PREVALENCE AND ASSOCIATED RISK FACTORS OF POLYCYSTIC OVARY SYNDROME IN ASIAN COUNTRIES

By

Bodron Nesa Eathan
17126017
Ananya Mahmud
18326017

Thesis submitted to the Department of Mathematics and Natural Sciences in partial fulfillment of the requirements for the degree of
Bachelors in Microbiology

Mathematics and Natural Sciences

Brac University

September, 2022

Declaration

It is hereby declared that

1. The thesis submitted is our own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. We have acknowledged all main sources of help.

Student's Full Name & Signature:

Bodron Nesa Eathan 17126017	Ananya Mahmud 18326027

Approval

The thesis titled “Prevalence and Associated Risk Factors of Polycystic Ovary Syndrome in Asian countries” submitted by

1. Bodron Nesa Eathan (17126017)
2. Ananya Mahmud (18326027)

of (Summer), (2022) has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelors in Microbiology on 29-09-2022

Examining Committee:

Supervisor:
(Member)

_____
Dr. Fahim Kabir Monjurul Haque
Assistant Professor
Microbiology Program
Mathematics and Natural Sciences,
Brac University

Program Coordinator:
(Member)

_____
Dr. Mahbubul H. Siddiqee
Associate Professor
Microbiology Program
Mathematics and Natural Sciences, Brac University

Departmental Head:
(Chair)

_____
Dr. A.F.M Yusuf Haider
Chairperson
Mathematics and Natural Sciences, Brac University

Ethics Statement

Hereby, we assure that for the manuscript ‘Prevalence and associated risk factors of Polycystic Ovary Syndrome in Asian countries’ the following is fulfilled:

- This material is the author’s own original work, which has not been previously published elsewhere.
- The paper reflects the author’s own research and analysis in a truthful and complete manner.
- The paper properly credits the meaningful contributions of co-authors and co-researchers.
- All sources used are properly disclosed (correct citation). Literally copying of text must be indicated as such by using quotation marks and giving proper reference.
- All authors have been personally and actively involved in substantial work, leading to the paper and will take public responsibility for its content.

The violation of the Ethical Statement rules may result in severe consequences. We all the authors agree with the above statements.

Date: 29-09-2022

Corresponding author’s signature:

Abstract

Polycystic ovary syndrome is one of the most common endocrinal disorders which 1 in 10 women are suffering from, worldwide. This disease is a multifaceted disease and does not come alone, but brings with it, few to many co-related diseases. Despite the high rate in prevalence, the exact etiology is yet to be known. But there are factors which are believed to play key roles in the initiation of the disease such as- insulin resistance, genetics, psychological disorders, Bisphenyl A, hormonal imbalances, etc. In this review article, the prevalence of the disease among Asian women are explored on a number of basis which include obesity, mental health, socio-economic features and an overall idea of the prevalence condition Asia-wide. This review article also focuses on the most common risk factors which are and have always been associated with the disease such as cardiovascular diseases, hirsutism, hyperandrogenism, etc.

Keywords

Polycystic ovary syndrome; risk factors; obesity; mental health; Asian women.

Dedication

To our wonderful parents and our beloved faculties.

And, to all the female scientists and researchers. Nevertheless, they persist, and inspire.

Table of Contents

Glossary

Thesis:	An extended research paper that is part of the final exam process for a graduate degree. The document may also be classified as a project or collection of extended essays.

List of Tables

Chapter:1

INTRODUCTION

In today's time, polycystic ovary syndrome (PCOS) is one of the most emerging endocrine disorders in women. This disorder directly results in the improper functioning of the endocrine system, responsible for the hormones, receptors and the direct organs associated with PCOS. PCOS can be distinguished if there are presence of irregular menstrual cycle, hyperandrogenism and polycystic ovarian morphology are seen (Islam et al., 2022). PCOS is a multifaceted disease which can begin as early as from conception and can continue even

after menopause is reached (Islam et al., 2022). This disease is the result of female sex hormone imbalance, which leads to formation of cysts in the ovaries, impairing ovarian morphology and welcoming a series of co-related health problems (Patel S., 2018). Cysts are water-filled sacs which develop in the follicles where eggs are stored in under-developed condition. Cyst formation disturbs the ovulation process, leading to infertility issues as the whole menstrual cycle gets affected. When cysts are present in large numbers in the ovaries, it leads to PCOS (Patel S., 2018). Not only does PCOS interfere with ovulation and the hormones needed to do so, this disease leads to produce an unhealthy amount of androgen hormone, which is typically a male hormone present in female body in minute quantity. The failure to ovulate, leads to several cyst formation in one or both ovaries and these cysts in turn, produce excessive androgen contributing to issues with menstrual cycle and all linked symptoms and co-related diseases (Azziz et al., 2016). In short, PCOS is an endocrine disorder with abnormal hormone production alongside ovulatory dysfunction and polycystic ovarian morphology.

The exact etiology of the discussed endocrine disorder is yet to be known. That being said, there are factors which play key roles in the occurrence of the disease. Factors like insulin resistance, hormonal imbalance, genetics, Bisphenyl A (BPA), ovarian follicular defect and even, psychological disorders are suspected to contribute towards the etiology of the disease (Muhas et al., 2018).

Insulin resistance: Insulin resistance can occur due to hyperinsulinemia followed by type 2 diabetes in 10% women. Hyperinsulinemia can develop as a result of increased production of insulin as well as decreased insulin clearance from the body. It can be said that anovulatory women with PCOS are hyperinsulinemeniac and resistant to insulin compared to ovulatory women without PCOS. Selective insulin resistance is central to the etiology of PCOS. Level of insulin production in the body is also corelated with the generation of androgen production from the ovaries. Apart from that, insulin concentration alters gonadotropin secretion, decreasing the SHBG synthesis in the liver and so, free flow of testosterone increases in female body (Muhas et al., 2018).

