A STUDY OF RETINAL CHANGES IN WOMEN WITH POLYCYSTIC OVARIAN SYNDROME

Thesis

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AIIMS, Jodhpur **Dr. Sakshi Shiromani**

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DECLARATION

I hereby declare that this project titled "**A study of retinal changes in women with Polycystic Ovarian Syndrome**" is the bonafide record of my original research. It has not been submitted to any other institution for the award of any degree or diploma. Information derived from the published or unpublished work of others has been duly acknowledged in the text.

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CERTIFICATE

This is to certify that the thesis titled "**A study of retinal changes in women with Polycystic Ovarian Syndrome"** is the bonafide work of **Dr. Sakshi Shiromani** under my guidance and supervision, in the Department of Ophthalmology, All India Institute of Medical Sciences, Jodhpur.

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Dr. Sakshi Shiromani

LIST OF ABBREVIATIONS

OCT	Optical Coherence Tomography
PCOS	Polycystic Ovarian Syndrome
RNFL	Retinal Nerve Fibre Layer
USG	Ultrasonography
ESHRE	European Society for Human Reproduction & Embryology
ASRM	American Society of Reproductive Medicine
AE-PCOS	Androgen Excess & PCOS
NIH	National Institutes of Health
HA	Hyperandrogenism
OA	Oligo-anovulation
PCOM	Polycystic Ovarian Morphology.
IOP	Intraocular Pressure
NGF	Nerve Growth Factor
HD-OCT	High Definition- Optical Coherence Tomography
NOM	Nasal Outer Macula
TOM	Temporal Outer Macula
CCT	Central Corneal Thickness
IGF-I	Insulin Growth Factor- I
MUC5AC	Mucin 5 AC
OSDI	Ocular Surface Disease Index
FBU	Fluorescein Break Up
AIIMS	All India Institute of Medical Sciences
NEI	National Eye Institute
SPSS	Statistical Package of Social Sciences
IQR	Inter Quartile Range
SD	Standard Deviation
TBUT	Tear film Break Up Time
MGD	Meibomian Gland Disease
GCL	Ganglion Cell Layer
IPL	Inner Plexiform Layer
BMI	Body Mass Index
HDL	High Density Lipoprotein
LDL	Low Density Lipoprotein

SYNOPSIS

Optical Coherence Tomography (OCT) is a non-invasive diagnostic technique that provides an in vivo cross sectional view of the retina. It is analogous to an ultrasound, the difference being that it uses light instead of sound[1].The functional principle that it utilizes is interference of light to create a cross-sectional map of the retina. In an inhomogeneous sample, different structures within the sample will have different indices of refraction and light will be backscattered when it encounters an interface between materials of different refractive index. Detection of this backscattered light helps to form an image of the various layers of the retina.[2-4]

The retinal nerve fibre layer is formed by the expansion of the fibres of the optic nerve which is thickest near the optic disc and diminishes towards the ora serrata. Posterior to this is the ganglion cell layer which consists of retinal ganglion cells, the dendrites of which extend into the inner plexiform layer and the axons are sent into the nerve fibre layer. The thickness of these layers varies with different physiological and pathological processes, some of which have been enumerated in the introduction below. The thickness of these two layers can be measured on the OCT machine. The macula is the most important sensory channel of the eye concerned with visual acuity, form sense, colour sense and stereopsis. The macular thickness, which again varies with different physiological and pathological conditions, can be measured on the OCT machine.

Polycystic ovary syndrome (PCOS) is one of the commonest endocrine disorders in women of reproductive age group.[5,6,7] It has a heterogeneous presentation, the most important ones being hyperandrogenism and ovulatory dysfunction.[8,9] It may be associated with metabolic syndrome, insulin resistance, glucose intolerance, type 2 diabetes, cardiovascular disease, obesity, and dyslipidemia.[10-12]

The prevalence of PCOS reported in earlier studies varies between 2.2% to 26%[13]. These variations are due to difficulties in hormonal evaluation and lack of consensus on diagnostic criteria. Using different criteria, prevalence has been estimated as 4.0%–11.9% in the community from 3 different countries[14]. Calculated prevalence of PCOS in women between the ages of 18-25 years from Lucknow, north India, is 3.7%.[15] However, there is paucity of data from India.

Insulin resistance plays a major role in the pathogenesis of PCOS. Indians are known to have high prevalence of insulin resistance and therefore PCOS is not uncommon in our population.

The relationship between eye changes in PCOS is unexplored especially in the Indian population. Since PCOS is known to be associated with metabolic syndrome and changes in glucose metabolism, it was interesting to study retinal changes in these patients as compared to healthy females of reproductive age group. Furthermore, the presence of sex steroid hormone receptors in various ocular tissues, especially the retina and choroid, leads us to believe that hormonal changes such as hyperandrogenism may also cause changes in the posterior segment of the eye.

The aim of this study was to compare Optical Coherence Tomography based Retinal Nerve Fibre Layer and Ganglion Cell Layer thickness at the posterior pole, total macular thickness in women with Polycystic Ovarian Syndrome vs healthy reproductive age group females.

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INTRODUCTION

INTRODUCTION

Optical coherence tomography (OCT) is a noninvasive, noncontact technology. It produces two dimensional retinal images with the help of near infrared, low coherence light moving through a Michelson interferometer. The resolution is approximately 5–10 μm in the axial plane[16]. This noninvasive technique allows us to diagnose subclinical retinal changes early. Using it, we can obtain detailed information on the retinal microstructure with remarkable resolution, precision, and repeatability. A coupler which is present in the machine splits the light from a low-coherence source into two channels, and these are directed along two distinct arms of an interferometer. The principle it uses is that when light passes through a non-homogeneous sample, distinct structures within the sample will have varying indices of refraction and light will be backscattered when it comes in contact with an interface of materials with different refractive indices. This backscattered light is utilized to create two dimensional images of the retina and assess the thickness of its layers.

The optic nerve fibres expand to produce the retinal nerve fiber layer (RNFL) or the stratum opticum, which is thickest near the optic disc, gradually thins out as it approaches the ora serrata. RNFL is a delicate structure. Some processes can stimulate its natural apoptosis (dangerous situations such as high intraocular pressure, its fluctuation, inflammation, vascular disease and any kind of hypoxia), modifying its thickness which we can evaluate on the OCT machine quadrant-wise and clock hour-wise.

The ganglion cell layer or the ganglionic layer is located posterior to the nerve fibre layer. It consists of retinal ganglion cells of various sizes and displaced amacrine cells. The cells have a flask-shaped form; with a rounded internal surface that rests on the nerve fibre layer, and sends off an axon that extends into it. Numerous dendrites extend from the opposite end into the inner plexiform layer, where they branch and arborize at various levels. Thinner RNFL, older age, longer ocular axial length, and being male are the factors linked with thinning of this layer[17].The thickness of this layer can also be determined using the OCT machine.

The macula is the focal point of the eye, optically, functionally and organically as it is the most important sensory channel. It deals with visual acuity, form sense, colour sense, and stereopsis. It contains one additional layer of ganglion cells as compared to the peripheral retina. The fovea is the thinnest part of the retina and is composed solely of a high density of cone photoreceptors and their nuclei together with Müller cells. Female sex, advanced age, and longer axial length are all linked to thinner overall average macular thickness, whereas

female sex and shorter axial length are linked to thinner central foveal thickness[11]. A frequent cause of increased macular thickness is macular edema. The thickness of the macula can be measured by the OCT machine, and one can also visualize macular edema by looking at the OCT image. [18-21]

Polycystic ovary syndrome (PCOS) is one of the most frequent endocrine disorders in women of the reproductive age group[6]. It presents in a variety of ways, the most important ones being hyperandrogenism and ovulatory dysfunction.[8,9] This syndrome also leads to other comorbidities such as metabolic syndrome, insulin resistance and glucose intolerance. Type 2 diabetes, cardiovascular disease, obesity, and dyslipidemia are also among its consequences.[12]

Currently the Rotterdam diagnostic criteria (2013) are being followed for the diagnosis of polycystic ovarian syndrome. The Rotterdam criteria requires the presence of two of the following: [22-24]

1. Hyperandrogenism (clinical or biochemical)
2. Ovulatory Dysfunction (oligo or anovulation)
3. Polycystic ovaries on USG (At least one ovary with i)12 follicles of 2-9mm ii) volume > 10 ml)

Ocular structures such as the lacrimal and meibomian glands, conjunctiva, cornea, lens, iris, ciliary body and retina, all carry estrogen, progesterone and androgen receptors.[25-27] Though studies regarding ocular changes in the anterior and posterior segment of the eye are sparse, especially in the Indian context, a few studies conducted overseas have found significant differences between anterior and posterior segment parameters in females with Polycystic Ovarian Syndrome as compared to healthy females of reproductive age group.[28-30]

We conducted an anterior segment examination of the patient and that followed by posterior segment examination using an indirect ophthalmoscope and then imaging was done on an OCT Machine.

All findings were recorded and compared with healthy reproductive age group females.

AIM & OBJECTIVES

AIM AND OBJECTIVES

RESEARCH QUESTION: Is there any significant difference between the Optical Coherence Tomography based Retinal Nerve Fibre Layer and Ganglion Cell Layer thickness at the posterior pole, and total macular thickness of women with Polycystic Ovarian Syndrome vs healthy reproductive age group females?

AIM: To compare Optical Coherence Tomography based Retinal Nerve Fibre Layer and Ganglion Cell Layer thickness at the posterior pole, total macular thickness in women with Polycystic Ovarian Syndrome vs healthy reproductive age group females.

OBJECTIVES:

1. To compare the Retinal Nerve Fibre Layer thickness in women with Polycystic Ovarian Syndrome vs healthy reproductive age group females.
2. To compare the Ganglion Cell Layer Thickness in women with Polycystic Ovarian Syndrome vs healthy reproductive age group females.
3. To compare the total macular thickness in women with Polycystic Ovarian Syndrome vs healthy reproductive age group females.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Polycystic ovary syndrome (PCOS) is one of the most frequent disorders in reproductive age group females. With diverse presentations due to hyperandrogenism and ovulatory dysfunction, it also causes morbidity to the patient due to metabolic syndrome, insulin resistance, glucose intolerance, type 2 diabetes, cardiovascular disease, obesity, and dyslipidemia.

The relationship between eye changes in PCOS is unexplored especially in the Indian population. The retinal changes that develop in these patients can be attributed to the alterations in glucose metabolism and metabolic syndrome caused by it. The hormonal imbalance in these patients stimulates the androgen receptors in the tissues of the eye such as the ciliary body and choroid which can partly explain these changes.

POLYCYSTIC OVARIAN SYNDROME

PCOS, or Polycystic Ovarian Syndrome is a highly frequent endocrine–metabolic condition in reproductive-aged women. The pivotal account of Stein and Leventhal was the first tangible report in modern clinical literature. Formerly thought of as unrelated, they linked the triad of polycystic ovaries, hirsutism, and oligo-amenorrhea. Yet, despite tremendous advances in understanding the inner workings of this disorder over the past two decades, medical practitioners continue to misdiagnose and mistreat the disorder.[31- 33]

Presenting with a myriad of signs and symptoms, this disorder often poses a diagnostic dilemma in front of the clinician. Hirsutism, which is defined the presence of excess terminal hairs in a male-like pattern is what the clinician most frequently comes across. Clinical hyperandrogenism can also be confirmed by the presence of excess androgen concentrations in the blood. One needs to enquire the time between the episodes of vaginal bleeding in order to diagnose oligo-ovulation. An investigation that can be done to confirm polycystic ovarian morphology is transvaginal ultrasonography. It can also be detected histopathologically. [31]

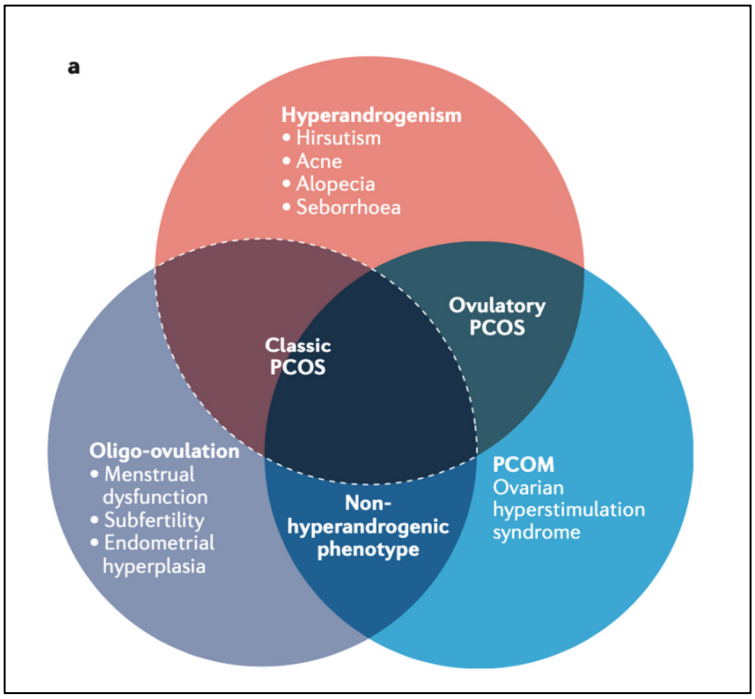


Figure 1: The Diagnostic Criteria for Polycystic Ovarian Syndrome

(Adapted from REF. 38, Macmillan Publishers Limited.)

The syndrome is also morbid to the patients in other aspects. These include excess adiposity leading to obesity, chronic insulin resistance unexplained by an increased body mass index, increased risk of abnormal vascular function, subfertility associated with abnormal ovulatory function ad greater risk of anxiety and depression.

