



The Relation Between Intraocular Pressure Level and Polycystic Ovarian Disease

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ABSTRACT

Background: Polycystic ovarian syndrome (PCOS) is the most common endocrinopathy among women of reproductive age. PCOS affects around one in every five females in the reproductive age group, with a frequency of around 17 percent. Recently, female sex hormones have been demonstrated to possess systemic as well as ocular effects. Androgen, estrogen, progesterone receptors are present in the lens, cornea, the ciliary body, iris, the retina, lacrimal glands, meibomian glands, and the conjunctiva.

Objective: The purpose of this study is to measure the intraocular pressure (IOP) and central corneal thickness (CCT) in patients with poly cystic ovarian syndrome and compare it with IOP and CCT in age matched non polycystic females.

Patients and Methods: The study was conducted in the ophthalmology outpatient clinic in Alsadar Medical City in the period between November 2020 and May 2021. One hundred patients with PCOS enrolled from AL Sader hospital fertility center IOP and CCT measured and compare with the same measurement of one hundred age matched females without polycystic ovarian syndrome from outpatient clinic, a total of 200 eyes of polycystic ovarian syndrome females were compared to 200 eyes of non-polycystic age-matched females.

Results: The PCOS mean age group was 29.3 (17-41) years old, while the non -PCOS group mean age was 27.78 (16-41) years old ($P=0.1$). The mean body mass index (BMI) in the PCOS group was 29.56 kg/m² (18.7-45), while the mean BMI in the non -PCOS group was 24.5 kg/m² (17.1 -37.2) with a statistically significant difference between the two groups (p -value 0.0001). The mean IOP level acquired through air puff tonometer in the PCOS group was 19.50±0.2 mmHg, whereas the IOP values mean in the non -PCOS group was 15.80±0.2 mmHg, with a statistically significant difference between the two groups (p -value 0.001). The central corneal thickness CCT measurement in the PCOS group was at 562.9±1.6 μm and in the non -PCOS group was at 525.5±1.8 μm, with a statistically significant difference between the two groups (p -value 0.001).

Conclusion: PCOS affects the eye's physiology and it has structural alterations. Hormonal disruption is a key factor in these changes. The PCOS group has considerably higher IOP and CCT level than the non -PCOS group.

Keywords:

PCOS, women

Introduction

1.1 Background:

Polycystic ovarian syndrome (PCOS) is the most common endocrinopathy among women of reproductive age. PCOS affects around one in every five females in the reproductive age group, with a frequency of around 17 percent. Chronic anovulation is the key physiopathological factor, high levels of testosterone and androstenedione, the active type of androgens generated predominantly by the ovaries ⁽¹⁾. Recently, female sex hormones have been demonstrated to possess systemic as well as ocular effects.

Androgen, estrogen, progesterone receptors are present in the lens, cornea, the ciliary body, iris, the retina, lacrimal glands, meibomian glands, and the conjunctiva ⁽²⁾. An great illustration is the fact that women are more likely to suffer from dry eyes, especially after menopause, which rises during pregnancy and lactation while decreases with hormonal replacement treatment ⁽³⁾. The researchers wanted to see how (CCT) central corneal thickness and (IOP) intraocular pressure differed between PCOS patients and healthy people. It looked at the correlation between the findings of the two groups.

1.2: Polycystic ovarian syndrome:

PCOS is the most prevalent cause of hyperandrogenism in women of reproductive age and oligo-anovulation, both of which have significant psychological, social, and economic repercussions as well as one of the most common endocrine illnesses in those women ⁽⁴⁾. Polycystic ovarian syndrome (PCOS) is prescribed generally based on the proceedings of an expert conference held in April 1990 that was sponsored by the National Institutes of Health (NIH), which recognized the disorder to be including the following 1) hyperandrogenism and/or hyperandrogenemia, 2) oligo-ovulation and finally 3) exclusion of known disorders ⁽⁵⁾.

In May 2003, another expert conference held in Rotterdam established PCOS ESHRE/ASRM (Rotterdam), 2003 To consist of two of the following, in addition to the related disorders should be excluded:

1) Oligo- or anovulation

2) Clinical and/or biochemical signs of hyperandrogenism

3) Polycystic ovaries ⁽⁶⁾

1.2.1: Exclusion of Related Disorders

It's critical to rule out other illnesses that have a similar clinical presentation to PCOS, such as congenital adrenal hyperplasia, Cushing's syndrome, and androgen-secreting tumors. A basal 17-hydroxyprogesterone level at morning, with a ranging cutoff values between 2 and 3 ng/mL, can be used to rule out 21-hydroxylase deficient non-classical adrenal hyperplasia (NCAH) ⁽⁷⁾.

1.2.2: Clinical Hyperandrogenism:

Hirsutism is the most common symptom of androgen excess ⁽⁶⁾. The following points, however, should be highlighted:

- In large populations, there is still a paucity of normative data.
- Hirsutism is diagnosed using a subjective approach, with only a small percentage of doctors using standardized grading methodologies in practice.
- Hirsutism is frequently treated before the patient's endocrinological status is assessed.
- Hyperandrogenic women of east Asian ancestry may have a lower prevalence of hirsutism.

1.2.3: Biochemical Hyperandrogenism:

The majority of PCOS patients have hyperandrogenemia, and new research suggests that circulating androgen levels may be a genetic marker for androgen excess. ⁽⁸⁾ The most sensitive way of detecting hyperandrogenism was supposed to be measuring free T or the free T (free androgen) index. ⁽⁹⁾ ⁽¹⁰⁾. Equilibrium dialysis, computation of free T ⁽⁹⁾ from sex hormone-binding globulin and total T values, and ammonium sulfate precipitation were used to produce free T. ⁽¹¹⁾.

1.2.4: Polycystic Ovaries (PCO)

PCO should now be included as one of the potential PCOS criteria. PCO is defined as presence of 12 or more follicles in each ovary measuring 2–9 mm in diameter, and/or increased ovarian volume (10 mL) ⁽⁶⁾. Because the oral contraceptive pill affects both normal

and PCO women's ovarian morphology, this criterion does not apply to them. Only one ovary that fits these criteria is required for diagnosis (6).

1.2.5: Luteinizing Hormone:

In women with PCOS, both the overall level of circulating LH and its relationship to FSH levels are greatly raised (12). Due to the increased amplitude and frequency of LH pulses, elevated LH concentrations (above the 95th percentile

of normal) can be seen in roughly 60% of women with PCOS. (13)

1.3: Intraocular pressure (IOP):

In a healthy eye, aqueous humor flow against resistance produces an intraocular pressure (IOP) of about 15 mmHg, which is required for the globe's appropriate shape and optical qualities (14).

The angle and the normal pathways of aqueous humor flow are illustrated schematically in the Figures 1.