Hormonal imbalance: High testosterone levels are linked with hyperandrogenism. Low sex hormone binding globulin (SHBG) is also linked with hyperandrogenism. High levels of LH increase chances of improper functioning of ovaries. At the same time, hypothalamic-pituitary axis (HPA) abnormalities lead to unusual secretion of gonadotropin-releasing hormone (GnRH) and LH, which increases the ovarian androgen production as LH stimulates the theca cells in the ovaries to synthesize androgens, leading to hyperandrogenism (Muhas et al., 2018).

Genetic factors: It can be assumed that genetics come in play and contributes towards the chance of developing the disease. During intrauterine life, excess androgen exposure can lead to a permanent effect on gene expression, contributing towards PCOS and insulin resistance. Not only genes, but environmental factors also contribute to PCOS. A single gene is not responsible for the disease alone, rather there are a few genes involved along with environmental factors. At the same time, low birth weight and fetal exposure to the hormone androgen can contribute towards the development of PCOS phenotype (Muhas et al., 2018).

Bisphenyl A (BPA): This common industrial compound is linked in initiating ovarian dysfunctionality (Muhas et al., 2018).

Ovarian follicular defect: Compared to healthy women, women who tend to have PCOS, are more likely to have 2 to 6-fold more follicles. This rapid increase in the number, is due to excessive androgen production, contributing towards follicular defect (Muhas et al., 2018).

Psychological disorders: Increased stress and depression can disturb with the menstrual cycle and in turn, interfere with the hormonal cycles as well. Stress can increase the concentration of cortisol and prolactin hormones in the body, delaying the monthly cycle. If the delays continue to happen every month or frequently, the body's natural cycle loses integrity and can be a contributing result to PCOS (Muhas et al., 2018)

The main theories to explain the pathophysiology or consequences of the disease are as follows-

Endometrial progesterone resistance- Women with PCOS has low endometrial response. A study has confirmed that total endometrial progesterone receptor expression is higher in the affected females. The progesterone expression is much higher in the epithelial cells compared with the stromal cells which is why, more epithelial cells are blocked, resulting in reduction of binding of progesterone with the stromal cells (Muhas et al., 2018).

Insulin resistance- This feature can be present in both obese and non-obese women, having PCOS. Insulin resistance means the body cells fail in the uptake of glucose from the blood,

resulting in build-up of glucose in the body as insulin was supposed to help in the uptake of the sugar to the liver. As a result of this build-up, pancreas starts producing more insulin to help with the uptake of glucose (NIDDK, Insulin resistance and diabetes). Insulin resistance contributes to hyperandrogenism in two possible ways, one of which is the inhibition of hepatic synthesis of serum sex hormone binding globulin or in short, SHBG. Another way is the inhibition of hepatic production of 1GFBP-1 which is known to allow higher local activity of IGF-1 (Muhas et al., 2018).

Ovarian defect- PCOS can occur if there is a defect in the ovaries due to gonadotropin-dependent hyperandrogenism. This defect can lead to intraovarian androgen excess levels which is common in PCOS patients along with elevated levels of androstenedione in response to LH (Muhas et al., 2018).

In this review, the prevalence of PCOS based on obesity, mental health condition, socio-economic features and insulin resistance are studied among the Asian countries of the world. Apart from the mentioned criteria of the prevalence that are studied, associated risk factors of the disease polycystic ovary syndrome are studied. This review study has the following purposes-

1. To review previous papers to find out about the prevalence of the disease based on dependent factors.
2. To summarize the associated risk factors of the disease.

Chapter:2

PREVALENCE OF POLYCYSTIC OVARY SYNDROME BASED ON DIFFERENT FACTORS

2.1 Prevalence of Polycystic Ovary Syndrome in different Asian countries.

From the given data of tables, it is clear that Bangladesh, India, Pakistan, Afghanistan, Japan, Indonesia, Iran and Taiwan have greater prevalence of PCOS due to regional, economical and mental health than other countries in Asia. The prevalence of PCOS in Chinese women has increased significantly over the past 10 years and become a significant public health problem in women of reproductive age in China (Yang R, 2022). Among Chinese, Filipina and South Asian women the prevalence of PCOS was 1%, 1.5% and 3.3% but now that has increased (Lo J, 2021).

Table 1: Prevalence of Polycystic Ovary Syndrome in different Asian countries.

City, country	Age	Prevalence of PCOS	Number of. Studied population	Common symptoms	References
Dhaka, Bangladesh	16.8 ± 1.7	22%	8,000-9,000	Irregular period, weight gain, hirsutism	Mirza, 2014; Hasan et al.,2020
Lucknow, India Mumbai Tamil Nadu	18-25 15-24 12-19	3.7 % 22.5% 18%	1520 600 126	Amenorrhea, infertility, hyperandrogenemia	Ganie et al., 2019
Islamabad, Pakistan	15-44	52%	440	Abnormal hair growth on face and face, acne	Sindra et al., 2019
Thimphu, Bhutan	15-50	5-10%	550	Irregular period, hair loss from the head, difficulty with pregnancy	The heart of fertility care, 2018
Afghanistan	20-24	50.1%	216, 686	Darkening of skin, heavy periods, sleeping problems	Asghari et al., 2022
China, republic of China	19-45	5.6%	15,924	Higher rates of infertility, lower rate of obesity, insulin resistance	Li et al., 2013
Tokyo, Japan	20++	2.5% - 32.8%	21,29	Chronic ovulatory dysfunction, hyperandrogenism	Kubota et al., 2013; Miyoshi et al., 2013