In today's world, there are three diagnostic criteria for PCOS. Although the diagnostic schemes of these criteria varies slightly, they all use the same elements in general. An examination of the criteria reveals that two of them (the 2003 Rotterdam and the 2006 Androgen Excess & PCOS Society) are extensions of the first (the 1990 National Institutes of Health criteria).(Figure 1) (Table 1)[34-36]

Currently the Rotterdam diagnostic criteria (2013) are being followed for the diagnosis of polycystic ovarian syndrome.

Table 1: The diagnostic Criteria for Polycystic Ovarian Syndrome

	1990 NIH	2003 ESHRE/ASRM (Rotterdam)	2006 AE-PCOS Society	2012 NIH Consensus
Criteria	2 of 2 criteria required 1. HA 2. OA	2 of 3 criteria required 1. HA 2. OA 3. PCOM	2 of 2 criteria required: 1. HA 2. Ovarian Dysfunction (OA, PCOM or both)	Recommended the use of the 2003 Rotterdam criteria, but with the specification that the specific phenotypes included can be identified • Phenotype A: HA+OA+PCOM • Phenotype B: HA+OA • Phenotype C: HA+PCOM • Phenotype D: OA+PCOM
Exclusions	Exclusion of similar or mimicking disorders			

The treatment of PCOS largely depends on the concerns of the patient. The main goals of treatment are 1) decreasing androgen secretion and activity, 2) preserving the endometrium and alleviating menstrual dysfunction, 3) improving metabolic state, and 4) increasing ovulatory fertility.[37,38]

OPTICAL COHERENCE TOMOGRAPHY

Optical coherence tomography (OCT) is a noninvasive, noncontact technology. It produces two dimensional retinal images with the help low coherence light travelling through a Michelson interferometer. The wavelength it uses is close to the infrared region. The resolution is approximately 5–10 μm in the axial plane.[16] This noninvasive technique allows us to diagnose subclinical retinal changes early. Using it, we can obtain detailed information

on the about the various layers of the retina. We can also maintain a numerical record of the data which is extremely beneficial in the treatment, monitoring and follow up of patients. [2]

The light from a low-coherence source is directed into two paths by a coupler sending it along two different arms of an interferometer. When the light passes through a non-homogeneous sample, distinct structures within the sample will have varying indices of refraction and light will be backscattered when it comes in contact with an interface of materials with different refractive indices. This backscattered light is utilized to create two dimensional images of the retina and assess the thickness of its layers.. [1]

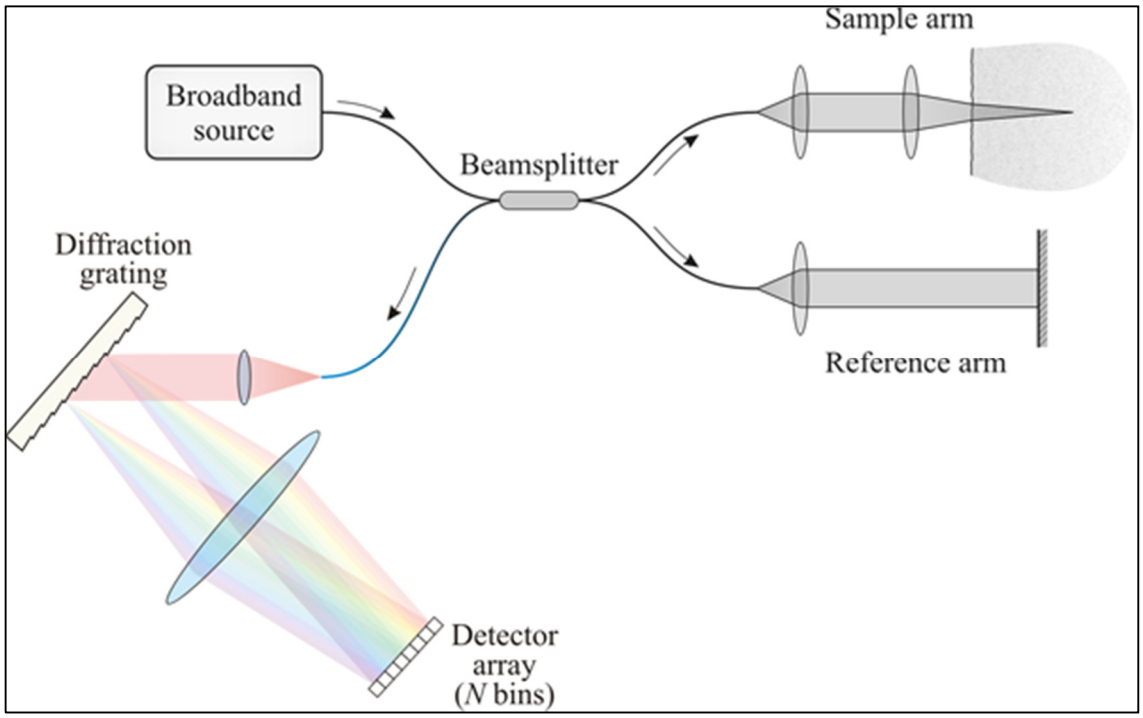


Figure 2: The Basic Principle of Optical Coherence Tomography (Adapted from http://obel.ee.uwa.edu.au/research/fundamentals/introduction-oct/)

The retina consists of a number of layers formed by three strata of cells and their synapses.

- The visual cells (lying externally)
- A relay layer of bipolar cells (lying intermedially), and,
- A layer of ganglion cells (lying internally), the axons of which run into the central nervous system.

The optic nerve fibres expand to produce the retinal nerve fiber layer (RNFL) or the stratum opticum, which is thickest near the optic disc, gradually thins out as it approaches the ora serrata. RNFL is a delicate structure. Some processes can stimulate its natural apoptosis

(dangerous situations such as high intraocular pressure, its fluctuation, inflammation, vascular disease and any kind of hypoxia), modifying its thickness which we can evaluate on the OCT machine quadrant-wise and clock hour-wise

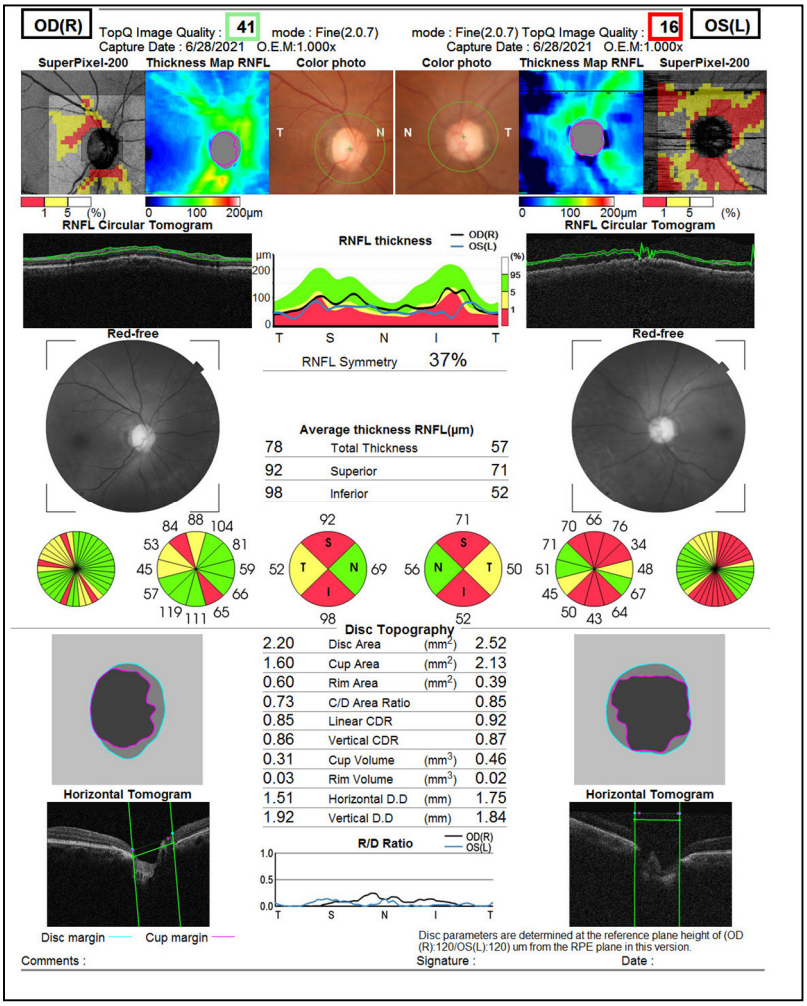


Figure 3: The OCT RNFL Values Quadrant-wise and Clock hour-wise
(Source: Department of Ophthalmology, AIIMS Jodhpur)

The ganglion cell layer or the ganglionic layer is located posterior to the nerve fibre layer. It consists of retinal ganglion cells of various sizes and displaced amacrine cells. The cells have a flask-shaped form; with a rounded internal surface that rests on the nerve fibre layer, and sends off an axon that extends into it. Numerous dendrites extend from the opposite end into the inner plexiform layer, where they branch and arborize at various levels. Thinner RNFL, older age, longer ocular axial length, and being male are the factors linked with thinning of this layer[17].The thickness of this layer can also be determined using the OCT machine.

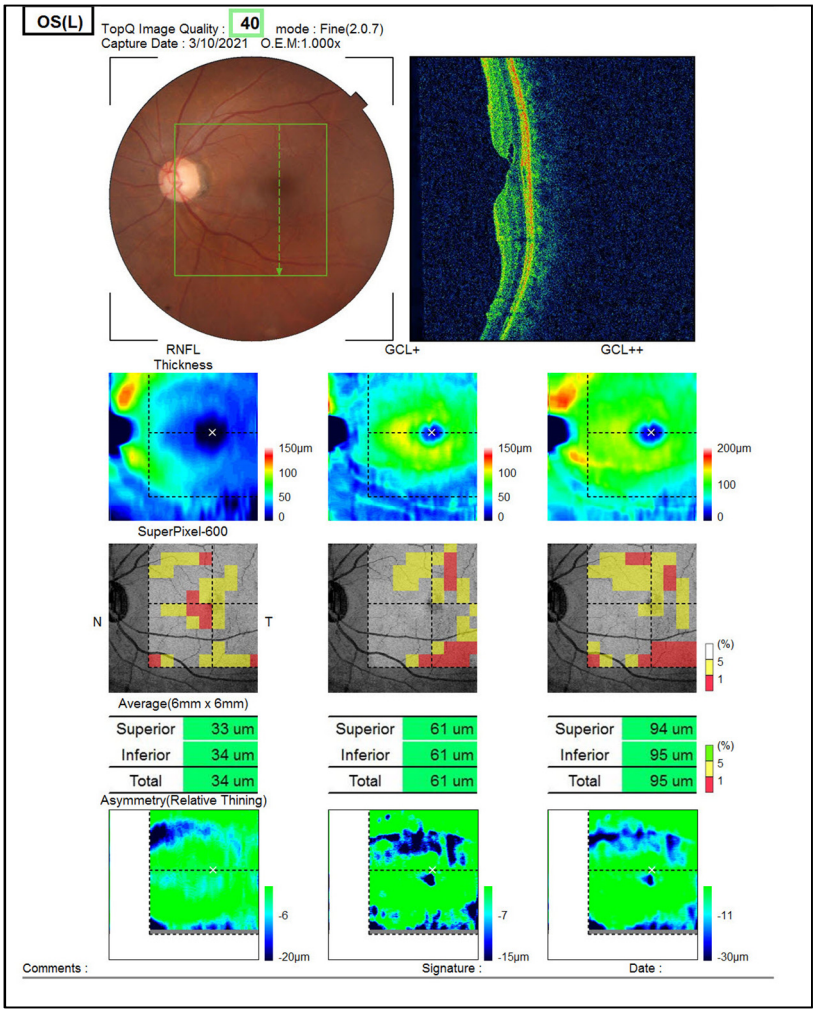


Figure 4: The GCL+, GCL++ and Macular RNFL thicknesses

(Source: Department of Ophthalmology, AIIMS Jodhpur)

The macula is the focal point of the eye, optically, functionally and organically as it is the most important sensory channel. It deals with visual acuity, form sense, colour sense, and stereopsis. It contains one additional layer of ganglion cells as compared to the peripheral retina. The fovea is the thinnest part of the retina and is composed solely of a high density of cone photoreceptors and their nuclei together with Müller cells. Female sex, advanced age, and longer axial length are all associated with thinner overall average macular thickness, while female sex and shorter axial length are associated with thinner central foveal thickness.[11] A frequent cause of increased macular thickness is macular edema. The thickness of the macula can be measured by the OCT machine, and one can also visualize macular edema by looking at the OCT image. [18-21]

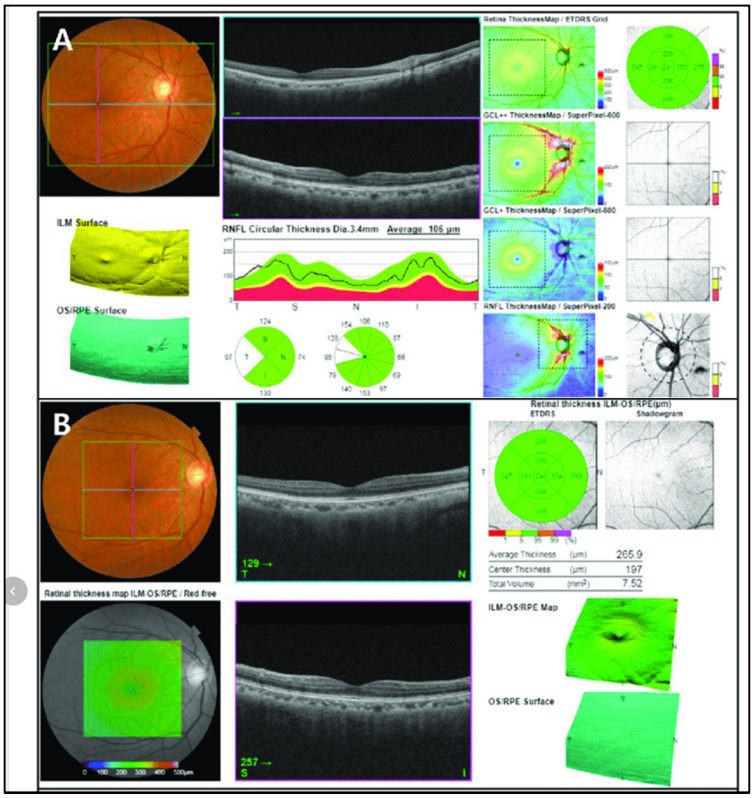


Figure 5: The Central and Average Macular Thicknesses

(Source: Department of Ophthalmology, AIIMS Jodhpur)