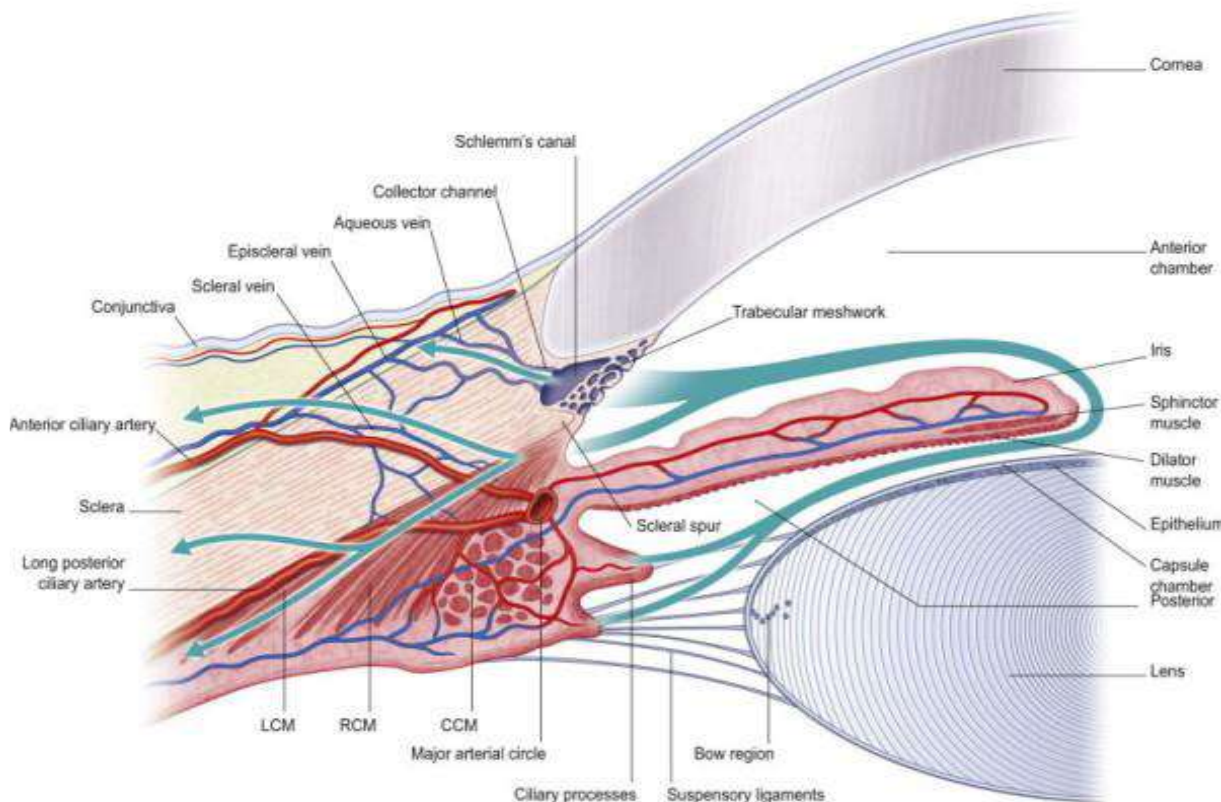


Figure (1) Schematic representation of the primate anterior ocular segment.

There are two primary routes for the drainage of aqueous humour: one that is pressure-dependent, and another that is not.

1 Outflow of the trabeculae (pressure-dependent outflow)

Most of the aqueous humour leaves the anterior chamber of the eye through the venous system, which consists of the trabecular meshwork, the juxtacanalicular connective tissue, Schlemm's canal, the collecting channels and aqueous veins, and the episcleral venous system (19).

Outflow from the uvea and sclera (pressure-independent outflow)

In a healthy eye, uveoscleral outflow occurs instead of trabecular outflow. Uveoscleral outflow is also known as pressure-independent outflow. One of the mechanisms is the passage of aqueous humour from the anterior chamber via the ciliary muscle and on to the supraciliary and suprachoroidal areas. Typically, it makes up between 5% to 15% of total aqueous outflow (21), but recent studies show it may make up a larger proportion of total outflow in the eyes of healthy young adults.

Flow Dynamics During Inflows

At the ciliary body arterioles, blood is delivered at a rather high hydrostatic pressure of 30 mm Hg, and is transformed into aqueous humour

by mechanisms that are not well described but are likely to include comp ex. The produced aqueous humour moves from the anterior chamber to the posterior chamber by convective bulk flow via the pupil, where the pressure is 16 mm Hg lower. (22)

1.3.4, The Dynamics of the Outflow:

Water diffuses through the trabecular meshwork and gathers in the Schlemm canal, where the lower pressure of the episcleral venous system (9 mm Hg) compared to the anterior chamber (16 mm Hg) aids the return of aqueous humour to the systemic circulation. The uveoscleral route is important for aqueous outflow in humans (22).

Intraocular Pressure and Its Affecting Factors

Increased intraocular pressure (IOP) caused by: 1. the Valsalva manoeuvre; 2. playing musical instruments; 3. a tight collar; 4. stooping; 5. raised central venous pressure; and 6. intubation. Blepharospasm, squeezing, and sobbing all put pressure on the eye (raise intraocular pressure), particularly in young children. Thirdly, intense physical activity lowers intraocular pressure.

4. a higher core body temperature is associated with increased aqueous humour production. Ketamine and other depolarizing muscle relaxants like succinylcholine are among the most often used anaesthetics. Hormone Effects, Number Six: (lower during pregnancy and higher with hypothyroidism) Seven substances that lower eye pressure but aren't used in treatment (Alcohol, heroin, and marijuana) Eighth, various medications that boost IOP (LSD, Corticosteroids: cause an open-angle glaucoma, anticholinergics: precipitate angle closure in some patients) IOP is affected by the blood's pH level, and systemic acidosis causes a decrease in IOP.

Ten. Outside variables that affect IOP

Among the potential causes of this increase is: • Age, IOP is somewhat greater after the age of 40. Until age 40, men and women have the same intraocular pressure (IOP). The average intraocular pressure (IOP) of women increased more than that of men as they aged. Incorrect refractive power The intraocular pressure (IOP) of myopes is often greater than that of emmetropics. (15)(21)

Measurement of intraocular pressure

Both new cases of glaucoma and the progression of the disease are linked to elevated intraocular pressure. (23)

IOP MEASUREMENT

IOP Evaluation Using Transpalpebral Methods Use of the thumb and index finger to feel the skin. TGDc-01, Version 2 Eye pressure measurement using the Proview

To begin with, let's talk about manometry

A needle is inserted into the anterior chamber or vitreous and then attached to a mercury or water manometer, providing the sole direct measurement of intraocular pressure (18).

Tonometry.

Tonometry based on the a-index:

It's predicated on the observation that a plunger is more effective in indenting a soft eye than a hard eye (18). An example of a tonometer using the Schitzz principle

It was originally the most popular tonometer, but now it is utilised mostly in operating rooms and other non-ophthalmologic or non-optometric situations where its accuracy, low cost, portability, and autoclavability are still valued. A weight is used to force a plunger, which may move freely, against the cornea, indenting it.

Tonometry through applanation of the eardrum. A dry thin-walled sphere's internal pressure (P) is proportional to the force (F) required to flatten its surface (i.e., $P = F/A$) using the Imbert-Fick principle (28). a Tonometer that Uses a Constant Force During Applanation

1-Maklakoff. 2-Posner. Tones in a Fixed Applanation Area

1.Goldmann acoustic tonometer (GAT):

The most common technique, based on the Imbert-Fick principle, calculates the amount of pressure required to flatten a circular section of cornea with a diameter of 3.06 mm. This diameter was chosen to strike a good balance between the resistance of the corneal material to flattening and the capillary attraction of the tear film meniscus to the tonometer head. In addition, the IOP may be calculated by multiplying the flattening force (in grams-force) by 10. (in mm Hg). Using a split-image

prism, the examiner can quickly and reliably identify the distorted region. Fluorescein dye is injected into the tear film with a topical anaesthetic to create an outline of the region of flattening. Semicircles of fluorescein, or mires,

are seen via a split-image prism; these mires travel with the ocular pulse and stop when their inner edges intersect halfway through their movement.

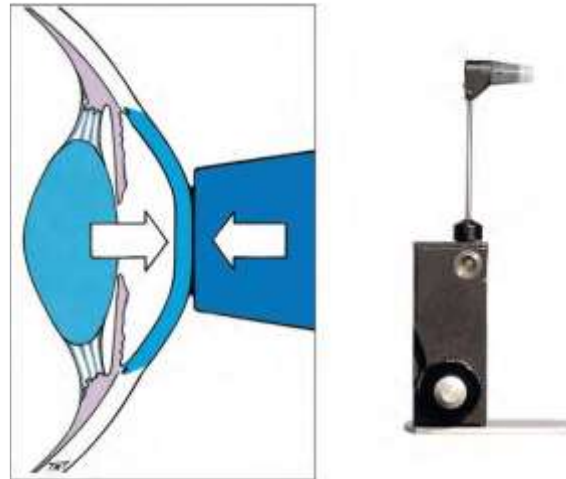


Figure (2) goldmann applanation tonometer

Air Puff Tonometer:

It's a type of non-contact tonometer that uses a puff of air to flatten the cornea, removing the need for the instrument to touch the eye⁽³²⁾. It is an applanation method that flattens the cornea with a standardized puff of air and avoids the use of topical anesthetics or the risk of corneal abrasion⁽²⁸⁾.

A central air plenum is flanked on either side by a light emitter and detector in this system. The convex corneal surface scatters light emitted when the cornea is in its resting state. The corneal surface behaves like a plane mirror reflecting light to the detector as the pressure of the air pulse directed to the cornea increases, deforming the cornea⁽²⁸⁾.