Jakarta, Indonesia	18-35	8% - 10%	125	Excessive androgen, male-pattern baldness	Wiweko et al., 2018
Sri Jayewardenepura, Sri Lanka	15-39	6.3%	3030	Hair loss, weight gain, increased androgen levels	V, 2008
Hamadan, Iran	27	7.1 %	200	Infertility, hirsutism	Moghadam, 2018
Tashkent, Uzbekistan	>35	10% - 15 %	240	Trouble to lose weight, depression	Jumayev et al., 2012
Kathmandu, Nepal	20-25 25-30 30-35	11% 26% 37%	10 23 33	Heavy bleeding, darkening of the skin, anxiety, mood swings, insomnia	Pandey, 2020
Singapore, Republic of Singapore	18-35	10%	225	Dark skin patches, thinning of scalp hair	Salim, 2022
Bangkok, Thailand	>40	5.29%	180	Prolonged menstrual cycles/missed period, spotting due to thick lining	Kaewnin, 2018; Pronmoi et al., 2009
Kuala Lumpur, Malaysia	26.01±7.14	12.6%	675	infertility, depression	Dashti,2018
Taiwan	18-45	20%	Random	Android obesity, androgenic alopecia	Hsu, 2015
Istanbul, Turkey	18-45	6.1%	392	Cysts on the ovaries, excess flaps on the neck or armpits area	BO et al., 2021

2.2 Prevalence of Polycystic Ovary Syndrome based on mental well-being among Asian countries.

In Pakistan, prevalence of PCOS varied from married to unmarried girls of reproductive age where 82.7% for married and 17.3% for unmarried women due to psychological disorders, sexual dysfunction, women identity and health related quality of life (Sindra S, 2019). There are different factors behind the prevalence of PCOS among them diagnostic criteria are one of the influencing factors that cause various prevalence for different ways of diagnostic. In addition, prevalence of PCOS, in Sri Lanka varied for diagnostic criteria and is 5-10% depending on Overall life-style, food habits, hygiene (Deswal R, 2020).

Table 2: Prevalence of Polycystic Ovary Syndrome based on mental conditions among Asian women

Country	Age	Psychological features with prevalence of PCOS (%)	Studied populations	Influential factors	References
Bangladesh	24-45	Loneliness- 71% Anxiety disorder- 80% Depressive illness- 60%	444	Several mental disorders, Socio-economic and demographic with lifestyle, relatively poor mental health	Hasan et al.,2022
India	18-45	Anxiety- 38.6 Depression- 25.7%	70	Infertility, alopecia, hirsutism, quality of life	Chaudhuri et al., 2018
Pakistan	26-35	Depression- 5 to 10%	152	Marital status, living locations	Malik et al., 2020
China	19-45	Positive anxiety-26.6% Positive depression- 23.6%	433	Dysfunctional sleeping	Yang et al., 2021
Iran	27	8%	316	Income source, quality of life	Moghadam, 2018

Table 3: Prevalence of PCOS depending on socio-economic conditions in Asia

Country	Sociological features	Prevalence of PCOS	Influencing factors	References
India	Rural area /lower income Urban area/ better income	8.9% 1%	Oligomenorrhea, hirsutism, treatment of allopathy or naturopathy, lack of awareness of PCOS	Bharathi et. al., 2017
Bhutan	Under privileged women	6-10%	No private toilets, no hygiene system and less knowledge	Chen et al., 2018

Afghanistan	Comparatively poor	50% (from 1990 to 2019)	Lower resource ability, lower income, less awareness	Asgharik,2022
China	Less privileged	Workers-10.37 %, students-16.37 %	Population of the living region, occupation	Wu et al., 2020
Japan	High-middle class women	41.33% (2007-2017)	Quality of life	Liu et at.,2022

2.3 Prevalence of Polycystic Ovary Syndrome based on obesity among different Asian countries

According to the World Health Organization (WHO), obesity is defined as the excessive fat deposition in the human body, leading to an abnormal increase in body mass, often contributing to multiple health risks. If BMI (body index mass) is over 30, then, the person is considered to be obese. Obesity is measured using BMI of each person and if it stands out to be 30 or more, the person is considered obese. Body Mass Index is calculated by dividing a person's weight in kilograms by his/her height in meters squared (kg/m^2). Whatever the value is obtained, it is then compared with weight classification numbers on the pre-formed BMI chart where underweight, normal weight, overweight and obesity are defined based on specific cut-offs.

The study of prevalence of obesity has been done on various studies and put together on table: 5 to show the prevalence of PCOS based on obesity in different Asian countries where obesity means the population studied were all equal to over 30 kg/m^2 according to the weight status established by World Health Organization (WHO, 1998).

Table 4: WHO classification of weight status.

Weight Status	**Body Mass Index (BMI), kg/m^2**
Underweight	<18.5
Normal range	18.5-24.9
Over weight	25.0-29.9
Obese	≥ 30
Obese Class 1	30.0-34.9
Obese Class 2	35.0-39.9
Obese Class 3	≥40

Obesity is one of the most findings in women who have PCOS. It has a wide range of prevalence from as low as 15% to as high as 80% as shown in (Table: 5). Prevalence of obesity has been studied to see the real scenario among the Asian countries. Typically, it is seen that if a larger group of population is studied, the rate of prevalence is seen to be low and if a smaller population is studied, prevalence of obesity is found to be higher as for example- according to Table: 5, Malaysia has a very high prevalence rate, which is 77.1% but it only has 62 people in the study whereas Japan has a comparatively low prevalence which is only 25.9% and the study had a large population of 1498 people. Apart from this, another interesting observation is that of China- from the table:5, it is clearly seen that the prevalence of obesity keeps increasing with age. Age below 25 has the least prevalence at 15.9% whereas the obesity % kept increasing significantly as Chinese women aged, as women older than 41 has the highest obesity prevalence which is 57.1%. The highest prevalence is in Islamabad, Pakistan at 80% and the lowest is in China with 15.9% but the age range and number of patients studied, are uneven and hence, a perfect comparison between the data cannot be drawn. Apart from China, other countries do not follow the age and obesity pattern perfectly such as- countries like Pakistan, Malaysia has shown a very high obesity prevalence in younger women but in countries like, India and Sri Lanka show lower prevalence in younger women. So, only China showed the obesity% increase with age which is not the case in other countries as younger women in different countries have shown both high and low prevalence of obesity.