PCOS AND THE EYE

PCOS, also known as ovarian hyperandrogenemia is the most common endocrinopathy in reproductive- aged females.[39] Target organs experience an unopposed hyperestrogenemic effect that cannot be counteracted by progesterone. Target organs respond to estrogen by producing certain proteins (e.g. cathepsin D, alpha- 2-macroglobulin, and aromatase cytochrome P45) which are involved in vital cellular functions like differentiation, proliferation and maturation and were described by Ogueta et al.[40] As expected, ocular tissues such as the ciliary body and retinal pigment epithelium show the presence of most of these proteins. Elevated sex steroid levels in PCOS influence ocular anatomy and function in the same way they affect the cardiovascular system and endometrium.[41] Basic cellular processes like growth, differentiation and proliferation have a role of steroid hormones.[40] The potent vasodilatory action of estrogen was described by Magness et al.[42], while Sarrel[39] reported that progesterone has the opposite effect. Yucel et al.[43] proposed the effect of unopposed high progesterone levels and said that in the presence of low estrogen, the ocular perfusion might be reduced due to vasoconstriction.[25]

Previous authors have written about the aqueous layer deficiency and dry eye disease (evaporative) due to hormonal imbalances.[44–48] Androgens have been studied to affect gene expression and lipid synthesis in meibomian glands, making them a target organ for these hormones. Meibomian gland dysfunction and evaporative dry eye syndrome can be caused by androgen deprivation. Estrogen inhibits the function of the meibomian glands, which may contribute to the development of evaporative dry eye. Na et al.[49] described the effect of exogenous estrogen in post-menopausal women taking hormonal therapy and reported a significant increase in dry eye syndrome. IOP elevation was thought to be associated with the steroidogenic effect of estrogen replacement therapy.

The functions of the lacrimal gland are influenced by sex hormones, particularly androgens. Androgens cause the lacrimal gland to produce more tears. Furthermore, androgens' anti-inflammatory impact on the lacrimal glands can help individuals with keratoconjunctivitis sicca and Sjogren syndrome improve tear fluid volume. The action of estrogens on the lacrimal gland is debatable; although some writers say that estrogens counteract the effects of androgens by reducing tear production, others claim that estrogens enhance Goblet cell density and alleviate ocular discomfort. At least in the early phases of PCOS, hyperandrogenism is not a factor that lowers tear production from the lacrimal glands. Insensitivity and/or down-regulation of androgen receptors may occur over time as a result of long-term exposure to androgen.

It has been found previously that in females with PCOS, the levels of nerve growth factor (NGF) are elevated.[50] This, in conjunction with androgens has a trophic action on nerves.[51–53]

Ciccone et al. demonstrated how a single dosage of nasal 17-b-estradiol enhances ocular artery perfusion.[54] In a study, Atalay et al studied ocular hemodynamic parameters using Doppler, similar to Ciccone et al. They discovered that hormone replacement therapy with estradiol 17-valerate 2 mg and cyproterone acetate 1 mg improves ocular vascular Doppler indices, which could be an indicator of cerebral vascular health.[29] However, Sogawa et al[55] investigated the relationship between the choroidal thickness and the choroidal blood flow in healthy young individuals. In healthy young people, they found no significant associations between subfoveal choroidal thickness and total choroidal blood flow or subfoveal choroidal blood flow; however, decreasing subfoveal choroidal thickness was linked to lower refractive error and axial length..[55] They assumed that the increased choroidal thickness seen in PCOS

patients is due to an increased estrogen-dependent vasodilatory action in the ophthalmic artery caused by unopposed estrogen levels.[55,29]

Though studies regarding ocular changes in the anterior and posterior segment of the eye are sparse, especially in the Indian context, a few studies conducted overseas have found significant differences between anterior and posterior segment parameters in females with Polycystic Ovarian Syndrome as compared to healthy females of reproductive age group.

Posterior Segment

José Edvan de Souza-Júnior et al[30] conducted a study in 2015 to compare macular thickness (MT) and retinal nerve fiber layer (RNFL) thickness between women with polycystic ovary syndrome and healthy women using HD-OCT. The study included 45 women with PCOS and 47 ovulatory women who underwent gynaecological and ocular evaluations, including optical coherence tomography measurements of the MT, RNFL, and optic disc characteristics. PCOS patients had substantially thicker superior RNFL around the optic nerve than healthy volunteers (P = 0.036). After stratification based on insulin resistance, the temporal inner macula (TIM), inferior inner macula (IIM), nasal inner macula (NIM), and nasal outer macula (NOM) were significantly thicker in the PCOS group than in the control group (P 0.05). This suggests that PCOS may operate as a protective factor in the RNFL around the optic nerve, possibly via testosterone. PCOS, on the other hand, when combined with metabolic disorders, can be a dangerous factor in the macular region.

In addition to these two parameters, **Acmaz et al[56]** conducted a study in 2014 which also included the choroid thickness alterations using spectral-domain optical coherence tomography. The study group included 64 PCOS patients and the control group included 60 healthy volunteers. There was a statistically significant difference in choroid thickness between the PCOS and control groups (P.001), indicating that the thickness of the choroid was greater in PCOS patients. The PCOS group had considerably lower foveal centre thickness and temporal inner macula than the healthy control group (P =.009 and P =.033, respectively). In contrast to these results, the PCOS group's nasal outer macula (NOM) and temporal outer macula (TOM) were statistically thicker than the control group (P =.001 and P.001, respectively). They said that in patients with PCOS, increased choroid thickness and RNFL may result in an increase in both retinal volume and retinal thickness in the peripheral side of the retina, making the NOM and TOM regions susceptible areas.

A similar study was done by **Demir et al**[28] in 2013 to compare the retinal nerve fibre layer thickness between women with polycystic ovary syndrome and healthy women. They studied 88 eyes from 44 women with PCOS (group 1) and 84 eyes from 42 healthy women (group 2). The average RNFL, superior average RNFL, and inferior average RNFL thicknesses in women with PCOS were substantially higher than in healthy women (P = 0.003, P= 0.012, P = 0.009). Therefore, patients with PCOS have a higher density of nerve fibres. Women with PCOS have been found to have high levels of nerve growth factor (NGF). Androgens and nerve growth factor are thought to have trophic effects on nerves, which could explain the observed modifications.

Anterior Segment

In addition to retinal changes, anterior segment changes have also been evaluated in women with PCOS side by side. **Seda Karaca Adıyeke et al**[25] conducted a study in 2017 to investigate the anterior segment in women with polycystic ovary syndrome (PCOS) and to compare them with those of healthy reproductive-age female volunteers. In the study, 50 eyes each of PCOS and healthy females were chosen. The PCOS group had significantly greater mean central corneal thickness values (p=0.001). The mean intraocular pressures of the two groups were identical. The Schirmer's test scores and tear film break-up time values were significantly lower in the PCOS group (p=0.001 and p=0.001, respectively). Serum estradiol levels had a weakly negative (r=-0.393) correlation with tear film break-up time, a moderately positive (r=0.552) correlation with mean central corneal thickness, a slightly positive (r=0.351) correlation with intraocular pressure, and a moderately positive (r=0.552) correlation with intraocular pressure. Schirmer's test results (r=-0.562) and tear film break-up time (r=-0.502), as well as intraocular pressure (r=0.342) and central corneal thickness (r=0.303), all revealed weak negative relationships with serum free testosterone levels. It was thus concluded that PCOS affects the eye's physiological and structural changes. Patients with PCOS had more severe dry eye symptoms and higher central corneal thickness assessments. These are linked to testosterone and estrogen levels in the blood.

Kebapciplar et al [57]also conducted a study to compare the corneal thickness on PCOS subjects with those of healthy women and demonstrate cornea in PCOS patients as a possible target of IGF-1 action and insulin resistance. This cross-sectional study included 43 patients with PCOS and 30 healthy persons who were age and gender matched. PCOS patients had a substantially larger mean central corneal thickness than the control group (P = 0.001, P =

0.001, respectively). Women with PCOS had higher levels of insulin resistance and serum testosterone. IGF-1 was independently and positively linked with right central corneal thickness (beta = 0.768, P0.001). Left central corneal thickness was significantly correlated with insulin resistance and serum testosterone in women with PCOS (P=0.001; P = 0.022). IGF-1 regulates keratocytes and the development of corneal stromal extracellular matrix, as well as having well-known effects on proteoglycan biology. This study emphasises the importance of biomechanical anomalies in PCOS patients, which might lead to IGF-1-related ocular problems.

An interesting study was conducted by **Bonini et al**[58] to define the ocular symptomatology in women with Polycystic Ovaries and signs of hyperandrogenism. Sixteen out of sixty-two patients of Polycystic Ovaries on ultrasound were identified as having clinical and biochemical signs of hyperandrogenism. A thorough eye examination was performed on all women with a history of ocular symptoms (20/62 total patients [32.3 percent], 15/16 polycystic ovary syndrome (PCOS) patients [93.7 percent], and 5/46 PCO patients [10.8%]. Conjunctival hyperemia (P.001), dryness (P.001), itching (P.001), mucous discharge (P.001), and contact lens intolerance (P.001) were all higher in PCOS patients than in PCO patients. When compared to both PCOS patients and healthy subjects, patients with PCOS had a substantial decrease in tear film but a significant increase in goblet cell number and conjunctival MUC5AC messenger ribonucleic acid expression. Also, their conjunctival tissue localisation was shown to be significantly reduced, accompanied by significantly higher conjunctival mRNA expression of MUC5AC. These findings were accompanied by a 177% increase in MUC5AC tear levels in the three patients whose tears were collected. The aberrant shift in location of these receptors from conjunctival tissue to tears in PCOS patients appears to be harmful and may be the source of abnormal mucous filaments accumulating on the ocular surface.

Another study to evaluate the tear osmolarity and ocular surface changes in patients with polycystic ovary syndrome (PCOS) was conducted by **Gonen et al.**[59] They enrolled a total of forty-eight patients with recently diagnosed PCOS and thirty-three control volunteers and calculated their Ocular surface disease index (OSDI). They used the TearLab Osmolarity System to measure the tear osmolarity. PCOS patients had a higher mean OSDI score than controls (P = 0.001). Tear osmolarity was similar in both groups (P = 0.404) and so were the Schirmer I test results, TBUT, and ocular surface flourescein staining scores (P > 0.05).

However, a statistically significant squamous metaplasia was observed in temporal bulbar conjunctival impression cytology specimens in PCOS group (P = 0.032).

Yavas et al. [60] conducted another crucial investigation to assess meibomian gland abnormalities in Polycystic Ovarian Syndrome. In the study, twenty-seven women with PCOS and twenty-two healthy people aged 18 to 42 were enrolled. Dry eye problems were reported frequently or all of the time by fifteen patients in the PCOS group (55.55 percent) and five patients in the control group (22.73 percent) (p = 0.025). Six (22.2%) PCOS patients had translucent or waxy white secretions at meibomian gland orifices or lid margin telangiectasia, compared to three (13.6%) PCOS patients in the control group (p = 0.35). The only test that showed a difference between women with PCOS and normal participants was the FBU, which was 10.46 seconds in women with PCOS and 15.86 seconds in normal people (p = 0.034). There was no significant difference between schirmer test, rose Bengal staining scores, and goblet cell count between the two groups. There was no significant change in cytology between the PCOS and control groups. There was no squamous metaplasia in any group. Because the meibomian gland carries the mRNA for all of the major steroidogenic enzymes, they can produce and metabolise their own androgens, the change in meibomian gland function was attributed to increased peripheral 5-reductase activity in women with PCOS.

Last but not the least, **Ryan et al[61]** presented a case report about a 30-year-old female with diagnosis of PCOS with no other co-morbidities. She had 3 recurrent uveitis episodes within one year. However, her inflammatory markers were very high compared to other PCOS patients. Initially it seemed that the uveitis was due to an idiopathic cause. The patient's medical history was insignificant but blood work showed several proinflammatory factors which leaned on towards PCOS as an etiological factor. She was given medications to alleviate her symptoms from her polycystic ovarian syndrome. The decrease in the frequency and severity of uveitis episodes could be attributed to metformin which has anti-inflammatory properties. The risk of rebound inflammation posed a treatment challenge. Fortunately, the general treatment for uveitis along with metformin significantly helped the patient ameliorate her symptoms and the risk of sight-threatening complications.

In conclusion, significant findings have been found in the ocular signs and symptoms in patients with PCOS. These changes also correspond to the hormonal imbalances found in the patients, suggesting a role of expression of androgen receptors in the eye. Since the number

of studies carried out are less, it emphasizes the need for more research on this subject and also whether treatment of PCOS helps to improve ocular symptomatology or reverse retinal changes.