The central cornea's applanation is measured by collecting light reflected from it, a parallel

beam of light, at an angle of 30 degrees, is aimed onto the central cornea, and the reflected light is measured by a photodetector at a 30-degree angle of reflection. When the cornea is flat and acting as a plane mirror rather than a curved mirror, at this angle, the reflected beam of light will be the strongest. The amount of air pressure needed to flatten the cornea will be measured by the device which in turn exhibit the intraocular pressure that is equal to that force.

The air tonometer should be held at a specific distance from the cornea, which is made easier by the instrument's optical alignment system⁽³²⁾. It can be utilized without anesthesia and reduces the risk of infectious pathogens being transmitted from one eye to the other via the tonometer tip⁽³²⁾.



Figure (3) air puff tonometer

3. Perkin appplanation tonometer:

It is a portable version of the GAT, also requiring topical instillation of fluorescein. It has the advantage of being easily transported from site to site for screening examinations ⁽³³⁾



Figure (4) The Perkins appplanation handheld tonometer

4. Reichert ocular response analyzer.

5. Dynamic observing tonometer.

6. Tonopen :

Portable light-weighted contact electronic appplanation tonometer.



Figure (5) tonopen

7. pneumatic tonometer



Figure (6) pneumatic tonometer

8

. pulse air tonometer.

Tonometry and central corneal thickness

Measurements obtained with the most common types of tonometers are affected by central corneal thickness (CCT). Measurement with the Goldmann tonometer is most accurate when the CCT is 520 μm . Thicker corneas resist the deformation inherent in most methods of tonometry, resulting in an overestimation of IOP, while at the same time, thinner corneas may give an artificially low estimation. there may be an underestimation of IOP readings measured after photorefractive keratectomy and laser in situ keratomileusis because of differences in corneal thickness caused by these and other refractive procedures ⁽¹⁶⁾.

AIM:

1.To compare IOP levels and CCT in patients with PCOS with age-matched non polycystic females at childbearing age as IOP is the most prevalent factor associated with developing glaucoma.

2. Define any effect of abnormal sex hormones on IOP and /or CCT.

Subject and methods:

3.1: study design:

The study is a retrospective cohort comparative study. It was undertaken after approval had been acquired from the Ethical

committee in al Najaf health district. All participants gave their verbal agreement. The study's methods were done in accordance with the institutional research committee's ethical requirements and was conducted in Alsadar medical city in the ophthalmology outpatient clinic.

3.2: Patient profile:

Women who visited the fertility clinics and the ophthalmology outpatient clinics in Alsadar medical city between November 2020 and May 2021 were enrolled in the study. A total of 200 eyes of polycystic ovarian syndrome females and compared with 200 eyes of non-polycystic age-matched females in the reproductive age group. The mean age was 29.3 years (17-41) in the PCOS group, and 27.78 years (16-41) among the non-PCOS group (*p-value 0.1*)

Take into consideration the 2003 Rotterdam criteria for the diagnosis of PCOS, a comprehensive gynecological screening and examination done by an obstetrician-gynecologist specialist to diagnose PCOS. ⁽⁶⁾

Inclusion criteria:

- Poly cystic ovarian syndrome females: Those with at least two of the following criteria were included in this study:
 1. Oligomenorrhea-amenorrhea.
 2. The clinical and/or biochemical findings of hyperandrogenism

3. Polycystic ovaries assessed on the US (existence of 12 or more follicles 2-9 mm in diameter in ovaries) were enrolled into the study.
- Non polycystic female: with the normal or regular menstrual cycle were included in the non -PCOS group and they were incompatible with the 2003 Rotterdam PCOS diagnostic criteria.

Exclusion criteria:

1. Metabolic irregularity including diabetes mellitus and any endocrinopathy (thyroid disease, Hyperprolactinemia, Cushing's syndrome, congenital adrenal hyperplasia, glucocorticoid, hormonal treatment)
2. Addiction to smoking and alcohol.
3. Pregnancy.
4. Ophthalmologic disorders, malignancy, history of any ocular trauma and or surgery.
5. Family history of primary open glaucoma and high refractive error.
6. Any medical illness such as hypertension, ischemic heart disease.
7. Systemic medication having IOP lowering effect (beta blocker, antihypertensive) and taking anti psychiatric medication.
8. Any neurological disorder

3.3 Examination and equipment:

3.3.1 Examination:

1. Demographic history including age, marital status, occupation and address obtained for all participants.
2. All participants' weight and height are recorded.
3. A questionnaire introduced for the hormonal status, past ocular and medical history.
4. All visual symptoms recorded including blurring of vision, floaters, halos and eye pain.
5. All Participants were examined between 10 am and 12 pm.
6. All Participants' VA (unaided and aided) were recorded, VA tested by NIDEK electronic chart.

7. Participants' refractive status measured by auto refractometer.
8. IOP was measured via air-puff tonometry.
9. Bio microscopic slit lamp detailed examination of the anterior segment (cornea, lens and anterior chamber).
10. Angle examined and classified using three mirror gonioscopes
11. Fundus examination was done after dilatation with Tropicamide 1% with 78 D Non-contact lens.
12. CCT measurement by corneal tomography.
13. For patients from fertility clinics, their data was collected from their files in the archive unit after obtaining approval.

All the PCOS females were sent for an abdominal ultrasound on day 15 of the menstrual cycle to the radiology department and examined by the same doctor and sent for LH, FSH, testosterone, estradiol E2, and TSH level.

3.3.2 Equipment:

1. Electronic illiterate E chart for visual acuity NIDEK SC-1600.
2. TOPCON slit lamp, fundus examination done after dilatation with Tropicamide 1% with 78D non-contact lens.
3. Auto refractometer HRK 7000A.
4. TOPCON computerized tonometer CT-80
5. Oculus pentacam HR type 70900.

3.4 Statistical analysis:

Using SPSS (the statistical package for social sciences) version 25, IBM,US; for managing and analyzing the data of the 200 patients. Cross tabulation and Mann Whitney test used to assess the significance of relationship between IOP level in PCOS and age matched non polycystic females. Level of significance, P. value, set at ≤ 0.05 , the value at which the difference or correlation is significant. Finally, results presented in tables and figures with an explanatory paragraph for each using the Microsoft Word and Excel Software, version 2016.

Result

The average age of PCOS sufferers was 29.3 (range: 17-41) years old, whereas those without the disorder were 27.78 (range: 16-41) (P=0.1). There is a statistically significant difference between the mean body mass index (BMI) of 29.56 kg/m² (18.7 - 45) in PCOS and the mean BMI of 24.5 kg/m² (17.1 - 37.2) in the non-PCOS group (p-value 0.0001). The average IOP measured with an air puff tonometer was 19.50.2 mmHg in the PCOS group and 15.80.2 mmHg in the non-PCOS group; this was a statistically significant difference (p0.001). In the PCOS group, the mean CCT was 562.91.6 m, whereas in the non-PCOS group it was 525.51.8 m; this was a statistically significant difference (p0.001). The mean IOP after CCT correction was 18.50.2 mmHg in the PCOS group and 16.70.2 mmHg in the non-PCOS group, with a statistically significant difference between the two groups (p 0.001). There was no statistically significant

difference between the PCOS and non-PCOS groups in terms of best-corrected visual acuity (1.00 in PCOS and 0.99 in non-PCOS) (p-value 0.3). Both groups' right eyes were compared. The PCOS group had a BCVA of 1.0, whereas the control group had a BCVA of 0.99. (p-value 0.3). There was a statistically significant difference (p0.001) between the two groups, with the PCOS group having an IOP of 19.50.3 mmHg and the other group having an IOP of 15.650.3 mmHg. The PCOS group had a significantly higher mean CCT (562.03 2.1 m) than the non-PCOS group (525.4 2.5 m; p 0.001). Both groups' left eyes are compared. In the PCOS group, the BCVA was 1.0, while it was 0.99.1 in the other group. The PCOS group had an average IOP of 19.40.3 mmHg, whereas the non-PCOS group had an average IOP of 15.90.3 mmHg (p0.001). Mean CCT was 563.72.4 m in PCOS against 525.52.5 m in the non-PCOS group, a statistically significant difference (p0.001).

