease was referred to by its eponym stein leventhal syndrome.

By the year 1947 Kierland et al added the presence of skin darkening and skin tags in women with hyperandrogenism and diabetes mellitus. In the next decade Keetel (1957) and his associates investigated on the eponymous 'Stein-Leventhal'syndrome and noted increase concentration of androgens and LH in women with polycystic ovaries. Adding to the findings, polycystic ovarian syndrome in the recent times benefited from ultrasound technology.^[17]

It was Swanson *Et al* in the year 1981 who first defined the ultrasound appearance of polycystic ovaries and by the year 1985, Adams et al added detail to the USG findings such as follicle number and ovarian volume. The ultrasound description of the stein leventhal

syndrome gave the name polycystic ovarian syndrome to the disease.^[10]

Developments in the Management of Pcos

The management of PCOS became a dilemma for the clinicians due to the ambiguous etiology and complex patho-physiology. Historically, for many years wedge resection was the only treatment for PCOS along with histological assessment of the ovaries. The ovarian wedge resection though improved menstruation had the inconvenience of potential peri-ovarian adhesion formation. With the discovery of anti-estrogens this surgical technique became obsolete.^[11] The therapeutic approach in PCOS now became symptom oriented. In the year 1961, Greenblatt found that clomiphene citrate may induce ovulation in patients with secondary amenorrhea and infertility. Thus, the first successful induction was reported in 1961.^[12] In the year 1967, the scientist duo Palmer and De Brux studied laproscopic ovarian biopsies. This was later modified and used as a method of treatment in the form of ovarian diathermy by Gjonnaess. It was Huber and his colleagues who popularized the laproscopic ovarian drilling in the year 1990.^[13] During this decade insulin sensitizing agents also gained popularity. The use of insulin sensitizing agents in PCOS was discovered accidentally when the relation of insulin resistance and the syndrome was reported. By the end of 1996, it was reported that metformin not only reduced circulating insulin levels but was also associated with decreases in ovarian 17, 20-lyase activity and ovarian secretion of androgens.^[14] During the 20th century the mainstay of treatment was insulin sensitizing agents and brought under evaluation of other hypoglycemic agents troglitazone, rosiglitazone & pioglitazone (thiazolidinedione agents). Though troglitazone has been withdrawn due to adverse effects in the year 2000, the other two thiazolidinediones are still being used at various dosages for ovulation induction.^[14]

Recent Development in the Alternative System of Medicine

Complementary medicine (CM) use by women has increased during the past ten years. A number of herbal medicines which may have potential benefit without the possible side effects of abnormal uterine bleeding, weight gain, and liver failure are being tried in the management of PCOS. Pre clinical and clinical studies are undertaken on an array of single drugs such as *Cimicifuga racemosa*, *Cinnamomum cassia*, *Curcuma longa*, *Glycyrrhiza spp.*, *Matricaria chamomilla*, *Mentha piperita*, *Paeonia lactiflora*, *Silybum marianum*, *Tribulus terrestris* and *Vitex agnus-castus* etc. A prospective, clinical study, on PCOS subjects using cinnamomum zeylanicum supplements suggested improvement in the menstrual cyclicity and assured it to be an effective treatment option for some women with PCOS.^[15] The role of regimental therapy in *Unani* system of medicine is time tested. Ongoing clinical trials and published case reports.^[16] reveal that the use of *Hijamah* therapy helps

in regularizing menstrual cycles in amenorrheic subjects suffering from PCOS. The *hijamah* therapy also helped in restoration of ovulation in patients suffering from infertility due to PCOS.^[17] Other mode of therapy widely in practice is acupuncture. Recent data revealed that acupuncture increased pregnancy rates from 26.3% to 42.5% when performed both pre- and post- IVF transfer.^[18,19] To bring these therapies into fore and to generalize the results scientific validation to the mechanism of action is still awaited.

CONCLUSION

Taken together, this historical review suggests that PCOS is known from centuries. It is the discovery of sophisticated investigation techniques which helped to decipher the disease concept, understanding the perception of the disease and presentation of the symptoms documented in ancient classical texts. This paper is first of its kind and written in order to gather knowledge about the syndrome in the ancient period and how the disease has evolved in the present times with multiple treatment options. Conventional and alternative systems assert to serve the purpose by providing an ample amount of drugs but still future researches for better achievement of results are ongoing.

Table 1: Summary of History of Evolution of Pcos.

Claudius Galen (129-200 AD)	Description of women with masculine features.
Hippocrates (460 BC-377 BC)	Robust and mannish women do not bear meager bleeding pattern, nor do they conceive.
Zakariya Razi (860-925 AD)	Described amenorrhic widowed women with hoarse voice and male like hair growth pattern. Association of amenorrhea with phlegmatic temperament. Liver as the cause of cessation of menstruation.
Ali Bin Abbas Majoosi (930-994 AD)	Liver diseases give rise to amenorrhea and obesity.
Moises Maimonides (1135-1204 AD)	Woman's nature tends to be transformed to the nature of a man does not arise from medications, but is caused by heavy menstrual activity.
Ambroise Pare (1510-1590 AD)	Used the term Viragines, that is to say stout or manly women; therefore their voice is loud and big, like unto a man, and they become bearded."
J. Lisfranc, 1830	Described the disease as an entity.
Chereau, 1844	Introduced the term sclerotic disease of the ovary or sclerocystic disease.
1900s	Ovarian micro-cystic degeneration in sclerotic ovaries with associated abnormal bleeding patterns.
Achard and Thiers, 1941	The diabetes of bearded women (diabete des femmes a barbe)
Stein (1945)	Defined the syndrome of oligomenorrhea, hirsutism, infertility and polycystic ovaries.
Kierland <i>et al</i> , 1947	Acanthosis nigricans, was reported to occur frequently in women with hyperandrogenism and diabetes mellitus.
Dr. Jo V Meigs, 1949	Term Stein-Leventhal's syndrome was used for the first time.
Keetel <i>et al</i> , 1957	Noted increased concentrations of androgens and LH in women with polycystic ovaries.
NIH, 1990	First diagnostic criteria for PCOS ^[19]

CONFLICT OF INTEREST

There is no conflict of interest among the authors.

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