MATERIALS & METHODS

MATERIALS AND METHODS

Study was conducted in the Department of Ophthalmology, AIIMS, Jodhpur in collaboration with the Department of Obstetrics and Gynaecology, AIIMS, Jodhpur

STUDY DESIGN: A Cross Sectional, Comparative study

INCLUSION CRITERIA	EXCLUSION CRITERIA
Study Group: 1. Consent to inclusion and participation in trial. 2. The women with PCOS among those who visit the Department of Obstetrics and Gynecology diagnosed according to Rotterdam Consensus (2013), according to which the syndrome should be diagnosed when two of the following three parameters are present: menstrual disorder, such as oligomenorrhea and/or amenorrhea; clinical and/or laboratory findings of hyperandrogenism; and ultrasound evidence of polycystic ovaries. Control Group: 1. Females of reproductive age group with normal menstrual cycles and no clinical signs of hyperandrogenemia.	1. Women with other endocrine disorders, renal or liver failure; chronic users of drugs that might interfere with the metabolism of carbohydrates, lipids and with renal function (such as diuretics, antihypertensives, antilipemic agents, and corticosteroids); smoking; alcohol consumption; or illicit drug use. 2. Women who have undergone any ocular surgery. 3. Women not giving written informed consent. 4. Uncooperative patients in whom the parameters cannot be measured.

SAMPLING

SAMPLE SIZE:

With reference to the study conducted by *Demir M et al 2013*, they have reported the SN RNFL in PCOS group as 126.18 ± 21.34 and in control group as 115.39 ± 18.85. Since this is a comparison of two means of two different samples,

$$n = \frac{[Z_{(1-\alpha/2)} + Z_{(1-\beta)}]^2 \, 2Sp^2}{\mu_d^2}$$

$Z_{(1-\alpha/2)} = 1.96$ at 5% level of significance

$Z_{(1-\beta/2)} = 0.842$ at $\beta = 20\%$

$Sp^2 = (\sigma_1^2 + \sigma_2^2)/2$

$\mu_d = \mu_1 - \mu_2$

$\sigma_1 = 21.34$ $\sigma_2 = 18.85$

$\mu_1 = 126.18$ $\mu_2 = 115.39$

Considering this, we estimated a sample size of 55 in each group i.e. 110 patients at 95% confidence interval and 80% power.

METHODS:

The study was conducted in the Department of Ophthalmology, All India Institute of Medical Sciences, Jodhpur in collaboration with the Department of Obstetrics and Gynaecology, All India Institute of Medical Sciences, Jodhpur. The patients diagnosed as Polycystic Ovarian Syndrome were advised to visit the Department of Ophthalmology. A written informed consent was taken and a Patient Information Sheet was provided. The diagnosis of PCOS was made by the Rotterdam's Criteria, 2013. Diagnosis is dependent on identifying at least two of the following three features, as per the criteria:

- Oligo/anovulation- women with menstrual cycles greater than 35 days apart or, conversely, with short cycles of less than 21 days. Women diagnosed with an-ovulatory infertility due to PCOS.
- Hyperandrogenism- Clinical or Biochemical evidence of hyperandrogenemia
  Clinical- evidence of acne, hirsuitism, male pattern balding, hyperandrogenemia
  Biochemical- Total Testosterone > 70 ng/dl, Androstenedione > 245 ng/dl, DHEA-S > 248 ng/dl
- Polycystic ovaries on ultrasound-when 12 small antral follicles (2-9 mm in diameter) are seen in each ovary or ovarian volume > 10 cc. A unilateral polycystic ovary is rare but still clinically significant.

Normal female- Females of reproductive age group (15 to 49 years of age) with no clinical signs of hyperandrogenemia (acne, hirsuitism, male pattern balding, acanthosis nigricans), anovulation (infertility, oligomenorrhoea or amenorrhoea) and normal menstrual pattern.

A detailed history regarding onset of symptoms, if any, duration, progression and any associated complaints was assessed. History regarding any major medical illness or addiction was recorded. After ensuring that our patient satisfied our inclusion criteria, the patient was informed about the nature of study and each patient was given a patient information sheet. After obtaining informed written consent patient was enrolled in the study. The demographic details of the patient were recorded. The baseline parameters including visual acuity (both unaided and best corrected) using Snellen's Charts, intraocular pressure (IOP) with applanation tonometer, central corneal thickness with the help of autorefractometer and Schirmer's test with Schirmer's strip were performed.

Figure 6: The Measurement of Central Corneal Thickness Using an Autorefractometer

(Source: Department of Ophthalmology, AIIMS Jodhpur)

The patient then underwent a thorough slit-lamp examination to evaluate the anterior segment; ocular surface staining score and Tear film Break-Up Time was measured. Patients were looked for any evidence of Meibomian Gland Dysfunction(MGD).

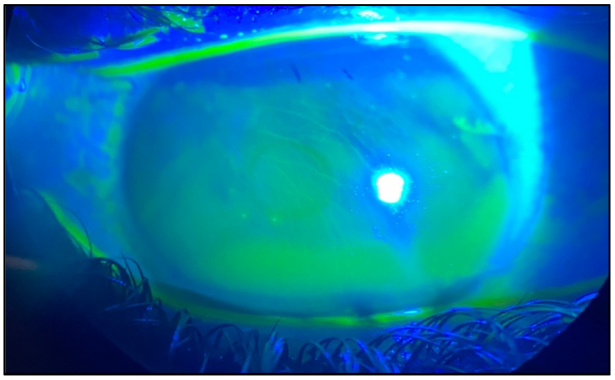


Figure 7: The Measurement of Tear Film Break Up Time on A Slit Lamp in Cobalt Blue Filter

(Source: Department of Ophthalmology, AIIMS Jodhpur)

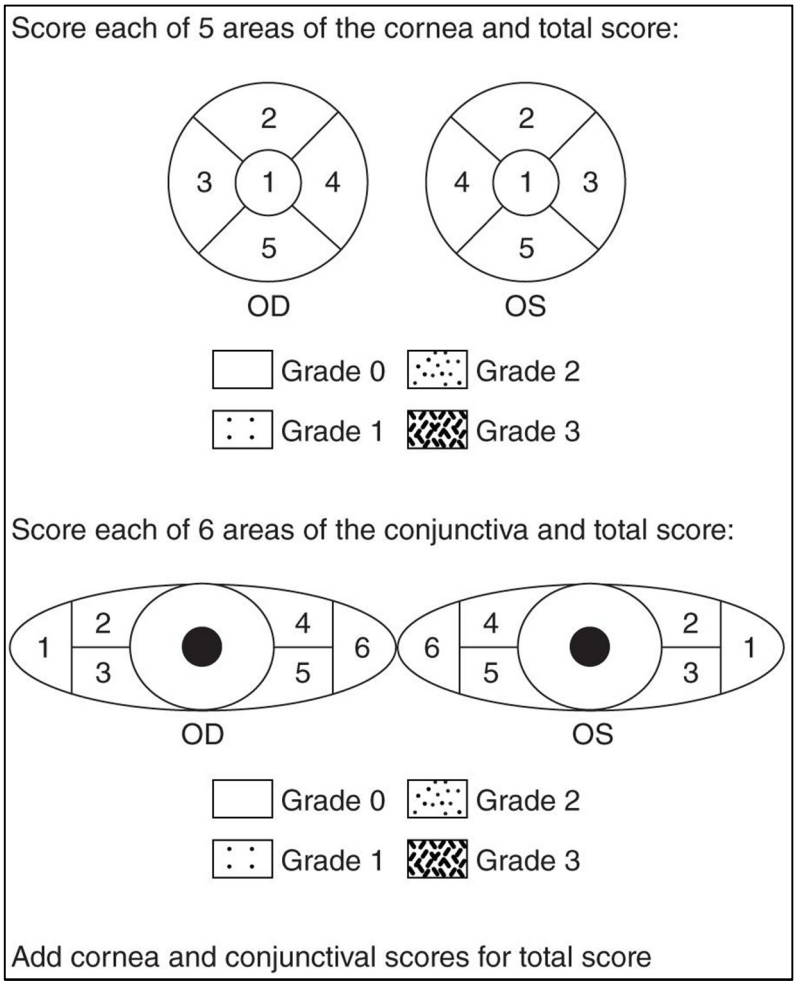


Figure 8: NEI Grading Scale for Dry Eye

(Adapted from https://www.aao.org/image/neiindustry-grading-system)

The NEI grading scale was used to calculate the Ocular Surface Staining Score. To aid measuring the fluorescein uptake, the NEI scale splits the corneal and conjunctival surfaces for grading fluorescein staining. For each of the five locations of each cornea, a consistent grading system of 0 to 3 is employed. When there is no staining, grade 0 is used, and the maximum score is 15.

This was followed by a dilated fundus examination with +90D lens. Indirect ophthalmoscopy with +20 D lens was also performed.

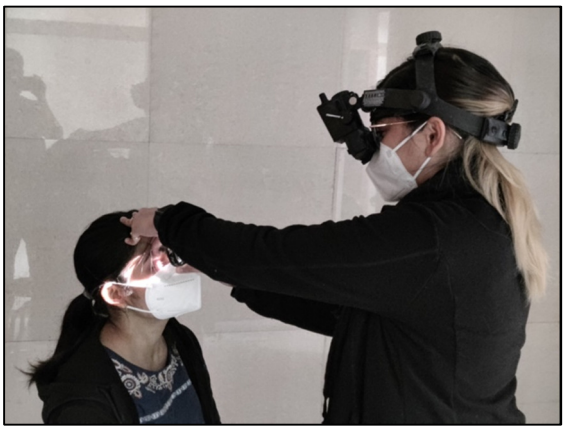


Figure 9a: Indirect Ophthalmoscopy

(Source: Department of Ophthalmology, AIIMS Jodhpur)

After recording all these findings, the patient was made to sit on the 3D Optical Coherence Tomography Machine (Spectral Domain OCT Machine).

Figure 9b: The Measurement of Retinal Thickness using an OCT machine

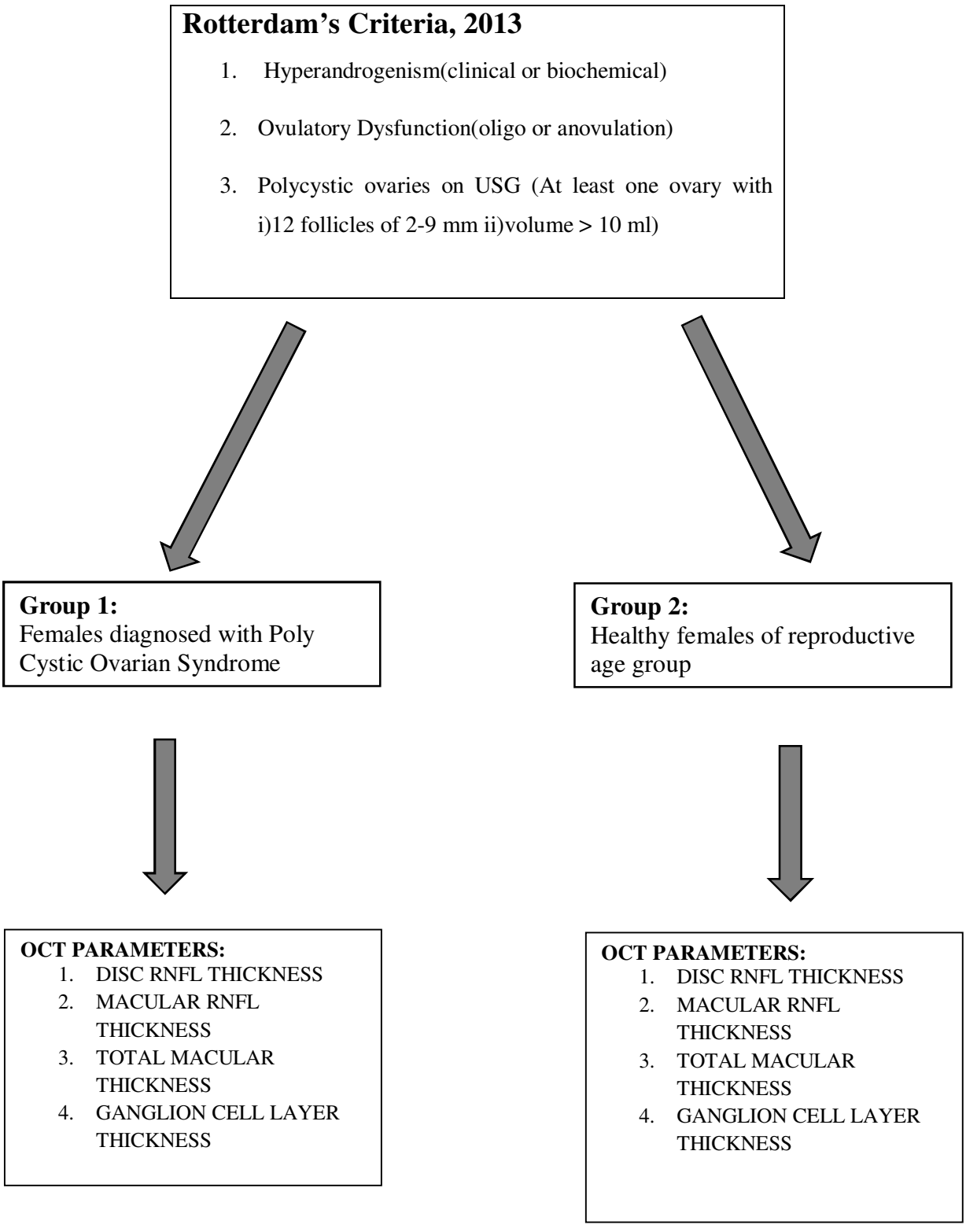
(Source: Department of Ophthalmology, AIIMS Jodhpur)

Images of the Optical Coherence Tomography based Retinal Nerve Fibre Layer thickness at the disc and macula were taken. Optical Coherence Tomography based evaluation of the Ganglion Cell Layer thickness was done. Optical Coherence Tomography based total macular thickness was measured.

Control group were healthy females of reproductive age group who volunteered to be part of the study.