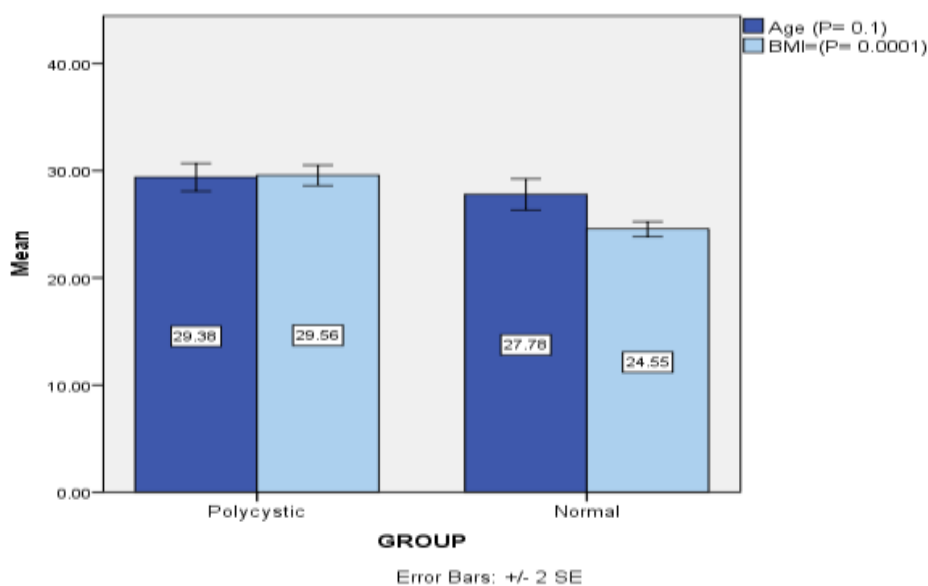


Figure (7) comparison of body mass index in PCOS group and non -PCOS group

Table (1) age distribution in the PCOS and non -PCOS group, BMI (body mass index) in the two groups classified to normal, over, under weights and obese (p value 0.0001)

		GROUP		Total	P
		Polycystic	non -PCOS		
Age group (years)	16-19	11 (11%)	17 (17%)	28 (14%)	0.04
	20-29	36 (36%)	45 (45%)	81 (40.5%)	
	30-39	48 (48%)	29 (29%)	77 (38.5%)	
	40-49	5 (5%)	9 (9%)	14 (7%)	

BMI (kg/m ²)	Underweight	0 (0%)	4 (4%)	4 (2%)	0.0001
	Normal	14 (14%)	52 (52%)	66 (33%)	
	Overweight	38 (38%)	36 (36%)	74 (37%)	
	Obese	48 (48%)	8 (8%)	56 (28%)	

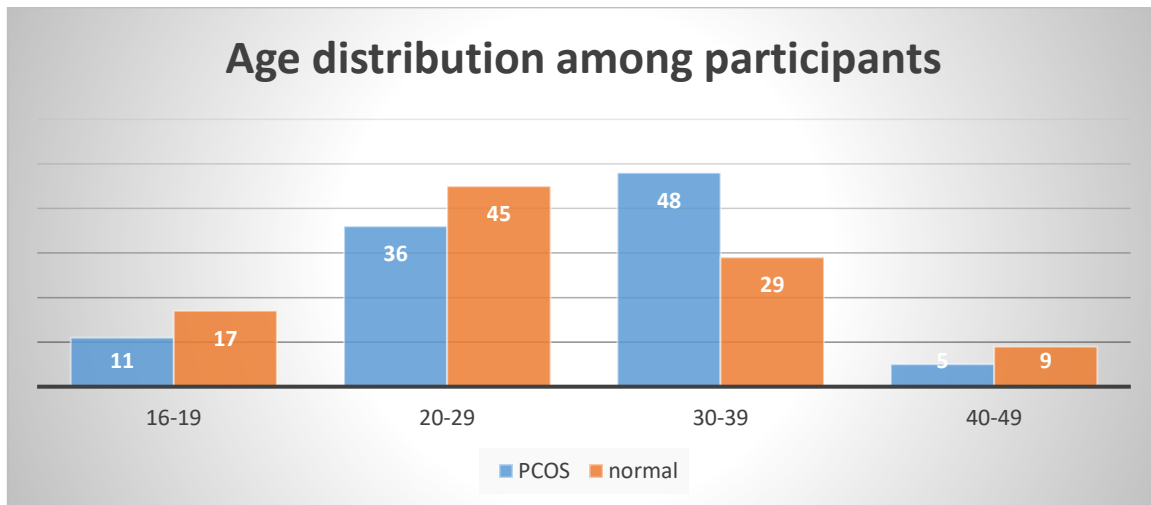


Figure (8) age distribution among participants in PCOS with blue line and comparison with orange one (P=0.1)

Table (2) Values of VA, BCVA, IOP, CCT, and IOP-CCT corrected of polycystic and non-polycystic groups

	Polycystic(N=200) Mean±SE	non -PCOS (N=200) Mean±SE	P value *
VA	0.4±0.03	0.8±0.02	0.01
BCVA	1±0	0.99±0.003	0.3
IOP	19.5±0.2	15.8±0.2	0.001
CCT	562.9±1.6	525.5±1.8	0.001
IOP-CCTcorrected	18.5±0.2	16.7±0.2	0.001

*Mann-Whitney U test

VA (visual acuity in decimel equivalent in minutes highest value 2.00 and the lowest value 0.001) , BCVA (best corrected visual acuity in decimel equivalent) , IOP (intra

ocular pressure in mmhg) . CCT (central corneal thickness in micrometer) , IOP-CCT (intraocular pressure in mmhg after correction with central corneal thickness) .

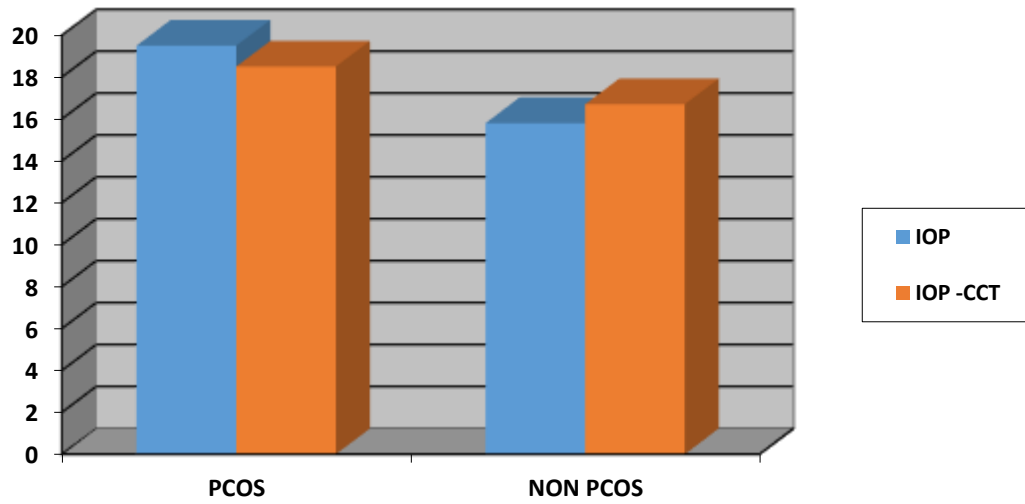


Figure (9) Comparison of the IOP level between PCOS and non -PCOS before and after correction with CCT