Table 5: Prevalence of Polycystic Ovary Syndrome based on obesity among different Asian countries

City, Country	Number of patients studied	Age groups (years)	Prevalence of PCOS based on obesity (%)	Related Factors	References
Islamabad, Pakistan	440	15-30	80%	Irregular menstrual cycle and infertility	Sidra et al., 2019

China	894	<25 (n=226) 26-35 (n=493) 36-40 (n=93) 41> (n=21)	15.9% 37.7% 55.9% 57.1%	Hyperandrogenism, PCO.	Li et al., 2013
Kuala Lumpur, Malaysia	62	22-26	77.1%	Hirsutism and non-insulin dependent diabetes mellitus	Tan et al., 2008
Taiwan	627	-	34%	High serum testosterone levels, but lower acne compared to non-obese PCOS patients	Hsu, 2015
Singapore city, Singapore	389	21-45	45.2%	Increased hair growth with modified Ferriman-Galwey (mfg.) score being 2.96-fold greater than non-obese females.	Neubronner et al., 2021
Japan	1498	-	25.9%	Increase in irregular menstrual cycle, infertility and amenohoerra.	Kubota, 2013
Lucknow, India	35	18-25	24%	Hypertension.	Gil et al., 2012
Gampaha, Sri Lanka	146	19-35	26%	Excessive hair growth	Kumarapeli et al., 2010

2.4 Prevalence of Polycystic Ovary Syndrome based on obesity in urban and rural regions of the Indian Sub-Continent.

A clear picture of the condition of PCOS related obesity in the Indian Sub-Continent has been shown in Table:6. Prevalence of obesity has been studied in both urban and rural regions of three countries- India, Bangladesh and Nepal. It is apparent from the table:6 that urban region in all three countries had very high prevalence of obesity compared to the rural region. The

study has been conducted in year 1996, 2000 and 2004 in both Bangladesh and Nepal and it is clearly seen that in all three years, the prevalence of obesity in the urban region has been a lot greater than in rural region. In fact, with the year increasing from 1996 to 2004, the prevalence of obesity in the urban region increased. So, it is clear that obesity has become more common with time in the urban region as obesity increased from 11.4% to 19.7% in Bangladesh and in Nepal, it increased from 5.8% to 25.5%. For India, study has been conducted in the years 1998 and 2005, where the same result has been observed- urban region has higher prevalence of obesity which increased over the years from 23.5% to 28.9%. Another observation that is very apparent from the study is that, Nepal had the highest increase of obesity prevalence as it increased from 5.8% to 25.5%, which is almost 5-fold increase, whereas Bangladesh had an increase of 8.3% and India had an increase of 5.4% only. When it comes to rural region, the prevalence of obesity increased in all three countries as well. The increase may not be as high as in urban region, but clearly, even in rural region, the % increased significantly. From years 1996 to 2004, Bangladesh had an increase of 4.1% prevalence of obesity followed by Nepal, increased by 6%. Whereas, India had only 2.7% increase from year 1998 to 2005. It is also clear that whether urban or rural, Nepal had the highest increase of prevalence of obesity, 19.7% in urban and 6% in rural and India had the least increase in the prevalence, 5.4% in urban and 2.7% in rural region only. (Check Table: 6) Not to mention, this study has been designed, keeping the age group constant, which means results observed are un-biased and accurate.

Table 6: Prevalence of Polycystic Ovary Syndrome based on obesity in Indian Sub-continent.

Country	Location	Year	Number of patients studied	Prevalence of PCOS based on obesity	Age group	References
Bangladesh	Urban	1996	570	11.4%	15-35 +	Balarajan and Villamor, 2009
		2000	1275	12.9%		
		2004	3593	19.7%		

	Rural	1996	3473	1.7%	15-35+	
		2000	3404	2.6%		
		2004	6896	5.8%		
Nepal	Urban	1996	304	5.8%	15-35+	Balarajan and Villamor, 2009
		2000	1070	24%		
		2004	2121	25.5%		
	Rural	1996	3116	1.4%	15-35+	
		2000	6889	4.4%		
		2004	5854	7.4%		
India	Urban	1998	24519	23.5%	15-35+	Balarajan and Villamor, 2009
		2005	36259	28.9%		
	Rural	1998	53090	5.9%	15-35+	
		2005	47887	8.6%		

2.5 Prevalence of Polycystic Ovary Syndrome depending on co-morbidity in Asian women.

Insulin resistance or IR is one of the most occurring side effects of polycystic ovary syndrome. Some of the Asian countries have been shown in Table: 7 where IR prevalence and total prevalence of PCOS in the countries are listed. From table: 7, one thing is clear that the studies which had lesser number of patients involved in the study, showed much higher prevalence of IR for example in Indonesia, Bangladesh and India, all showing prevalence between 40 to 80%. Whereas, the countries with higher number of populations studied like Japan and Nepal, the prevalence of IR was comparatively lower. Nepal had shown the least % prevalence of IR compared to all the countries, despite the differences in the number of populations studied. 0.5% is a very small number when a large population of 381 women are studied. It is almost like the Nepalis do not even have IR as the side effect of PCOS. On the other hand, Dhaka and Kolkata had a very similar population number studied and the IR

prevalence of both the cities were in the same range, which is from 44 to 70%. Japan showed only 33% IR prevalence with the largest population being studied and Indonesia had the highest prevalence of IR, up to 80% with a mediocre population number (check table: 7). Even though, there were no age group mentioned in the study of Nepal and Japan, the age range in Dhaka, Kolkata and Indonesia were similar, ranging from 16-33 and so, the studies could be compared effectively (check table: 7).