In addition to ocular evaluation, we also recorded the BMI, serum testosterone levels and the lipid profile of the PCOS patients.

The findings were recorded and the data was entered and analysed using the SPSS (Statistical Package for the Social Sciences) version 25.



STATISTICAL ANALYSIS

- Data was entered and analysed using the SPSS (Statistical Package for the Social Sciences) version 25. SPSS Statistics is a statistical analysis software package that allows you to perform interactive or batch statistical analysis. On August 8, 2017, SPSS Statistics released version 25. It was long created by SPSS Inc. before being acquired by IBM in 2009. IBM SPSS Statistics is the brand name for current versions (after 2015).
- The nominal, ordinal and continuous variables were identified.
- The data was cleaned and coded for analysis.
- All nominal variables were described using counts and percentages and analysed using Chi Square test or Fischer's Exact test.
- All ordinal variables were described using median and IQR and analysed using Mann Whitney U test.
- All continuous variables were described using mean and SD and analysed using Independent Sample t test.
- The analysed data was organized in tables.
- Graphs were plotted wherever necessary.
- A p value of less than 0.05 was considered statistically significant.

ETHICAL CONSIDERATION

- The following study was conducted after approval from the Institutional Ethics Committee.
- Informed consent was taken from the women being enrolled for the study by providing them a proper printed consent form along with patient information sheet and after properly explaining the purpose.

RESULTS

RESULTS

A total of 110 patients were enrolled in the study. 55 patients were diagnosed cases of PCOS according to Rotterdam's Criteria which formed the study group and 55 patients were healthy reproductive age group females satisfying the inclusion and exclusion criteria.

Table 2: Demographic Details of the Study Population

		Case	Control	p value
Residence	**Urban**	45 (81.81%)	49 (89.09%)	0.279
	Rural	10 (18.18%)	6 (10.90%)	
Systemic History	**Hypothyroidism**	3 (5.45%)	5 (9.09%)	0.304
	Others	4 (7.27%)	3 (5.45%)	
Family History	**DM**	8 (14.5%)	9 (16.3%)	0.806
	HTN	4 (7.27%)	4 (7.27%)	
	Others	6 (10.9%)	4 (7.27%)	
Education	**Illiterate**	3 (5.45%)	8 (14.54%)	0.146
	Early childhood, primary or secondary	22 (40%)	17 (30.9%)	
	Bachelor's or Masters level	26 (47.27%)	21 (38.18%)	
	Doctoral or equivalent level	4 (7.27%)	9 (16.36%)	

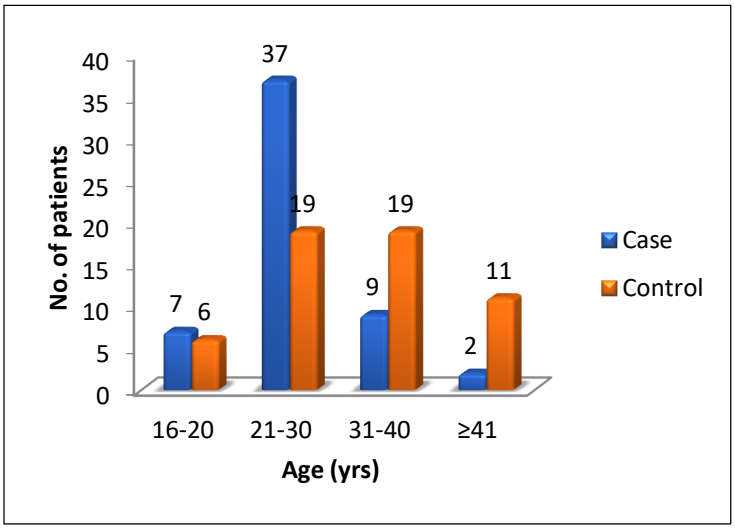
81.8% patients in the PCOS group and 89.09% patients in the control group resided in urban areas. 3 PCOS patients and 5 controls had a history of hypothyroidism. A family history of systemic diseases (DM, HTN, CAD, CKD, etc) was found in 18 PCOS patients and 17 controls. 47.27% patients of PCOS and 38.18% controls had an education of Bachelor's or Masters level. The difference between the two groups was not statistically significant**.** (Table 2)

TABLE 3: Age Distribution of the Study Population

Age (yrs)	Case		Control	
	N	%	N	%
16-20	7	12.73	6	10.91
21-30	37	67.27	19	34.55
31-40	9	16.36	19	34.55
≥41	2	3.64	11	20.00
Total	55	100.00	55	100.00
Median	26		33	
Range	16-45		19-45	
Mean±SD	26.32±5.84		32.09±7.83	
t & p value	4.374, <0.0001			

The mean age in the PCOS group was 26 years. This was significantly lower than the control group where the mean age was 32 years (p<0.0001). 67% patients in the PCOS group belonged to the age group of 21 to 30 years whereas almost 70% patients in the control group belonged to the age group of 21 to 40 years. (Table 3)

Figure 10: Age Distribution Cases vs Controls



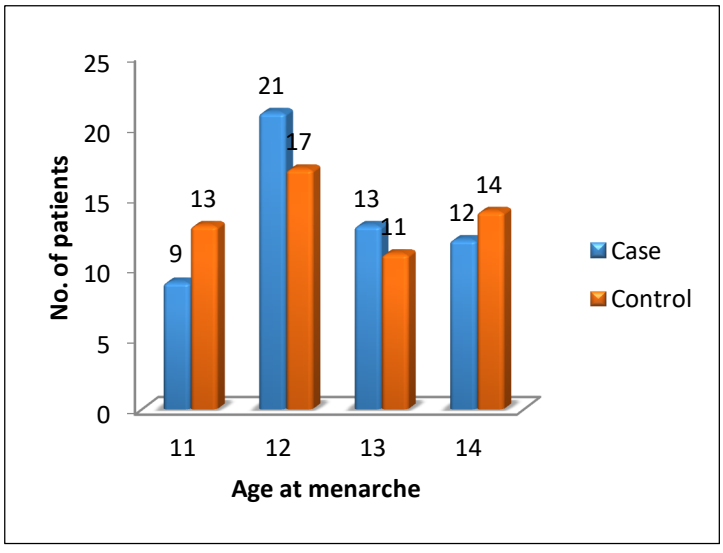
There were higher number of females in the age group of 21 to 30 years in the PCOS group as compared to the control group. The number of females above the age of 30 were higher in the control group. (Figure 10)

TABLE 4: Age at Menarche of the Study Groups

Age at menarche	Case		Control	
	N	%	N	%
11	9	16.36	13	23.64
12	21	38.18	17	30.91
13	13	23.64	11	20.00
14	12	21.82	14	25.45
Total	55	100.00	55	100.00
Median	12		12	
Range	11-14		11-14	
Mean±SD	12.50±1.01		12.47±1.12	
t & p value	0.178, 0.858			

The mean age at menarche was 12 years in both the groups. 38% patients in the PCOS group had menarche at the age of 12 years whereas 31% patients in the control group had menarche at the same age. (Table 4)

Figure 11: Age at Menarche of the Study Groups



21 PCOS patients had menarche at age 12 years whereas 17 healthy reproductive age-group patients had menarche at the age of 12 years. The minimum age at menarche was 11 years whereas the maximum age at menarche was 14 years in the study population. The distribution was similar between the two groups. (Figure 11)

Table 5 : The Diagnostic Criteria for PCOS

	No of Cases
Hyperandrogenism	35 (63.63%)
Oligo/anovulation	39 (79.90%)
Polycystic Ovarian Morphology on Ultrasound	34 (61.81%)

Clinical evidence of hyperandrogenism was found in 35 (63.63%) of the PCOS patients (history of hirsuitism). Oligo/anovulation was found in 39 (79.90%) patients (irregular menstrual cycles, dysmenorrhoea). 34 patients (61.81%) had evidence of polycystic ovaries on ultrasound. (Table 5)

TABLE 6: Distance Visual Acuity Among the Study Groups

DVA	Case		Control	
	N	%	N	%
0.00	70	63.64	54	49.09
0.20	14	12.73	22	20.00
0.60	16	14.55	14	12.73
0.80	8	7.27	12	10.91
1.1	2	1.82	8	7.27
Total	110	100.00	110	100.00
Chi square 4.188, P value 0.381				

63.64% PCOS patients had an unaided distance visual acuity of 0.00 on the logmar scale whereas 49.09% controls had the same. (Table 6)

The maximum no. of patients had a distance visual acuity of 0.00 on the logmar scale in both the groups. The BCVA was 0.00 on the logmar scale in all our patients.

Figure 12: Distance Visual Acuity Among the Study Groups

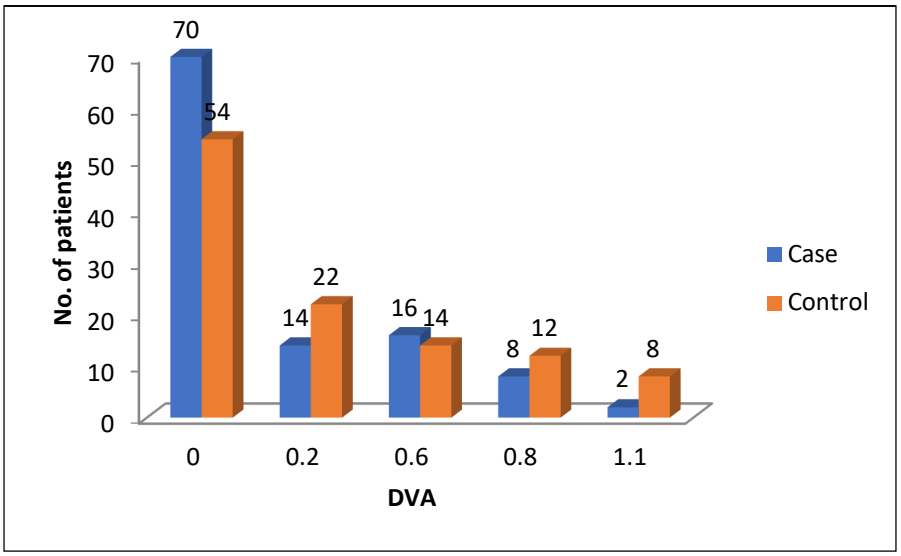


TABLE 7: IOP, CCT, SCHIRMER'S AND TBUT of the Study Groups

Variables		Case (Mean±SD)	Control (Mean±SD)	t value	p value
IOP	RE	14.13±2.65	13.69±2.36	0.913	0.363
	LE	13.56±2.57	14.31±2.65	1.496	0.137
CCT	RE	533.16±26.29	533.20±29.81	0.006	0.994
	LE	535.64±13.91	536.24±12.33	0.239	0.811
Schirmer test	RE	24.13±2.92	24.20±2.89	0.131	0.895
	LE	23.87±2.49	23.65±2.56	0.452	0.651
TBUT	RE	9.29±2.24	9.24±2.25	0.127	0.898
	LE	9.64±2.29	9.53±2.23	0.252	0.8

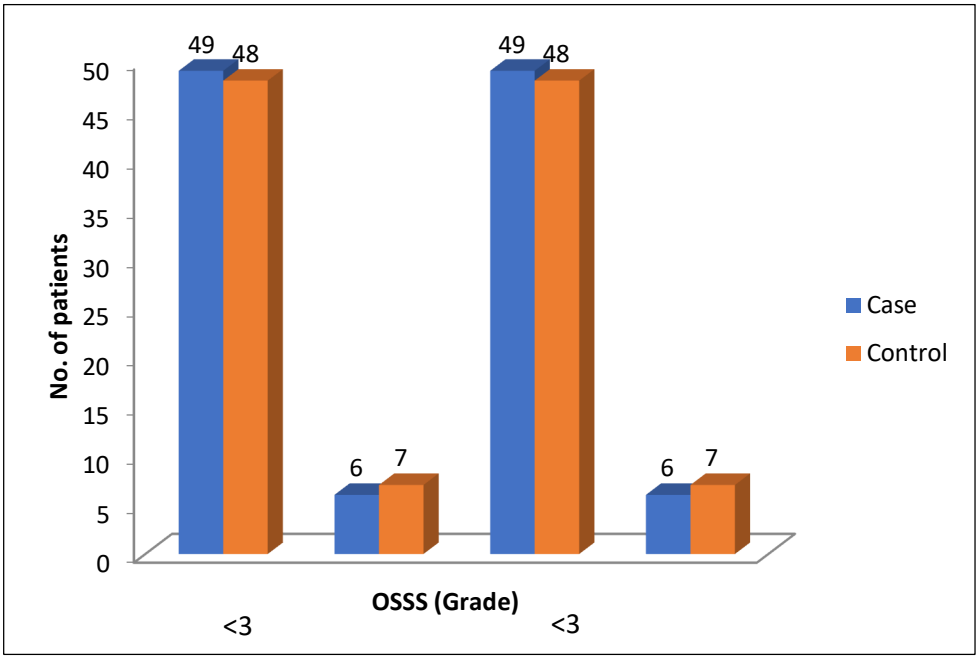
There was no significant difference between the IOP, CCT, Schirmer's test value and TBUT between the two groups. (Table 7)

TABLE 8: Ocular Surface Staining Score Among the Two Groups

OSSS (Grade)		Case		Control		chi square	p value
		N	%	N	%		
RE	<3	49	89.09	48	87.27	0.087	0.767
	>3	6	10.91	7	12.73		
LE	<3	49	89.09	48	87.27	0.087	0.767
	>3	6	10.91	7	12.73		

The ocular surface staining score was Grade 0 in 49 patients of the PCOS group and 48 patients of the control group. 6 patients in the case group and seven patients in the control group had a Grade of 1. (Table 8)

Figure 13: Ocular Surface Staining Score Among the Two Groups



The distribution of ocular surface training score was similar between the two groups and between the two eyes of all patients (Figure 13)

TABLE 9: Presence or Absence of MGD Among The two Groups

MGD		Case		Control		chi square	p value
		N	%	N	%		
RE	Present	7	12.73	6	10.91	0.087	0.767
	Absent	48	87.27	49	89.09		
LE	Present	7	12.73	6	10.91	0.087	0.767
	Absent	48	87.27	49	89.09		

The number of patients with MGD were similar in the two groups. The presence of MGD was found only in 7 patients in the PCOS group and 6 patients in the control group. (Table 9)

On dilated fundus examination of the patients, we found normal physiological findings in all patients. The C:D ratio ranged from 0.3 to 0.6:1 with a healthy neuroretinal rim. The retinal

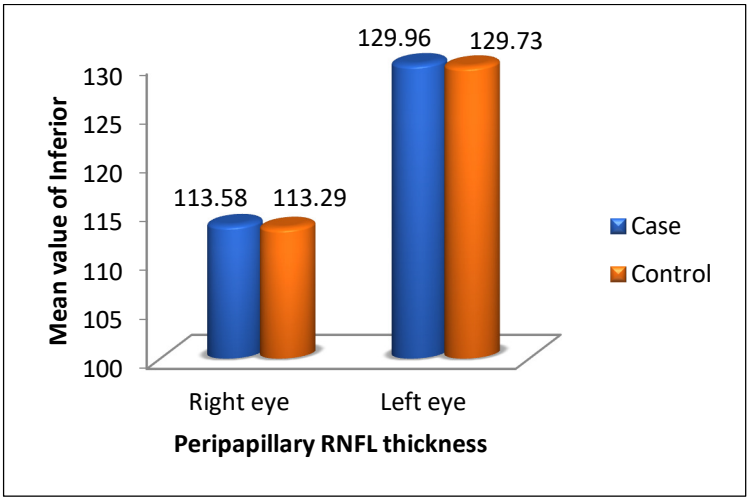
vasculature was normal in all patients and appearance of the background was within normal physiological limits. The foveal reflex was normal in all the patients.