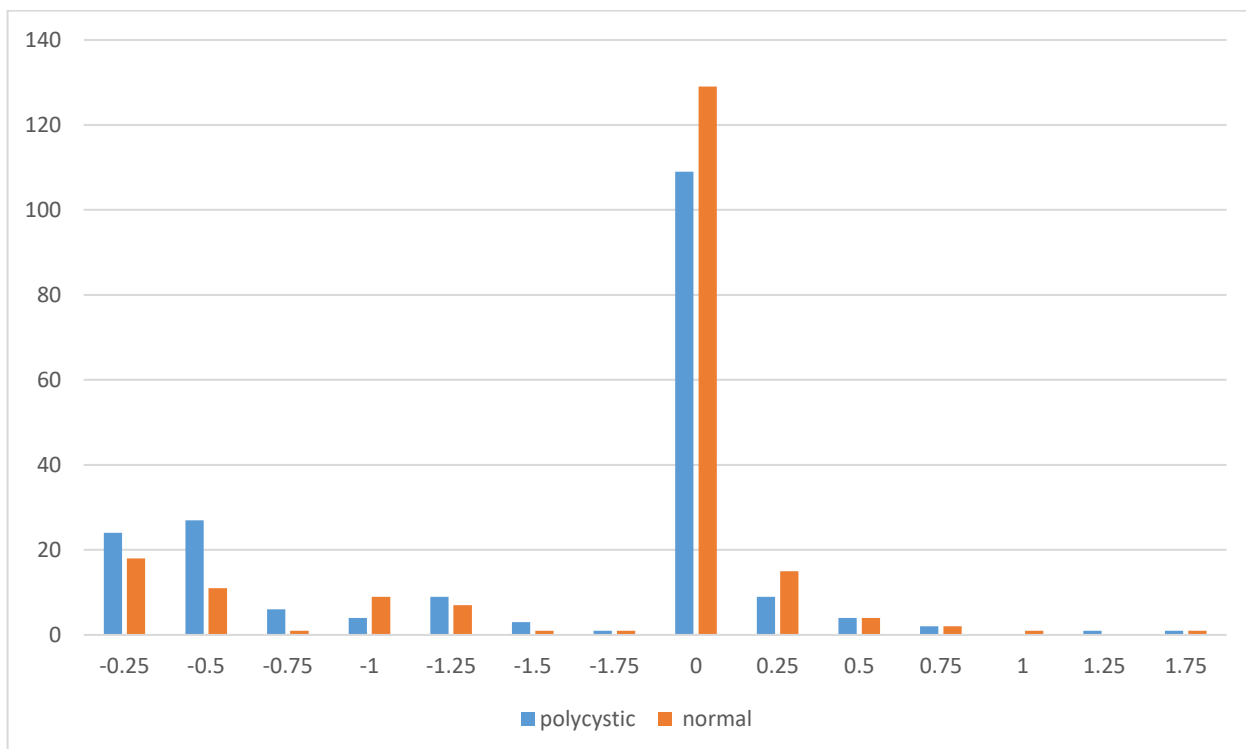


Figure (10) refraction distribution in PCOS and non -PCOS group between -0.25 and 1.75 with final p value 0.1, the blue one is PCOS and the orange one is non -PCOS

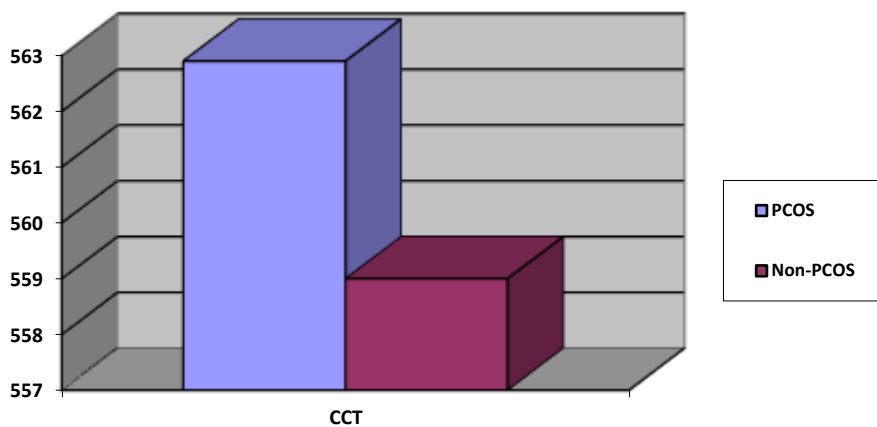


Figure (11) CCT level between PCOS and Non- PCOS measured in μm

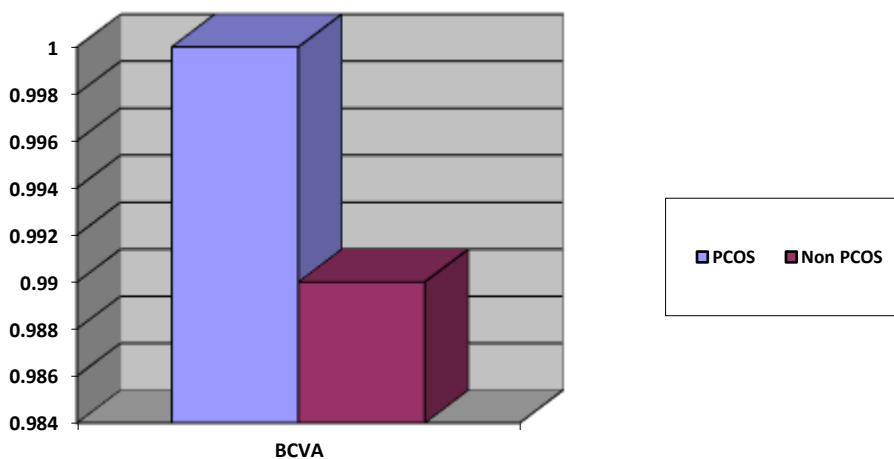


Figure (12) best corrected visual acuity between PCOS group and Non- PCOS group measure in decimel equivalent

Table (3) Values of VA, BCVA, IOP, CCT, and IOP-CCT corrected of polycystic and non-polycystic groups of the right eyes

	Polycystic(N=100) Mean±SE	non -PCOS (N=100) Mean±SE	P*
RBCVA	1±0	0.99±0.01	0.3
RIOP	19.5±0.3	15.65±0.3	0.001
RVA	.03±.01	0.8±0.03	0.001
RCCT	562.03±2.1	525.43±2.5	0.001
RIOP-CCT	18.5±0.3	16.6±0.2	0.001

*Mann-Whitney U test VA (visual acuity in decimel equivalent in minutes highest value 2.00 and the lowest value 0.001) , BCVA (best corrected visual acuity in decimel equivalent) ,

IOP (intra ocular pressure in mmhg) . CCT (central corneal thickness in micrometer) , IOP-CCT (intraocular pressure in mmhg after correction with central corneal thickness) .

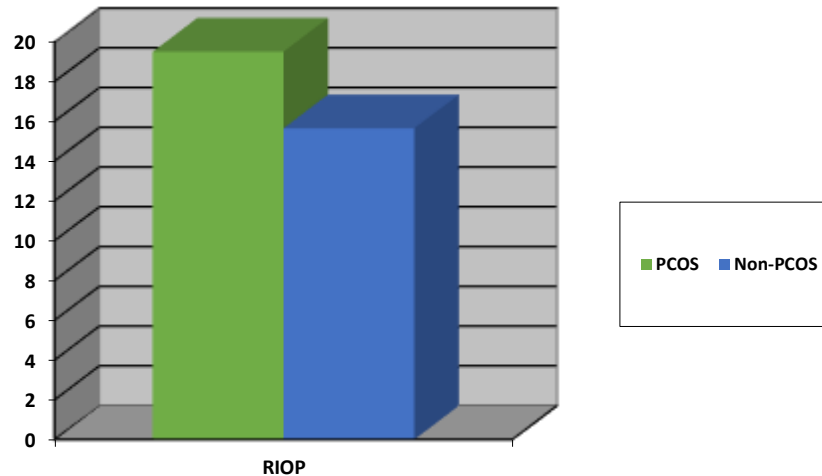


Figure (13) comparison between right eyes IOP between PCOS and Non-PCOS groups

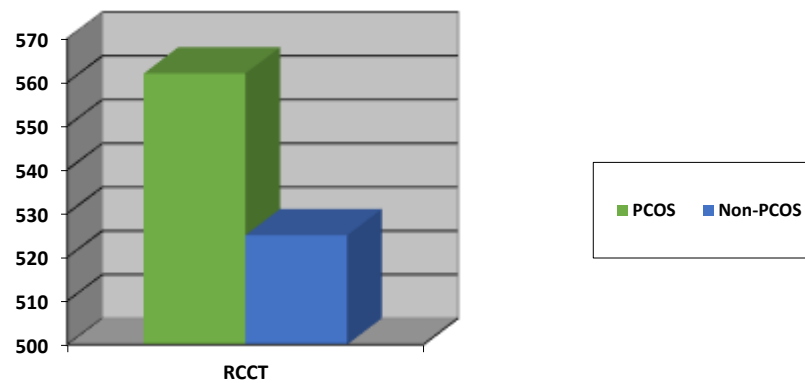


Figure (14) right eyes CCT level between PCOS and Non- PCOS measured in µm

Table (3) Values of VA, BCVA, IOP, CCT, and IOP-CCT corrected of polycystic and non-polycystic groups of the left eyes