Table 7: Prevalence of Polycystic Ovary Syndrome depending on co-morbidity in Asian women.

City, Country	Age group (years)	Number of patients studied	Prevalence of PCOS	Prevalence of PCOS based on Diabetes\ Insulin Resistance	Influencing factors	References
Kathmandu, Nepal	-	381	9.1%	0.5%	Cardiovascular diseases, hypertension, endometrial cancer	Shreeyanta K.C et al., 2020

Indonesia	25-30	125	15-20%	50-80%	Increased AMH	Wiweko et al., 2018
Dhaka, Bangladesh	22-23	73	37%	44-70%	Depression, hirsutism	Quadir F. et al., 2020
Japan	-	1498	27%	33%	Increase in irregular menstrual cycle, infertility and amenohoerra.	Kubota, 2013
Kolkata, India	16-33	66	3.7-22.5%	50-70%	Sleep apnea, diabetes mellitus	Bhattachary a et al., 2020

Chapter:3

Associated risk factors with Polycystic Ovary Syndrome

3.1 Cardiovascular risk factor

Cardiovascular disease is one of the first and foremost risk factor which has been associated with polycystic ovary syndrome, but CVD does not begin alone. There are many co-related factors and conditions which lead to cardiovascular disease. Starting from biochemical to clinical to metabolic syndrome, there are co-related factors which if present, can lead to CVD ultimately. If a patient has PCOS, it is most likely that she can develop conditions like- dyslipidemia, insulin resistance type 2 diabetes, hyperandrogenemia, hypertension etc. These conditions all contribute in the development of cardiovascular disease eventually. Insulin resistance is known to play key role in development of PCOS. Insulin resistance can

contribute towards the increase of BMI, leading to obesity, which is highly co-related with developing CVD. Another co-related factor is the hyperandrogenemia. The increase in hyperandrogenemia may contribute to insulin resistance as well (A.J. Cussons et al, 2006). However, insulin resistance has been associated with endothelial dysfunction and increased cardiovascular risk but hyperandrogenemia cannot be directly linked in the contribution of cardiovascular disease (A.J. Cussons et al, 2006).

Dyslipidemia is the most common metabolic abnormality in PCOS, with a prevalence of up to 70% by the National Cholesterol Education Program criteria. Dyslipidemia means there would be significant increase in the levels of triglyceride-rich proteins, leading to an increased level of LDL or low-density lipid and suppression of the good lipid which is high density lipid. These changes are related to insulin resistance as well. These qualitative changes in lipoprotein metabolism are thought to increase risk of cardiovascular disease in PCOS. If there are bad lipid involved in large amount, it would definitely mean higher chances of fat deposition in the arteries of the heart, meaning higher chance of Atherosclerosis. Also, dyslipidemia can contribute towards impaired glucose tolerance, leading to type 2 diabetes and of course, obesity. In short, it can be said that clusters of biochemical, clinical and metabolic syndrome can occur if patient has PCOS, which in turn, can lead to inflammation, adipocytokines, endothelial dysfunction. Myocardial dysfunction, atherosclerosis, leading towards clinical cardiovascular disease (A.J. Cussons et al, 2006).

3.2 Obstructive Sleep Apnea (OSA)

Obstructive sleep apnea is a chronic sleeping disorder where upper airway function is disturbed during sleep as well as consequential hypoxia and inconsistent sleeping pattern are conditions of OSA (Islam et al., 2022). OSA is one of the risk factors which is associated with not only OCOS but it also linked with hypertension, cardiovascular disease, stroke and abnormal glucose mechanism which surprisingly, are all associated PCOS in turn (Punjabi, 2008). The extremity of OSA can be defined by the number of obstructive events per hour of sleep, which is measured by apnea–hypopnea index or AHI, and can be classified as mild, moderate, or severe. Obstructive sleep apnea is an important contributor to both metabolic disturbances such as insulin resistance, type 2 diabetes, adverse cardiovascular as well as Polycystic ovary syndrome. Women with PCOS have been reported to develop OSA at rates which are higher than men. The high prevalence of OSA has been linked with the raised level of testosterone hormone which is considered to be one of the determining features of PCOS as well with obesity which is usually accompanied with the OSA (Ehrmann, 2012). OSA is generally more common in menopausal women with PCOS compared with premenopausal women with PCOS, with daytime sleepiness being a big concern in the menopausal women with PCOS (Tasali et al., 2008). Risk factor of OSA not only increases in menopausal women but in older women in general as well as obese women and women who tend to be regular smokers, sedative use, excessive alcohol intake and in certain ethnicities (Kahal et al., 2019).

OSA showed from 6 to 19% prevalence where data was collected from a recent systematic review. OSA is followed by recurring episodes of upper airway obstruction during sleep where not only consequential hypoxia occurs but also, oxygen desaturation, sleep fragmentation, changes in the intra-thoracic pressure, and increase in heart rate take place (Kahal et al., 2019).

3.3 Endometrial cancer

Among the many cancers possible, endometrial cancer has been linked with PCOS (Islam et al, 2022). It can be said that a woman who has PCOS, has a 2.7-fold increase in the chance of developing endometrial cancer. The interrelationship between the certain type of cancer and PCOS have been underlined over the years but other co-related factors are very much involved in the development of endometrial cancer if any. Factors like obesity, hypertension, family history, anovulation and diabetes are all involved in the formation of endometrial cancer (Dumesic et al, 2013). The risk of malignancy appears with the persistent exposure of the unopposed hormone estrogen in the absence of sufficient progesterone in the endometrium, which occurs due to anovulation. The first reference was published in 1949 showing association between PCOS and endometrial cancer. Since then, countless studies have confirmed the link between the two diseases (Dumesic et al, 2013) yet, routine screening for the diagnosis of the endometrial cancer is not recommended (Islam et al, 2022). Regular transvaginal ultrasound or endometrial biopsy should be encouraged in women with PCOS to stay updated on malignancy (Dumesic et al, 2013).