TABLE 10: Peripapillary RNFL Thickness Among the Two Groups

Peripapillary RNFL thickness		Case (Mean±SD)	Control (Mean±SD)	t value	p value
Right eye	I	113.58±7.08	113.29±7.19	0.213	0.831
	S	106.89±13.05	104.91±11.44	0.846	0.398
	N	78.09±4.57	77.96±4.64	0.372	0.71
	T	94.98±5.56	94.53±6.05	0.41	0.682
Left eye	I	129.96±8.87	129.73±8.62	0.141	0.887
	S	119.35±4.35	118.82±4.49	0.625	0.533
	N	70.22±4.98	69.69±4.69	0.571	0.568
	T	68.04±9.41	67.76±9.31	0.152	0.578
Mean	I	121.77±5.32	121.50±4.64	0.276	0.782
	S	113.11±7.8	111.86±6.43	0.972	0.333
	N	74.15±3.48	73.72±3.46	0.645	0.52
	T	81.05±5.36	81.14±5.39	0.354	0.723

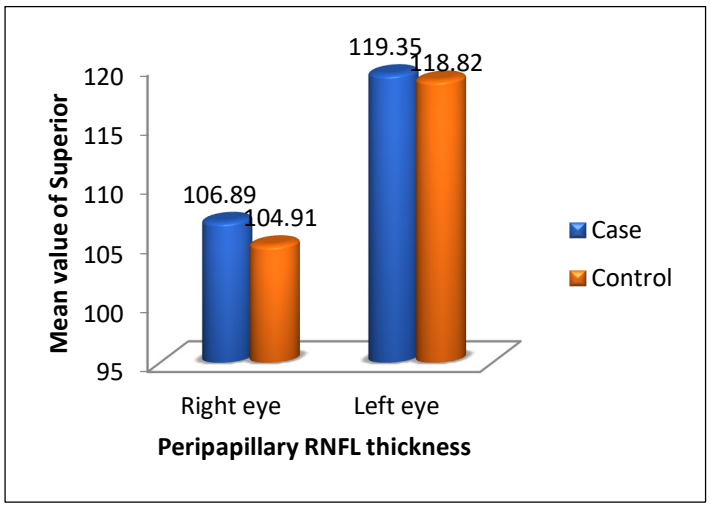
There was no significant difference between the peripapillary RNFL thickness between the two groups (Table 10)

Figure 14: Inferior Peripapillary Thickness Among the Two Groups



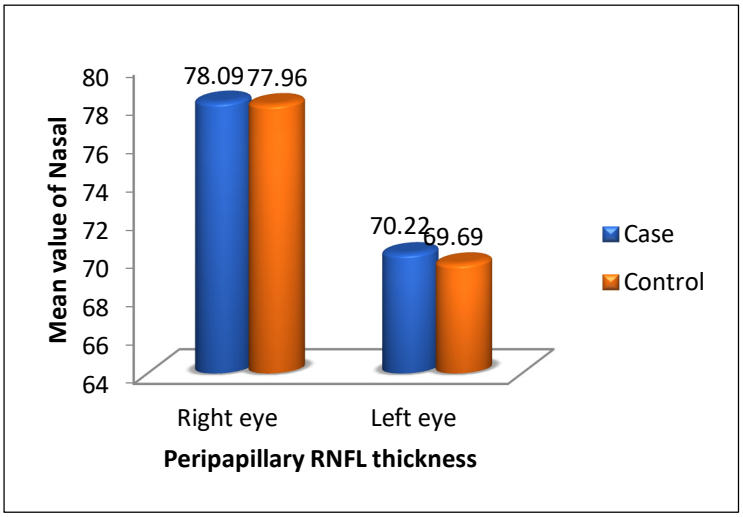
The mean peripapillary RNFL thickness in the inferior quadrant in the PCOS group was 121.77±5.32 in the PCOS group and 121.50±4.64 in the control group. It was found to be statistically insignificant. (Table 10) (Figure 14)

Figure 15: Superior Peripapillary Thickness Among the Two Groups



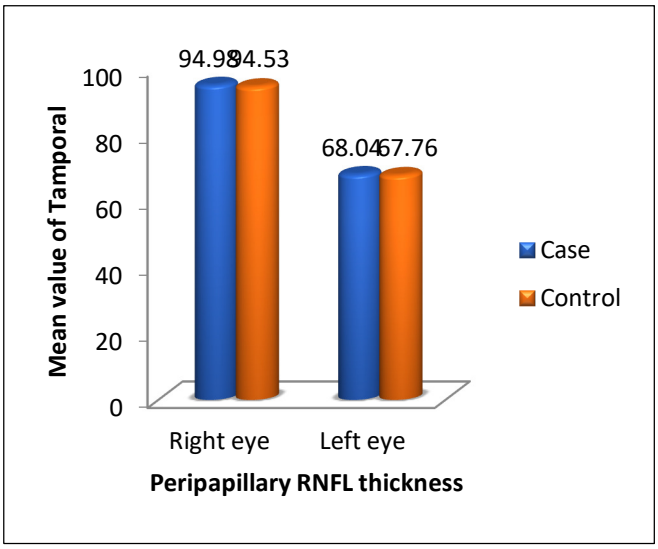
The mean peripapillary RNFL thickness in the superior quadrant in the PCOS group was 113.11±7.8 in the PCOS group and 111.86±6.43 in the control group. It was found to be statistically insignificant. (Table 10) (Figure 15)

Figure 16: Nasal Peripapillary Thickness Among the Two Groups



The mean peripapillary RNFL thickness in the nasal quadrant in the PCOS group was 74.15±3.48 in the PCOS group and 73.72±3.46 in the control group. It was found to be statistically insignificant. (Table 10) (Figure 16)

Figure 17: Temporal Peripapillary Thickness Among the Two Groups



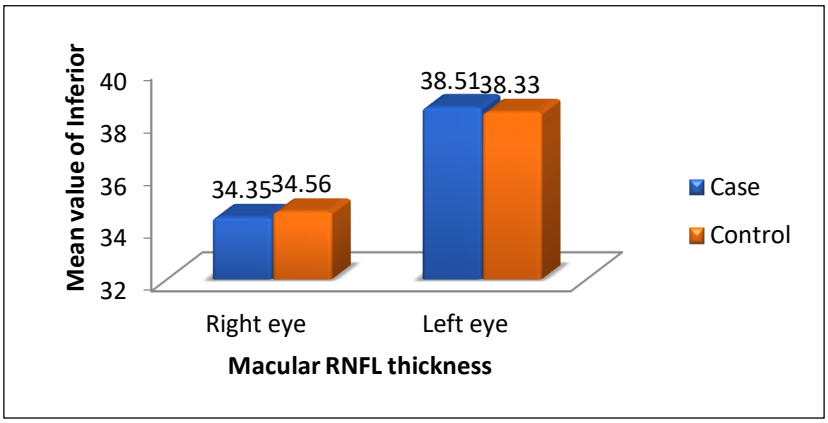
The mean peripapillary RNFL thickness in the temporal quadrant in the PCOS group was 81.05±5.36 in the PCOS group and 81.14±5.39 in the control group. It was found to be statistically insignificant. (Table 10) (Figure 17)

TABLE 11: Macular RNFL Thickness Among the Two Groups

Macular RNFL thickness		Case (Mean±SD)	Control (Mean±SD)	t value	p value
Right eye	I	34.35±2.70	34.56±2.46	0.442	0.659
	S	30.80±3.68	30.85±3.47	0.079	0.936
Left eye	I	38.51±3.80	38.33±3.95	0.246	0.806
	S	35.82±2.80	36.00±2.94	0.332	0.74
Mean	I	36.42±2.43	36.44±2.51	0.038	0.969
	S	33.30±2.28	33.42±2.36	0.266	0.79

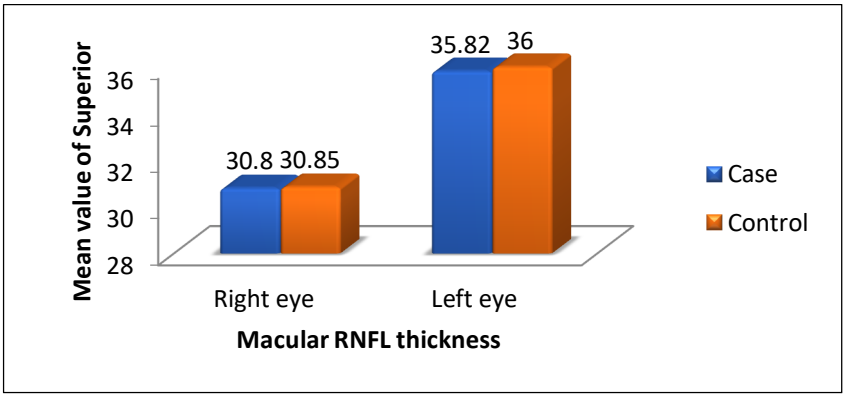
The Macular RNFL thickness was uniformly distributed between the two groups, with the mean in the inferior quadrant being 36.42±2.43 in the PCOS group and 36.44±2.51 in the control group. In the superior quadrant, the mean in the PCOS group was 33.30±2.28 and 33.42±2.36 in the control group. (Table 11)

Figure 18: Inferior Macular RNFL Thickness Among the Two Groups



There was no significant difference between the RNFL thickness in the inferior quadrant at the macula (Table 11) (Figure 18)

Figure 19: Superior Macular RNFL Thickness Among the Two Groups



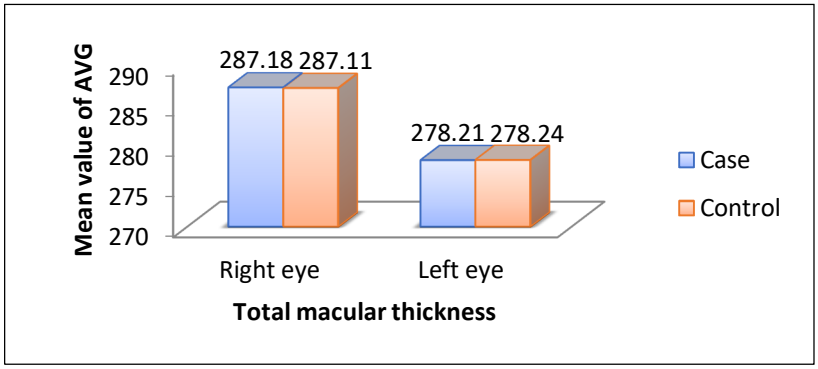
There was no significant difference between the RNFL thickness in the superior quadrant at the macula (Table 11) (Figure 19)

TABLE 12: Macular Thickness Among the Two Study Groups

Total Macular thickness		Case (Mean±SD)	Control (Mean±SD)	t value	p value
Right eye	AVG	287.18±6.20	287.11±6.21	0.061	0.951
	CMT	187.38±7.41	186.47±7.51	0.639	0.524
Left eye	AVG	278.21±5.35	278.24±5.70	0.02	0.983
	CMT	178.80±5.90	178.07±4.89	0.704	0.482
Mean	AVG	282.69±4.17	282.67±4.26	0.031	0.974
	CMT	183.09±5.33	182.77±4.94	0.833	0.406

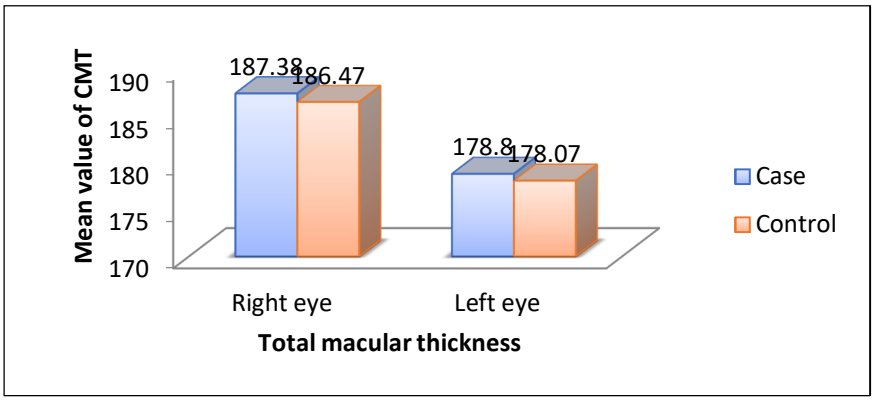
There was no significant difference between the macular thickness between the two groups. (Table 12)