	GROUP		P*
	Polycystic(N=100) Mean±SE	non -PCOS (N=100) Mean±SE	
LBCVA	1±0	0.99±0.01	0.3
LIOP	19.4±0.3	15.9±0.3	0.001
LVA	0.8±0.02	0.8±0.03	0.8
LCCT	563.7±2.4	525.5±2.5	0.001
LIOP-CCT	18.4±0.2	16.8±0.2	0.001

*Mann-Whitney U test

VA (visual acuity in decimel equivalent in minutes highest value 2.00 and the lowest value 0.001) , BCVA (best corrected visual acuity in decimel equivalent) , IOP (intra

ocular pressure in mmhg) . CCT (central corneal thickness in micrometer) , IOP-CCT (intraocular pressure in mmhg after correction with central corneal thickness)

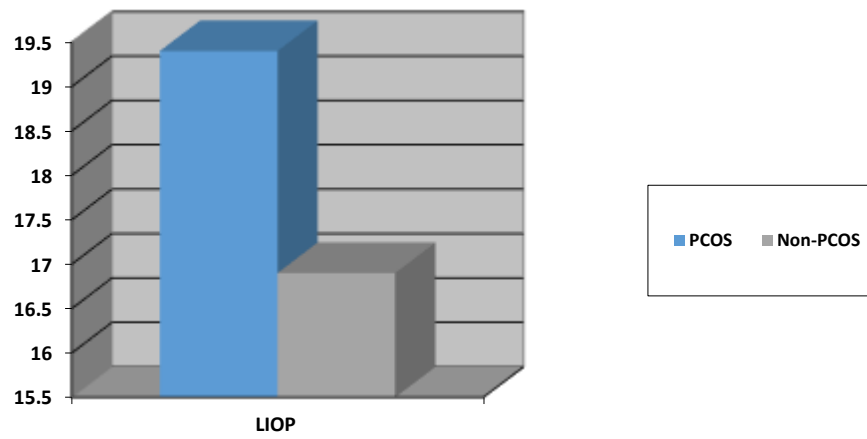


Figure (15) comparison of left eyes IOP level between PCOS and Non-PCOS groups

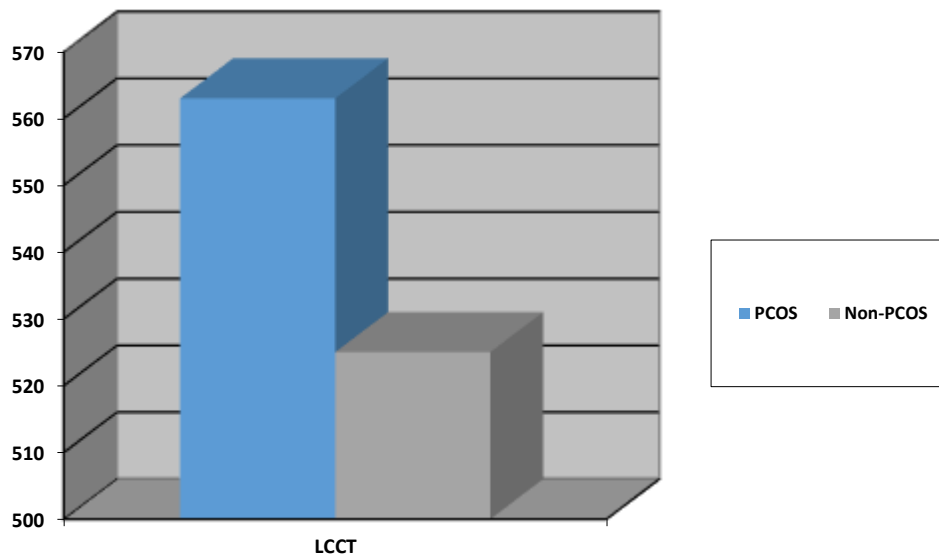


Figure (16) comparison of right eyes CCT level between PCOS and Non-PCOS measured in µm

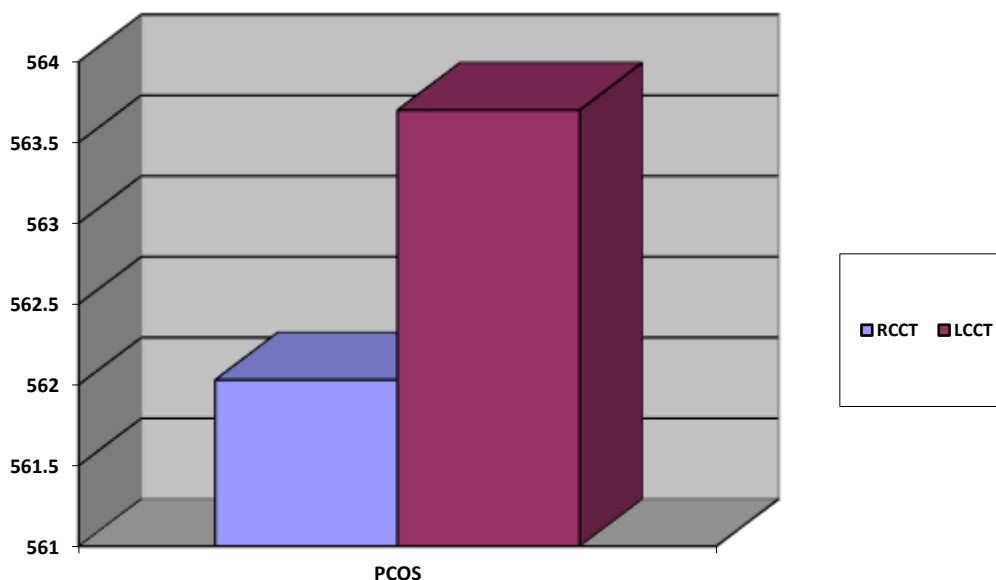


Figure (17) inter eye difference of CCT in PCOS groups

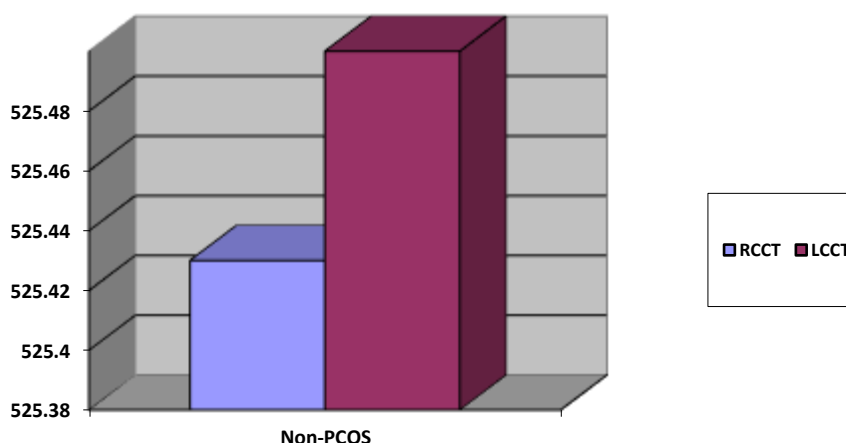


Figure (18) inter eye difference of CCT in Non-PCOS groups

Discussion:

Premenstrual syndrome (PCOS), also known as ovarian hyperandrogenemia, is the most common endocrinopathy in women of reproductive age. Target organ changes arise (5) because progesterone is unable to prevent the effects of hyperestrogenism. Estrogen-induced proteins (such as cathepsin D, alpha-2 macroglobulin, and aromatase cytochrome P45) are characterised by Ogueta et al.(37) as being involved in critical cellular processes such as differentiation, proliferation, and maturation.