3.4 Hyperandrogenemia and Hirsutism

Hyperandrogenism is one of the hallmark clinical features for PCOS which refers to the excessive presence of the male sex-hormones in women body that circulating testosterone in a high number, more active conversion of weaker androgens to stronger androgens, highly sensitive of the skin to DHT and effective of insulin and IGF-1 (Lakshmi C, 2013). This may lead to seborrhea (oily skin), acne, hirsutism, female pattern balding (alopecia) or male pattern balding in females, irregular menstruation, muscle mass and decreased breast size, infertility, Obesity and so on (Ashraf S. 2019). The first impact of androgen excess in PCOS is impaired with folliculogenesis. In this case, increased androgens in the early gonadotropin-independent stage stimulate the formation of primordial follicles and increase the number of small antral follicles (Nisenblat V, 2009). Normally, the gonadotropin-releasing hormone is secreted in a pulsatile manner by the hypothalamus that stimulates the pituitary gland to release gonadotrophins, LH and FSH. Luteinizing hormone acts primarily on the ovarian theca cells carrying LH receptors and induces the production of

androgens. Here, FSH acts on the ovarian granulosa cells and converts the androgens formed in theca cells into estrogens, principally estradiol which is responsible for the development of follicles. However, in women with PCOS, it has been hypothesized that irregular in the neuroendocrine system leads to an imbalance in the hypothalamic–pituitary– ovarian axis, leading to the overproduction of gonadotrophins. An increased hypothalamic GnRH favors the production of the β-subunit of LH over the β-subunit of FSH that in turn favors the production of LH over FSH (Van EJ, 1997), hence resulting in the classical hormonal hallmark of elevated LH/FSH ratio in PCOS. Owing to the increased LH stimulation, numerous follicles in the theca cells of ovaries get arrested mostly in the preantral and antral stages, causing hyperplasia of theca cells and subsequent accumulation of follicular fluid forming cyst-like structures along the periphery of the ovary giving it a string of pearls-like appearance. Furthermore, the hyperandrogenic state in PCOS also seems to be linked with the action of insulin. The increased insulin secretion possibly mimics the tropic action of luteinizing hormone on ovarian theca cells (Wu S, 2014), which further causes an increase in androgens. This is further validated by the fact that the improvement of insulin resistance in PCOS women decreases the level of hyperandrogenism.

Hirsutism is defined as the occurrence of terminal hair in a masculine pattern on the face or body. It is one of the main characteristics of hyperandrogenism in PCOS. The incidence of hirsutism in PCOS women ranges between 60 and 80% (Abid K, 2014). The extent of hirsutism also varies with the ethnicity of the population. The amount and distribution of hair growth is determined by the androgens, particularly testosterone. In PCOS women it is attributed to increased circulatory levels of free testosterone and more active form of testosterone. According to the FG score, hair is scored in nine parts of the body and the score of all nine areas is added up to get the final score used for diagnosis. Women with an FG score of 8 or higher are regarded as hirsute (Lakshmi C, 2013). This is observed in 10-15% of Asian women who has diagnosed with PCOS (Zhao X, 2011).

3.5 Genetical risk factor

PCOS has a strong connection with genital factors even before the birth or after it (Migala J, 2018). In most of the cases, this is a combination of genetic and environmental factors interplay, leading to PCOS. This means that you may have a genetic predisposition for the disorder, but something in the environment triggers it. So, our genetics may play a vital role to have PCOS. There is 40% chances to have PCOS if mother or sister have diagnosed with it (Migala J, 2018). The risk has even increased if the mothers do smoke during pregnancy (ESHRE, 2009). So, PCOS can be taken as a complex genetic trait which appears that there are multiple inherited, environmental or acquired factors that may increase the risk for developing PCOS (Unluturk U, 2006). Furthermore, most of the positive findings obtained with PCOS phenotypes have not been replicated in more than one population (Unluturk U, 2006).

Chapter:4

Conclusion

Polycystic Ovary Syndrome is a threat to women of the present world. As it is a multi-faceted disease, it does not stay limited to only the endocrinal system and the female reproductive system, but spreads throughout the vessel and is home, to few to many co-related risks and associated diseases some of which are discussed in this review article such as- cardiovascular diseases, hirsutism, hyperandrogenemia, endometrial cancer, etc. In this review paper, there are a few aspects of the disease and their prevalence have been highlighted, which are supposedly the most common aspects of PCOS in the Asian women. Obesity, Insulin resistance, mental health, socio-economic features are some of the most common reasons why the prevalence of the disease is so high among the Asian countries. Our goal was to list out the prevalence of PCOS, depending different and common aspects of the disease between the Asian countries as well as write about the most common risk factors which are associated with the disease.

THESIS finalReferences:

1) Islam H, Masud J, Islam N. Y, Haque F. K. M. An update on polycystic ovary syndrome: A review of the current state of knowledge in diagnosis, genetic etiology, and emerging treatment options. Women's health 2022; 18: 1-23.
2) Patel S. Polycystic ovary syndrome (PCOS), an inflammatory, systemic, lifestyle endocrinopathy. Journal of Steroid Biochemistry and Molecular Biology 2010.
3) Azziz R, Woods K.S, Reyna R, Key T.J, Knochenhauer E. S, Yildiz B. O. The prevalence and features of Polycystic Ovary Syndrome in an unselected population. The journal of clinical endocrinology and metabolism 2004; 89(6):2745–2749.
4) Muhas C, Nishad K.M, Ummunnoora K. P, Jushna K., Saheera K. V., Dilsha K. P. Polycystic Ovary Syndrome (PCOS)-an overview. Innovare Academic Sciences 2018; 10(6).