Figure 20: Average Macular Thickness Among the Two Study Groups



The mean average macular thickness in the PCOS group was 282.69±4.17 and 282.67±4.26 in the control group. The difference was statistically insignificant. (Figure 20)

Figure 21: Central Macular Thickness Among the Two Study Groups



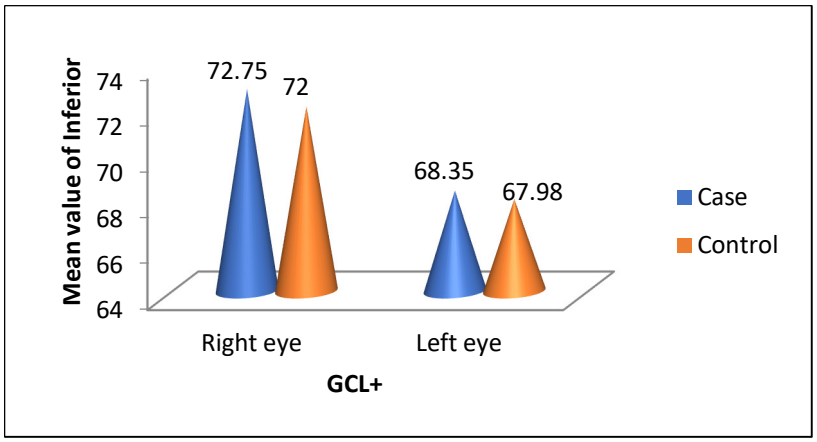
The mean central macular thickness in the PCOS group was 183.09±5.33 and 182.77±4.94 in the control group. The difference was statistically insignificant. (Table 12) (Figure 21)

TABLE 13: GCL + Thickness Among the Two Study Groups

GCL+		Case (Mean±SD)	Control (Mean±SD)	t value	p value
Right eye	I	72.75±8.58	72.00±8.15	0.467	0.641
	S	69.75±9.37	68.64±11.41	0.556	0.578
Left eye	I	68.35±7.56	67.98±7.48	0.253	0.800
	S	69.44±5.38	69.35±5.46	0.087	0.930
Mean	I	70.54±5.75	68.49±5.56	0.513	0.608
	S	69.59±5.72	68.99±6.53	0.512	0.609

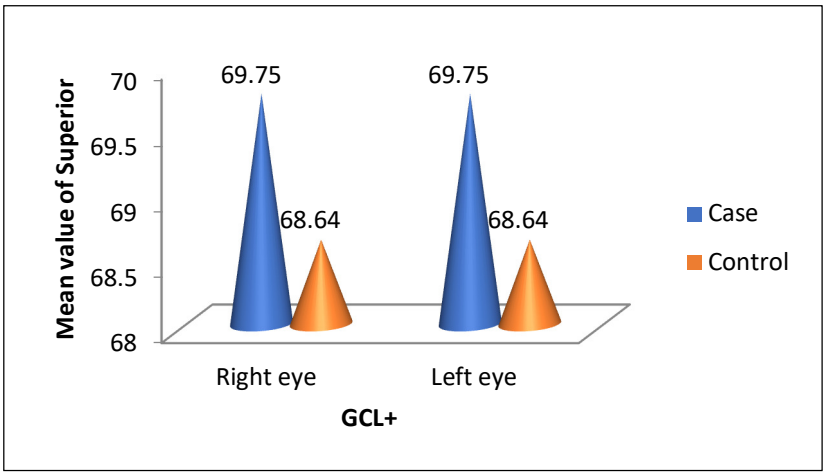
There was no significant difference between the GCL+ thickness (GCL + IPL) between the two study groups. (Table 13)

Figure 22: GCL+ Thickness in The Inferior Quadrant Among the Two Study Groups



The GCL+ thickness in the inferior quadrant was 70.54±5.75 in the PCOS group and 68.49±5.56 in the control group. (Figure 22) (Table 13)

Figure 23: GCL+ Thickness in The Superior Quadrant Among the Two Study Groups



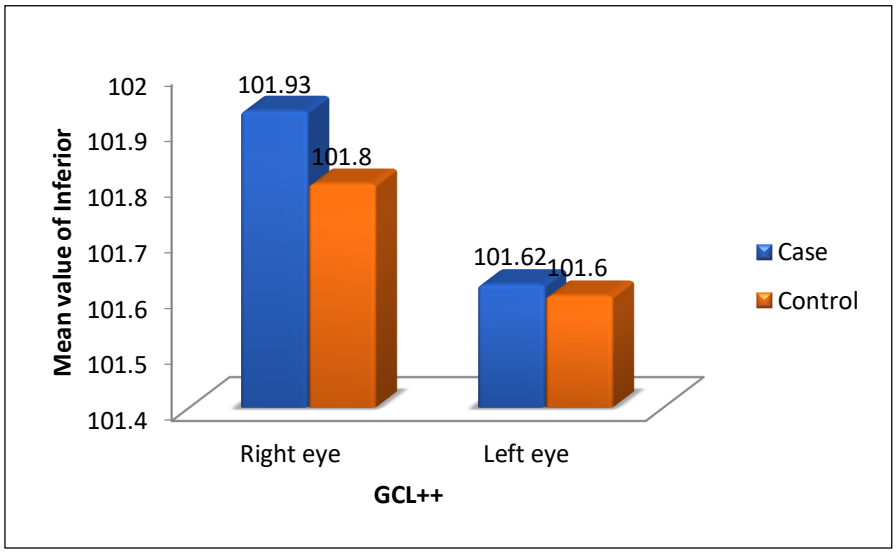
The GCL+ thickness in the superior quadrant was 69.59±5.72 in the PCOS group and 68.99±6.53 in the control group. (Figure 23) (Table 13)

TABLE 14: GCL ++ Thickness Among the Two Study Groups

GCL±±		Case (Mean±SD)	Control (Mean±SD)	t value	p value
Right eye	I	101.93±2.94	101.80±2.97	0.225	0.821
	S	99.49±4.12	99.40±4.10	0.116	0.907
Left eye	I	101.62±3.20	101.60±3.22	0.029	0.976
	S	100.47±3.07	100.73±2.99	0.440	0.66
Mean	I	101.77±2.26	101.7±2.38	0.164	0.869
	S	99.98±2.40	100.06±2.4	0.174	0.858

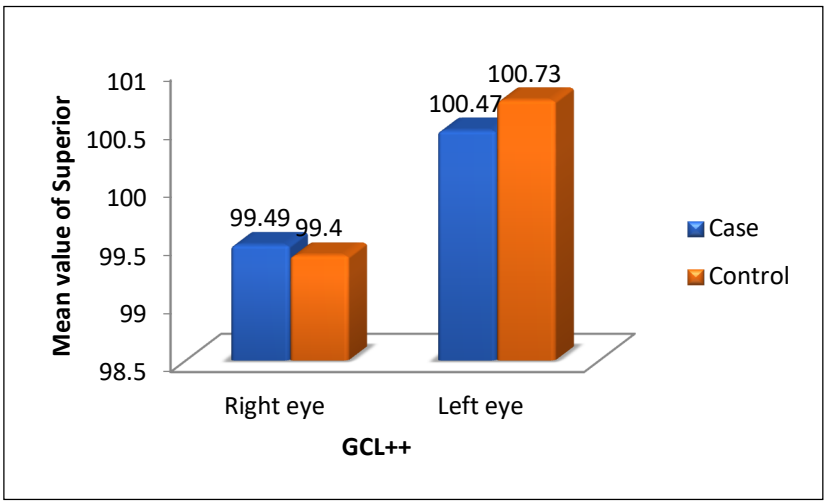
The mean GCL ++ thickness (RNFL + IPL + GCL) was similarly distributed between the two study groups. (Table 14)

Figure 24: GCL++ Thickness in The Inferior Quadrant Among the Two Study Groups



The mean GCL ++ thickness in the inferior quadrant was 101.77±2.26 in the PCOS group and 101.7±2.38 in the control group. (Table 14) (Figure 24)

Figure 25: GCL++ Thickness in The Superior Quadrant Among the Two Study Groups



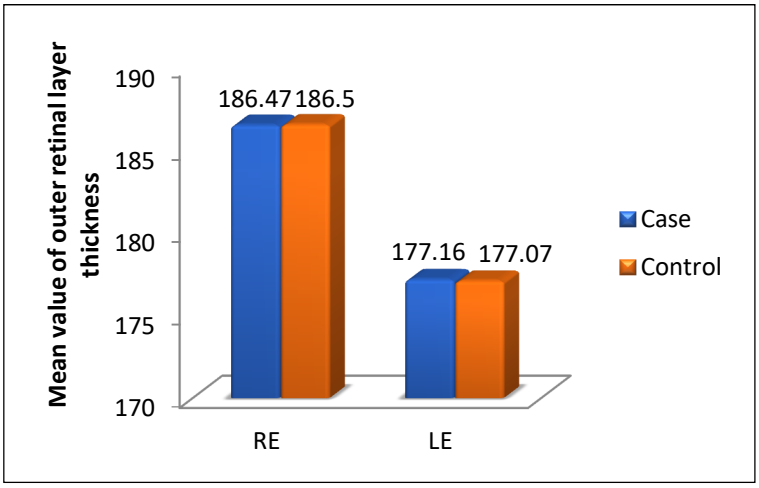
The mean GCL ++ thickness in the superior quadrant was 99.98±2.40 in the PCOS group and 100.06±2.4 in the control group. (Table 14) (Figure 25)

TABLE 15: Outer Retinal Layer Thickness Among the Two Study Groups

Outer retinal layer thickness	Case (Mean±SD)	Control (Mean±SD)	t value	p value
RE	186.47±6.20	186.50±6.16	0.03	0.975
LE	177.16±5.61	177.07±5.81	0.088	0.929
Mean	181.82±4.13	181.79±4.14	0.038	0.969

The outer retinal layer thickness which was similarly distributed between the two groups. (Table 15)

Figure 26: Outer Retinal Thickness Between the Two Groups



The outer retinal layer thickness in the PCOS group was 181.82±4.13 and in the control group was 181.79±4.14. (Table 15) (Figure 26)

TABLE 16: OCT Parameters Among the Two Groups

Variables		Case (Mean±SD)	Control (Mean±SD)	t value	p value
Peripapillary RNFL thickness	I	243.54±10.64	243.01±9.29	0.276	0.782
	S	226.23±14.16	223.72±12.86	0.972	0.333
	N	148.30±6.96	147.45±6.93	0.645	0.52
	T	163.01±10.73	162.29±10.78	0.354	0.723
Macular RNFL thickness	I	72.85±4.87	72.89±5.03	0.038	0.969
	S	66.61±4.57	66.85±4.73	0.266	0.79
Outer retinal layer thickness		363.64±8.26	363.58±8.28	0.038	0.969
Total Macular thickness	AVG	565.39±8.34	565.34±8.53	0.031	0.974
	CMT	366.18±10.67	364.54±9.89	0.833	0.406
GCL±	I	141.09±11.51	139.98±11.12	0.513	0.608
	S	139.18±11.44	137.98±13.07	0.512	0.609
GCL ±±	I	203.54±4.52	203.4±4.76	0.164	0.869
	S	199.96±4.81	200.12±4.80	0.174	0.858

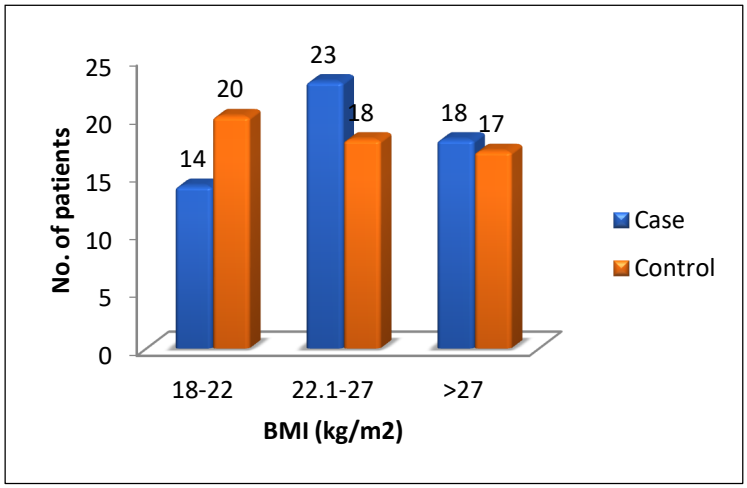
Above table displays the mean values of all OCT parameters among the two groups. All the OCT parameters were uniformly distributed between the two groups.