Some examples of ocular tissues that contain these proteins are the ciliary body and the retinal pigment epithelium. (2) (37)(52) . Increased sex steroid levels in PCOS affect ocular architecture and function in the same way they impact the endometrium and cardiovascular tissues. (53) Steroid hormones are crucial for cellular activities including proliferation, differentiation, and growth. (2)(36)(37) Interest amongst researchers has grown in the potential role of androgen in the physiology or pathophysiology of ocular tissues, and evidence to support this role has

gathered. Damage to the optic disc, nerve fibre layer, and visual field are hallmarks of glaucoma, a progressive optic neuropathy. Worldwide, it is the leading cause of permanent blindness. A high intraocular pressure (IOP) is the most important risk factor for the illness, while some individuals do not have it. Epidemiological factors like as age, sex, blood pressure, obesity, myopia, and family history have been associated with high IOP in the past. It remains an area of research focus to determine how hormone levels affect intraocular pressure. Results from the many human studies examining the effects of progesterone and oestrogen on intraocular pressure (IOP) have been contradictory. Some studies have found no link between IOP and female sex hormones, while others have found a correlation between increased testosterone levels and elevated IOPs in women receiving hormone replacement therapy.

Estradiol was proven to be a powerful vasodilator by Magness et al., whereas progesterone was found to have the opposite effect by Sarrel. A substantial difference in IOP was found in this research when comparing PCOS and age-matched non polycystic females when looking at IOP and CCT. A statistically significant increase ($P = 0.001$) was seen between the PCOS and non-PCOS groups in the mean IOP measured using an air puff tonometer. The PCOS group had a significantly higher mean CCT than the non-PCOS group ($p < 0.001$). High testosterone levels, long-term progesterone medication for monthly irregularities, and a higher body mass index (BMI) in PCOS patients compared to the age-matched normal population may all explain these findings. Statistically, this research shows that PCOS patients had a higher body mass index than reference females of the same age (p value 0.0001). Body mass index (BMI) is a significant predictor of elevated intraocular pressure (IOP). This research did not find any statistically significant differences in best corrected visual acuity or refractive status ($p = 0.3$ and 0.1 , respectively). After controlling for CCT, there was still a statistically significant difference in IOP levels across groups ($p < 0.001$). With the unexpected discovery that

four patients had IOPs higher than 25 mmHg during screening, we advised additional evaluation for possible glaucoma. We didn't exclude them out of the research since they didn't meet our exclusion criteria.

However, other studies have shown a considerable sexual predisposition in the development of secondary glaucoma (46), which contradicts the Blue Mountains Eye Study's finding of a marginally greater frequency of women among patients with open-angle glaucoma. Estradiol has a neuroprotective effect, which seems to be mediated at least in part via oestrogen receptors in the retinal ganglion cells in glaucoma animal models with a $p < 0.05$, as observed by Sait et al. According to research by Jong Soo Lee et al., there is a positive association between intraocular pressure and testosterone. Significant ($p < 0.05$) statistical evidence supported a link between intraocular pressure and testosterone.

Demir et al. compared 50 right eyes solely of PCOS and age-matched normal females and found that although IOP and CCT were similar in both groups, the PCOS group had substantially greater mean central corneal thickness values ($p = 0.001$). Positive linear connection was established between body mass index and intraocular pressure in a study by Cohen E et al. Both men and women have a steady and noticeable rise in IOP as their body mass index (BMI) rises; it is estimated that a rise in BMI by 10 kg/m² is related with a 0.7mm Hg rise in IOP. Both men and women showed a positive linear connection between BMI and IOP ($r = 0.166$, $P < 0.0001$ in males and $r = 0.202$, $P < 0.0001$ in women). According to Ayse Gul et al., those with PCOS had greater CCT than the general population. Higher levels of insulin-like growth factor-1 (IGF-1) seem to be the primary reasons of increased corneal thickness, suggesting that the eye is a target organ for PCOS. Compared to the control group, those with had considerably thicker central corneas on average (P value 0.001). Finally, PCOS patients have higher IOP and CCT than age-matched females; this needs to be further revised because IOP is the most known modifying factor for the development of POAG

and most cases are asymptomatic until advanced stages, regardless of whether the cause is a high body mass index (BMI), high testosterone level, or hormonal irregularities.

Constraints of the Study:

This research has several caveats: First, the COVID 19 epidemic meant that the GAT could no longer be used as the reference standard for intraocular pressure (IOP) measurement, therefore we switched to using the non-contact air puff tonometer instead. The epidemic has also had a dramatic impact on the number of people who visit our outpatient clinics. Two weeks of trouble with the air puff caused the research to be delayed substantially. The large range of testosterone levels prevented any meaningful correlation with intraocular pressure. Reasonable length of time between checks (4). For reasons including patient volume and hormonal shifts, extended follow-up is necessary.

Conclusion

Whether it's from a high testosterone level, a large body mass index, or the need for long-term hormonal treatment for PCOS, these factors all contribute to elevated intraocular pressure in people with PCOS. CCT was also greater in women with PCOS than in those without PCOS of the same age.

Recommendations

1. More research is needed, ideally with a bigger sample size and a longer follow-up period. All women with polycystic ovary syndrome should have an annual eye exam.

Third, the influence of PCOS on CCT should be reviewed with the patient and recommendations should be made to the refractive surgeon accordingly. Patients with PCOS should have their hormone levels under control before undergoing refractive surgery.

4. All patients with PCOS, particularly those on hormone medication, should have routine follow-up visits with an ophthalmologist. Since majority of the participants in this research did not know their IOP level, it is recommended that all primary health care clinics have access

to a tonometer for initial screening. Fertility and family planning centres should advise patients to get their IOP checked routinely.

References:

1. Adıyeke SK, Karaca İ, Yıldırım S, Adıyeke M, Uyar İ, Türe G. Anterior segment findings in women with polycystic ovary syndrome. *Turk Oftalmoloji Derg.* 2017;47(1):24-7.
2. Gupta PD, Johar K, Nagpal K, Vasavada AR. Sex hormone receptors in the human eye. *Surv Ophthalmol.* 2005;50(3):274-84.
3. Sullivan DA. Tearful relationships? Sex, hormones, the lacrimal gland, and aqueous-deficient dry eye. *Ocul Surf [Internet].* 2004;2(2):92-123. Available from: [http://dx.doi.org/10.1016/S1542-0124\(12\)70147-7](http://dx.doi.org/10.1016/S1542-0124(12)70147-7)
4. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. Position statement: Criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: An androgen excess society guideline. *J Clin Endocrinol Metab.* 2006;91(11):4237-45.
5. Azziz R. Diagnosis of the polycystic ovarian syndrome: The Rotterdam criteria are premature. *J Clin Endocrinol Metab.* 2006;91(3):781-5.
6. Azziz R, Tarlatzis R, Dunaif A, Ibanez L, Pugeat M, Taylor A, et al. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Revis 2003 Consens diagnostic criteria long-term Heal risks Relat to polycystic ovary Syndr.* 2004;81(1):19-25.
7. Dewailly D, Fox L, Ph.D., Boots LR, Ph D. Screening for 21-hydroxylase – deficient nonclassic adrenal hyperplasia among hyperandrogenic women : a prospective study. 1999;72(5):0-2.
8. Unaif AND. Evidence for a genetic basis for hyperandrogenemia in polycystic. 1998;95(December):14956-60.
9. Vermeulen A, Verdonck L, Kaufman JM. A