5) Sidra S, Tariq M. H, Farrukh M. J, Mohsin M. Evaluation of clinical manifestations, health risks, and quality of life among women with polycystic ovary syndrome: Clinical aspects and quality of life related to polycystic ovary syndrome. Plos One 2019; 14(10):0223329.
6) Li R, Zhang Q, Yang D. et al. Reproductive epidemiology: Prevalence of polycystic ovary syndrome in women in China: a large community-based study. Human reproduction 2013; 28(9): 2562 –2569.
7) Tan T. T, Lui S.K. Clinical and endocrine profiles of 62 Malaysian women with polycystic ovary syndrome 1989; Vol: 4.
8) Hsu M.I. Clinical characteristics in Taiwanese women with polycystic ovary syndrome. Clin Exp Reprod Med 2015;42(3):86-93.
9) Neubronner S. A, Indran I. R, Chan Y. H, Thu A. W. P, Yong E. L. Effect of body mass index (BMI) on phenotypic features of polycystic ovary syndrome (PCOS) in Singapore women: a prospective cross-sectional study. BMC Women's Health 2021; 21:135.
10) Kubota T. Update in polycystic ovary syndrome: new criteria of diagnosis and treatment in Japan. Reprod Med Biol (2013) 12:71–77.
11) Gill H, Tiwari P, Dabadghao P. Prevalence of polycystic ovary syndrome in young women from North India: A Community-based study: Indian Journal of Endocrinology and Metabolism 2012;16: S389-92.
12) Kumarapeli V, Seneviratne R, Wijeyaratne C. Health-related quality of life and psychological distress in polycystic ovary syndrome: a hidden facet in South Asian women. BJOG 2011; 118:319–328.
13) Shreeyanta K.C, Shah R. K, Singh A, Prasai A, Bhandari B, Aryal S, Khatri A, Thapa M. Prevalence of Polycystic Ovarian Syndrome among Medical Students of a Tertiary Care Hospital. J Nepal Med Assoc 2020 ;58(225):297-300.
14) Wiweko B, Indra I, Susanto C, Natadisastra M, Hestiantoro A. The correlation between serum AMH and HOMA-IR among PCOS phenotypes. BMC Res Notes 2018; 11:114.
15) Quadir F, Barua M, Pathan F, Kuryshi S.A, Chakma P. J, Barua B, Kabir M, Islam M. Frequency of Polycystic Ovary Syndrome among the Students of a Medical College in Dhaka City: International Journal of Diabetes & Metabolic Disorders 2020; 5(3).
16) Bhattacharya K, Sengupta P, Dutta S, Chaudhuri P, Mukhopadhyay L.D, Syamal A.K. Waist-to-height ratio and BMI as predictive markers for insulin resistance in women with PCOS in Kolkata, India: Endocrine (2021) 72:86–95.
17) Cussons A.J, Stuckey B.G.A, Watts G.F. Cardiovascular disease in the polycystic ovary syndrome: new insights and perspectives: Atherosclerosis 185, 2006; 227–239.
18) Punjabi N.M. The Epidemiology of Adult Obstructive Sleep Apnea 2008; 5: 136–143.
19) Ehrmann D.A. Metabolic dysfunction in PCOS: Relationship to obstructive sleep apnea: Steroids 2012; 77: 290-294.
20) Tasali E, Cauter E.V, Ehrmann D.A. Polycystic Ovary Syndrome and Obstructive Sleep Apnea: Sleep Med Clin 2008; 3: 37–46.
21) Kahal H, Tahrani A.A, Kyrou I, Dimitriadis G.K et al. The relationship between obstructive sleep apnea and quality of life in women with polycystic ovary syndrome: a cross-sectional study: Therapeutic Advances in Endocrinology and Metabolism 2020; 11: 1–12.
22) Dumesic D.A, Lobo R.A. Cancer risk and PCOS: Steroids 2013; 78: 782-785.