- Critical Evaluation of Simple Methods for the Estimation of Free Testosterone in Serum. 2015;84(10):3666-72.
10. Cibula D, Hill M, Starka L. The best correlation of the new index of hyperandrogenism with the grade of increased body hair. 2000;405-8.
 11. Tremblay RR, Dube JY. Plasma concentrations of free and non-TeBG bound testosterone in women on oral contraceptives. *Contraception*. 1;10(6):599-605..
 12. Fauser BCJM, Pache TD, Lamberts SWJ, Hop WIMCJ, Jong FHDE, Dahl KD. Serum Bioactive and Immunoreactive Luteinizing Women with Cycle Abnormalities, with or without. 2015;73(4):0-6.
 13. Van Santbrink EJ, Hop WC, Fauser BC. Classification of normogonadotropic infertility: polycystic ovaries diagnosed by ultrasound versus endocrine characteristics of polycystic ovary syndrome. *Fertility and sterility*. 1997 Mar 1;67(3):452-8.
 14. Nilsson SF, Ver Hoeve J, Wu S, Kaufman PL, Alm A. *Adler's Physiology of the Eye* E-Book. Elsevier Health Sciences; 2011 Mar 3.pp 530-880.
 15. Khurana V, Vadlapudi AD, Vadlapatla RK, Pal D, Mitra AK. Functional characterization and molecular identification of vitamin C transporter (SVCT2) in human corneal epithelial (HCEC) and retinal pigment epithelial (D407) cells. *Current eye research*. 2015 May 4;40(5):457-69.
 16. Louis B. Cantor, Christopher J. Rapuano, Colin A. McCannel .AAO. *Fundamentals and Principles of Ophthalmology* section 10 2020;2:430.
 17. Goel M, Picciani RG, Lee RK, Bhattacharya SK. Aqueous humor dynamics: a review. *The open ophthalmology journal*. 2010;4:52.
 18. Jordan B. *Central nervous control of autonomic function*. CRC Press; 1997 Jul 16. CRC Press; 6(11), 951-952.
 19. Johnson M. What controls aqueous humor outflow resistance? *Exp Eye Res*. 2006;82(4):545-57.
 20. Doneley B. *Clinical Anatomy and Physiology*. Avian Medicine and Surgery in Practice. 2016. 1-43 p.
 21. Ilginis T, Clarke J, Patel PJ. *Ophthalmic imaging*. *British medical bulletin*. 2014 Sep 1;111(1).
 22. Goel M, Picciani RG, Lee RK, Bhattacharya SK. Aqueous humor dynamics: a review. *The open ophthalmology journal*. 2010;4:52.
 23. Wang YX, Xu L, Wei W Bin, Jonas JB. Intraocular pressure and its normal range adjusted for ocular and systemic parameters. *The Beijing eye study 2011*. *PLoS One*. 2018;13(5):1-16.
 24. Mansouri K, Orguel S, Mermoud A, Haefliger I, Flammer J, Ravinet E, et al. Quality of diurnal intraocular pressure control in primary open-angle patients treated with latanoprost compared with surgically treated glaucoma patients: A prospective trial. *Br J Ophthalmol*. 2008;92(3):332-6.
 25. Nakamura Y, Ishikawa S, Nakamura Y, Sakai H, Henzan I, Sawaguchi S. 24-Hour Intraocular Pressure in Glaucoma Patients Randomized To Receive Dorzolamide or Brinzolamide in Combination With Latanoprost. *Clin Ophthalmol*. 2009;3(1):395-400.
 26. Topouzis F, Founti P. Weighing in Ocular Perfusion Pressure in Managing Glaucoma. *Open Ophthalmol J*. 2009;3(2):43-5.
 27. Goodman RL. *Ophtho notes: the essential guide*. Vol. 53, *Journal of Chemical Information and Modeling*. 2013. 1689-1699 p.
 28. Salmon JF, MD, FRCS Frco, Surgeon CO, Hospital OE, Oxford, Kingdom U. *KANSKI'S Clinical Ophthalmology A Systematic Approach Ninth Edition 2020*. Vol. 72, *British Journal of Ophthalmology*.477-477 p.
 29. Wolvaardt E, Stevens S. Measuring intraocular pressure. *Community eye health*. 2019;32(107):56..
 30. Yun SH, Specht K, Krummenauer F, Schwenn O, Troost A. Transpalpebral tonometry: Reliability and comparison

- with Goldmann applanation tonometry and palpation in healthy volunteers. *Br J Ophthalmol.* 2005;89(3):280-3.
31. Fresco BB. A new tonometer - The pressure phosphene tonometer: Clinical comparison with goldmann tonometry. *Ophthalmology.* 1998;105(11):2123-6.
 32. Heijnen JH. *Clinical Optics Third Edition* Andrew R. Elkington CBE, MA, FRCS, FRCOphth Consultant Ophthalmologist,(1994-1997). 2006. 1-9 p.
 33. De Moraes CG, Prata TS, Liebmann J, Ritch R. Modalities of tonometry and their accuracy with respect to corneal thickness and irregularities. *Journal of optometry.* 2008 Jan 1;1(2):43-9.
 34. Kirwan C, O'keefe M, Lanigan B. Corneal Hysteresis and Intraocular Pressure Measurement in Children Using the Reichert Ocular Response Analyzer. *Am J Ophthalmol.* 2006;142(6):990-2.
 35. US ethics guidelines for trials in the developing world. 2001;357:2001.
 36. Singh S, Shaul PW, Gupta PD. Conventional estrogen receptors are found in the plasma membrane of vaginal epithelial cells of the rat. 2002;67:757-64.
 37. Ogueta SB, Schwartz SD, Yamashita CK, Farber DB. Estrogen Receptor in the Human Eye : Influence of Gender and Age on Gene Expression. 1999;40(9):1906-11.
 38. Hales BAM, Chamberlain CG, Murphy CR, Mcavoy JW. Estrogen Protects Lenses against Cataract Induced by. 2006;185(2).
 39. Klein BE, Klein R, Ritter LL. Is there evidence of an estrogen effect on age- related lens opacities?: The Beaver Dam Eye Study. *Archives of Ophthalmology.* 1994 Jan 1;112(1):85-91.
 40. Farage MA, Neill S, MacLean AB. Physiological changes associated with the menstrual cycle: a review. *Obstetrical & gynecological survey.* 2009 Jan 1;64(1):58-72.
 41. Versura P, Fresina M, Campos EC. Ocular surface changes over the menstrual cycle in women with and without dry eye. *Gynecological endocrinology.* 2007 Jan 1;23(7):385-90.
 42. Suzuki T, Kinoshita Y, Tachibana M, Matsushima Y, Kobayashi Y, Adachi W. Expression of sex steroid hormone receptors in human cornea. 2001;22(1):28-33.
 43. Tachibana M, Kobayashi Y, Kasukabe T, Kawajiri K. Expression of Androgen Receptor in Mouse Eye Tissues AND. 2000;1999-2001.
 44. Ve P V, Kircher K, Kaminski S, Nagel G. Immunohistochemical detection of estrogen and progesterone receptor in human cornea. 2000;36:169-72.
 45. Akar Y, Yucel I, Akar ME, Taskin O, Özer HO. Menstrual cycle-dependent changes in visual field analysis of healthy women. *Ophthalmologica.* 2005;219(1):30-5.
 46. Mitchell P, Smith W, Attebo K, Healey PR. Prevalence of open-angle glaucoma in Australia: The blue mountains eye study. *Ophthalmology.* 1996;103(10):1661-9.
 47. Rudnicka AR, Mt-Isa S, Owen CG, Cook DG, Ashby D. Variations in primary open-angle glaucoma prevalence by age, gender, and race: A Bayesian meta-analysis. *Investig Ophthalmol Vis Sci.* 2006;47(10):4254-61.
 48. Patel P, Harris A, Toris C, Tobe L, Lang M, Belamkar A, et al. Effects of Sex Hormones on Ocular Blood Flow and Intraocular Pressure in Primary Open-angle Glaucoma: A Review. *J Glaucoma.* 2018;27(12):1037-41.
 49. Kang HY. Beyond the male sex hormone: Deciphering the metabolic and vascular actions of testosterone. *J Endocrinol.* 2013;217(3).
 50. Toker E, Yenice Ö, Temel A. Influence of serum levels of sex hormones on intraocular pressure in menopausal women. *J Glaucoma.* 2003;12(5):436-40.
 51. Roemer, Emily J., West, Kesley L., Northrup, Jessica B., Iverson, Jana M. HHS Public Access. *Physiol Behav.* 2016;176(12):139-48.
 52. Gharagozloo NZ, Brubaker RF. The correlation between serum progesterone

- and aqueous dynamics during the menstrual cycle. *Acta Ophthalmol.* 1991;69(6):791-5.
53. Wild RA, Carmina E, Diamanti-Kandarakis E, Dokras A, Escobar-Morreale HF, Futterweit W, et al. Assessment of cardiovascular risk and prevention of cardiovascular disease in women with the polycystic ovary syndrome: A consensus statement by the androgen excess and polycystic ovary syndrome (AE-PCOS) society. *J Clin Endocrinol Metab.* 2010;95(5):2038-49.