23) Hart R, Hickey M, Franks S. Definitions, prevalence and symptoms of polycystic ovaries and polycystic ovary syndrome: Best Practice & Research Clinical Obstetrics and Gynecology 2004; 18(5): 671–683.
24) Hasan K, Aalpona F, Selim S "Clinical, metabolic and hormonal profiles of Bangladeshi adolescents with polycystic ovary syndrome" *Touch views in Endocrinology* 2021; *17*: 17925
25) Ganie M, Vasudevan V, Wani I, Baba M et al., "Epidemiology, pathogenesis, genetics & management of polycystic ovary syndrome in India" *Indian J Med Res 150* 2019; *17*, pp 333-344
26) Okoro S, Chen G, Kiefer T "Menstrual hygiene management enables women and girls to reach their full potential" *World Bank Group* 2018
27) Asghari K, Nejadghaderi S, Alizadeh M, Sanaie S, Sullman M, Kolahi A, Avery J, Safiri S, "Burden of polycystic ovary syndrome in the Middle East and North Africa region" *Scientific Reports* 2022; *12*: 7039.
28) Miyoshi A, Nagai S, Takeda M, Kondo T, Nomoto H, Kameda H, Hirai A, Cho K, Kimachi K, Shimizu C, Atsumi T et al., "Ovarian morphology and prevalence of polycystic ovary syndrome in Japanese women with type 1 diabetes mellitus" *Journal of Diabetes Investigation* 2013; *04*,326-329
29) K Muhunthana, K Guruparana, "Clinicopathological features of polycystic ovarian syndrome in adolescence" *Sri Lanka Journal of Obstetrics and Gynecology* 2020; *42*: 91-98
30) Moghadam B Z, Fereidooni B, Saffari M, Montazeri A, "Polycystic ovary syndrome and its impact on Iranian women's quality of life: a population-based study" BMC *Women's Health* 2018; 18:164
31) Jumayev. I, Rashid H, Rustamov O, Zakirova N, Kasuya H, Sakamoto J, "Social correlates of female infertility in Uzbekistan" *Nagoya J. Med. Sci.* 2012; *74*: 273 ~ 283
32) Pandey R M, "Clinical profile of PCOS patients at a tertiary care center in Gandaki Province of Nepal" *Asian Journal of Medical Sciences* 2020; *11*: 5
33) Ko H, Teede H, Moran L, "Analysis of the barriers and enablers to implementing lifestyle management practices for women with PCOS in Singapore" *BMC Res Notes* 2016; *9*:311
34) Kaewnin K, Vallibhakara O, Vallibhakara S, Wattanakrai P, Butsripoom B, Somsook E, Hongsanguansri S, Sophonsritsuk A, "Prevalence of polycystic ovary syndrome in Thai University adolescents", 2018 *Gynecological Endocrinology*, *34*:6, 476-480
35) Dashti S, Abdul L L, Abdul H H, Saini SM, Shah A B A, Amirah N, Ismail M, Jafarzadeh Esfehani A, "Prevalence of Polycystic Ovary Syndrome among Malaysian Female University Staff" *Journal of Midwifery and Reproductive Health* 2019; *7(1):* 1560-1568
36) Miazgowski T, Martopullo I, Wedecka J, Miazgowski B, Brodowska A, "National and regional trends in the prevalence of polycystic ovary syndrome since 1990 within Europe: the modeled estimates from the Global Burden of Disease Study 2016" *Arch Med Sci.* 2021;*17*(2):343–351
37) Hasan M, Sultana S, Sohan M, Parvin S, Rahman A, Hossain J, Rahman SM, Islam R, "Prevalence and associated risk factors for mental health problems among patients with polycystic ovary syndrome in Bangladesh: A nationwide cross-sectional study" *PLOS ONE* 2022; *10*:1371

38) Chaudhari P A, Mazumdar K, Mehta D P, "Anxiety, depression, and quality of Life in women with polycystic ovarian syndrome" *Indian Psychiatric Society - South Zonal Branch* 2018; *40*(3)
39) Malik M, Latif F, Hussain A, "Health Related Quality of Life and Depression among Women with Poly Cystic Ovary Syndrome (PCOS) in Pakistan" *British Journal of Medical and Health Research* 2020; *7*(12): ISSN: 2394-2967
40) Yang R, Li Q, Zhou Z, Qian W, Zhang J, Wu Z, Jin L, Wu X, Zhang C, Zheng B, Tan J, Hao G et al., "Changes in the prevalence of polycystic ovary syndrome in China over the past decade" *www.thelancet.com* 2022; vol. *25*
41) Bharathi R, Swetha S, Neerajaa J, Varsha J, Janani D, Rekha S, Ramya S, Usha B, "An epidemiological survey: Effect of predisposing factors for PCOS in Indian urban and rural population" *Middle East Fertility Society Journal* 2017; *22*: 313-316
42) Wu Q, Gao J, Bai D, Yang Z, Liao Q, "The prevalence of polycystic ovarian syndrome in Chinese women: a meta-analysis" *Ann Palliat Med* 2021;*10*(1):74-87
43) Lakshmi C, "Hyperandrogenism" *Indian J Dermatol Venereol Leprol* 2013; *79*(3):322–37
44) Nisenblat V, Norman RJ, "Androgens and polycystic ovary syndrome" *Curr Opin Endocrinol Diabetes Obes*. 2009; *16*(3):224–231
45) Van EJ, Hop WC, Fauser BC, "Classification of normogonadotropic infertility: polycystic ovaries diagnosed by ultrasound versus endocrine characteristics of polycystic ovary syndrome", *Fertil Steril* 1997; *67*(3):452–458
46) Abbott DH, Barnett DK, Bruns CM, Dumesic DA, "Androgen excess fetal programming of female reproduction: a developmental etiology for polycystic ovary syndrome" *Hum Reprod Update* 2005; *11*(4):357–374
47) Wu S, Divall S, Nwaopara A, Radovick S, Wondisford F, "Obesity induced infertility and hyperandrogenism are corrected by deletion of the insulin receptor in the ovarian theca cell", *Diabetes* 2014; *63*(4):1270–1282
48) Abid K, Shah IH, Sheikh G, "Cutaneous manifestations of polycystic ovary syndrome: a cross sectional clinical study" *Indian Dermatol Online J.* 2014; *8*: 104–110
49) Zhao X, Ni R, Li L, Mo Y, Huang J, Huang M, Azziz R, Yang D, "Defining hirsutism in Chinese women: a cross-sectional study*" Fertil Steril* 2011; *96*(3):792-6
50) Migala J, "What Causes PCOS? 7 Factors That May Affect Your Risk", *everyday health* 2018
51) "Two Studies on Polycystic Ovarian Syndrome Shed Light on Its Causes and Its Effect on Brothers of Women with The Condition" *European Society of Human Reproduction and Embryology* 2009
52) Unluturk U, Harmanci A, Kocaefe C, Yildiz B, "The Genetic Basis of the Polycystic Ovary Syndrome: A Literature Review Including Discussion of PPAR-γ", *PPAR Research* 2006; *2007*
53) Lo J, "PCOS, diabetes risks among Asian women vary by ethnic subgroup*", Endocrinology* 2021
54) Dedwal R, Narwal V, Dand A, Pundir CS, "The prevalence of polycystic ovary syndrome: A brief systematic review", *J Hum Reprod Sci.* 2020*; 13:*261-71