Table 17: Distribution of BMI Among the Two Study Groups

BMI (kg/m^2)	Case		Control	
	N	%	N	%
18-22	14	25.45	20	36.36
>22-27	23	41.82	18	32.73
>27	18	32.73	17	30.91
Total	55	100.00	55	100.00
Median	25.4		24.2	
Range	18.80-33		18-30.90	
Mean±SD	25.17±3.50		24.27±4.01	
t & p value	1.246, 0.215			

41.82% patients in the PCOS group had a BMI ranging from >22-27 kg/m2, whereas 32.73% patients in the control group had a BMI ranging from 18-22. The mean BMI in the PCOS group was 25.17±3.50 kg/m2 and the mean BMI in the control group was 24.27±4.01 kg/m2. Even though it was higher in the PCOS group, the difference was statistically insignificant. (Table 17)

Figure 27: Distribution of BMI Among the Two Study Groups



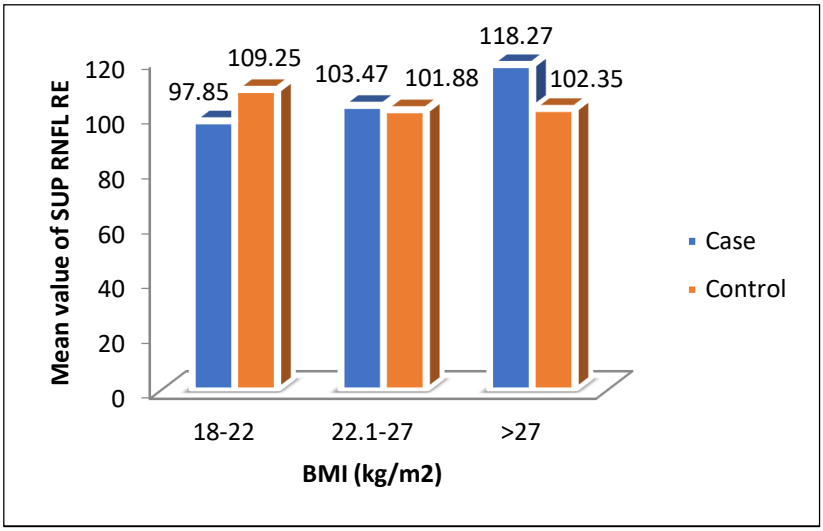
The maximum number of patients in the PCOS group belonged to BMI 18-22 whereas the maximum number of patients in the control group belonged to BMI >22-27 kg/m^2
(Figure 27)

TABLE 18: Superior RNFL Thickness (Right Eye) Among the Two Groups After Stratification According to BMI

BMI (kg/m^2)	SUP RNFL RE		t value	p value
	Case (Mean±SD)	Control (Mean±SD)		
18-22	97.85±11.55	109.25±9.89	3.084	0.004
22.1-27	103.47±7.91	101.88±10.08	0.566	0.574
>27	118.27±11.73	102.35±13.20	3.777	0.0006

After stratification according to BMI, the superior RNFL thickness was found to be significantly thicker in PCOS patients with BMI>27 kg/m^2 as compared to controls with BMI > 27 kg/m^2. (Table 18)

Figure 28: Superior RNFL Thickness (Right Eye) Among the Two Groups After Stratification According to BMI

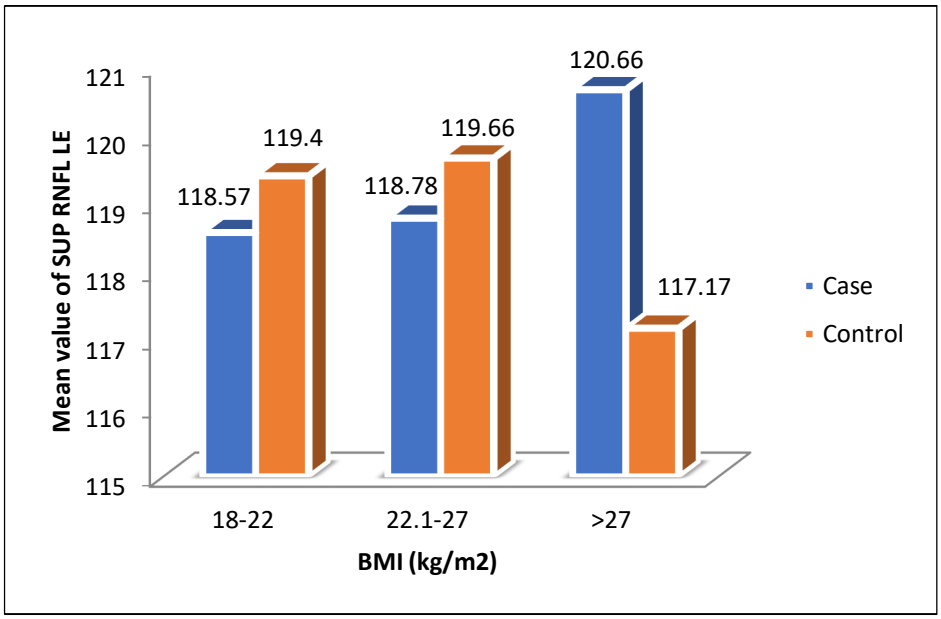


Patients with BMI>27 kg/m^2 have significantly thicker RNFL as compared to controls with BMI>27kg/m^2. (Table 18) (Figure 28)

TABLE 19: Superior RNFL Thickness (Left Eye) Among the Two Groups After Stratification According to BMI

BMI (kg/m2)	SUP RNFL LE		t value	p value
	Case (Mean±SD)	Control (Mean±SD)		
18-22	118.57±5.25	119.4±4.07	0.518	0.608
22.1-27	118.78±4.36	119.66±5.00	0.603	0.549
>27	120.66±3.39	117.17±4.14	2.733	0.01

Figure 29: Superior RNFL thickness (Left Eye) among the two groups after stratification according to BMI



After stratification according to BMI, the superior RNFL thickness was found to be significantly thicker in PCOS patients with BMI>27 kg/m^2 as compared to controls with BMI > 27 kg/$m^{2.}$ (Table 19) (Figure 29)

Table 20: Serum Testosterone Values Among the PCOS Patients

	Case (Mean±SD)	Range (mg/dl)	No of patients
Testosterone (ng/dl)	138.3 ± 23.2	<70	19 (34.54%)
		>70	36 (65.45%)

The mean serum testosterone level in patients with PCOS was 141.3 ± 23.2. 65.45% patients had a serum testosterone level more than 70 ng/dl. (Table 20).

Table 21: Lipid Profile of the PCOS Patients

	Case (Mean±SD)	Range (mg/dl)	No of patients
HDL (mg/dl)	43.4 ± 15.6	>50	24 (46.63%)
		<50	31 (56.36%)
LDL (mg/dl)	99.5 ± 21.7	<100	26 (47.27%)
		>100	29 (52.72%)
Total Cholesterol (mg/dl)	198.7 ± 27.3	<200	27 (49.09%)
		>200	28 (50.90%)

The mean HDL cholesterol in patients with PCOS was 38.1 ± 15.6. The mean LDL cholesterol in PCOS patients was 98.4 ± 21.7 and the mean total cholesterol in PCOS patients was 153.6 ± 27.3 (Table 21)

DISCUSSION

DISCUSSION

The aim of this study was to compare Optical Coherence Tomography based Retinal Nerve Fibre Layer and Ganglion Cell Layer thickness at the posterior pole, total macular thickness in women with Polycystic Ovarian Syndrome vs healthy reproductive age group females.

The study recorded the RNFL thickness at the disc and the macula, the total macular thickness, the GCL + and GCL ++ . Using these values, the outer retinal thickness was calculated.

The patients were then stratified in three groups according to BMI.

There was no significant difference between the total macular thickness between the two groups. Jose Edvan et al. conducted a major study and discovered that in the absence of insulin resistance, there were no statistically significant variations in the means of total macular thickness measures between the groups tested. [28]

Our study found no significant difference in the RNFL thickness at the disc and the macula. This could be due to the fact that patients in our study were relatively younger which means that they were diagnosed earlier.

However, on stratification according to BMI, we found that the superior RNFL thickness in the PCOS group was significantly thicker than the control group.

The RNFL in patients with PCOS were significantly thicker in the superior quadrant and those with BMI > 27 kg/m2. This was in correspondence with the studies conducted earlier by Jose Edvan et al, Demir et al and Acmaz et al [28,56] who also found a similar result. This could be due to the fact that since androgens have a trophic effect on the nerves and this could suggest that PCOS has a protective effect on the RNFL. In PCOS, the hyperestrogenemic impact is unbalanced by progesterone, resulting in alterations in the target organs. Estrogen-induced proteins in target tissues (such as cathepsin D, alpha-2 macroglobulin, and aromatase cytochrome P45) are engaged in critical cellular tasks such as differentiation, proliferation, and maturation, as detailed by Ogueta et al.[40] As expected, ocular tissues such as the ciliary body and retinal pigment epithelium show the presence of most of these proteins.

Our study found no significant difference between the RNFL layer thickness at the macula. This was in contrast to the study conducted by Jose Edvan et al [30] where they found significant thickening in the temporal inner macula (TIM), the inferior inner macula (IIM), the nasal inner macula (NIM), and the nasal outer macula (NOM). The nasal outer macula (NOM) and temporal outer macula (TOM) were significantly thicker in the PCOS group than in the control group, according to another study conducted by Acmaz et al. The PCOS group, on the other hand, had considerably lower fovea centre thickness and temporal inner macula than the healthy control group. Therefore it seems that the effect of PCOS at the macula is not clear needs further studies.

We also did not find any significant difference in the ganglion cell layer thickness or the outer retinal layer thickness. Demir et al also conducted a study where they compared the GCC thickness between the PCOS and control groups and found no significant difference between the same. There, however, have not been any previous studies comparing the outer retinal layer thickness in PCOS patients with that of healthy reproductive age group females. Acmaz et al measured the choroidal thickness in patients with PCOS using an EDOCT and found a significantly thicker choroid in patients with PCOS. Our study was however limited by the use an SD OCT which does not measure the choroidal thickness.[28,56]

PCOS is characterized by an menstrual irregularity, ovulatory dysfunction, and hyperandrogenism. Eye changes similar to those found in diabetes can theoretically be found in PCOS patients due to its metabolic alterations, insulin resistance. However we did not find any diabetic eye changes in our PCOS patients.

In addition to the above, we also assessed the IOP, CCT, Schirmer's and TBUT in these patients.

There was no significant difference in the IOP and CCT among the two groups. Androgen hormones act on meibomian glands and regulate gene expression and lipid synthesis in them.[25] Meibomian gland dysfunction and evaporative dry eye syndrome can be caused by androgen deprivation. Estrogen inhibits the function of the meibomian glands, which may contribute to the development of evaporative dry eye.[25] This was consistent with the studies done by Karaca et al and Demir et al [25,28] who did not find any significant difference between the IOP of the groups. However, in the study done by Karaca et al, a significant difference

was found between the CCT among the two group where the CCT in patients was found to be significantly thicker in PCOS patients.

Previous studies conducted by Bonini et al and Yavas et al [58,60] found no significant difference between the values of Schirmer's test between the two study groups. Our study also failed to find a significant difference. However, in the study conducted by Karaca et al[25], a significantly lower Schirmer's test value was found in PCOS patients. Interestingly, the TBUT was found to be significantly lower in PCOS patients in all three studies, unlike our study. This could be explained by the fact that factors like high temperature and windy climate which are present in our study region, would cause patients of dry eye to be equally distributed in our study and control groups. All in all, the higher prevalence of dry eye in our study region could be a confounding factor.

We also assessed the OSSS and found no significant difference between the two groups. This was consistent with the above findings. However, no other studies have evaluated the same.

Our results suggest that hyperandrogenemia can modify the retinal nerve fibre layer in patients with PCOS. Treatment of PCOS can probably ameliorate symptoms of dry eye in these patients. However, further studies need to be done to with a larger sample size to confirm the posterior segment changes in these patients and to compare the effect of treatment on the parameters that we assessed.

CONCLUSION & LIMITATIONS

CONCLUSION

1. A total of 110 patients were enrolled in the study. 55 patients were diagnosed cases of PCOS according to Rotterdam's Criteria which formed the study group and 55 patients were healthy reproductive age group females.
2. The mean age in the PCOS group was 26 years. This was significantly lower than the control group where the mean age was 32 years ($p<0.0001$).
3. The mean age at menarche was 12 years in both the groups. 38% patients in the PCOS group had menarche at the age of 12 years whereas 31% patients in the control group had menarche at the same age.
4. There was no significant difference between the IOP, CCT, Schirmer's and TBUT between the two groups.
5. The ocular surface staining score was 0 in 49 patients of the PCOS group and 48 patients of the control group. 6 patients in the case group and seven patients in the control group had a score of 1.
6. The number of patients with MGD were similar in the two groups. The presence of MGD was found only in 7 patients in the PCOS group and 6 patients in the control group.
7. The mean peripapillary RNFL thickness in the inferior quadrant in the PCOS group was 121.77±5.32 in the PCOS group and 121.50±4.64 in the control group. It was found to be statistically insignificant.
8. The mean peripapillary RNFL thickness in the superior quadrant in the PCOS group was 113.11±7.8 in the PCOS group and 111.86±6.43 in the control group. It was found to be statistically insignificant.
9. The mean peripapillary RNFL thickness in the nasal quadrant in the PCOS group was 74.15±3.48 in the PCOS group and 73.72±3.46 in the control group. It was found to be statistically insignificant.
10. The mean peripapillary RNFL thickness in the temporal quadrant in the PCOS group was 81.05±5.36 in the PCOS group and 81.14±5.39 in the control group. It was found to be statistically insignificant.
11. The Macular RNFL thickness was uniformly distributed between the two groups, with the mean in the inferior quadrant being 36.42±2.43 in the PCOS group and 36.44±2.51 in the control group. In the superior quadrant, the mean in the PCOS group was 33.30±2.28 and 33.42±2.36 in the control group.

12. The mean average macular thickness in the PCOS group was 282.69±4.17 and 282.67±4.26 in the control group. The difference was statistically insignificant.
13. The mean central macular thickness in the PCOS group was 183.09±5.33 and 182.77±4.94 in the control group. The difference was statistically insignificant
14. The GCL+ thickness in the superior quadrant was 69.59±5.72 in the PCOS group and 68.99±6.53 in the control group and in the inferior quadrant was 70.54±5.75 in the PCOS group and 68.49±5.56 in the control group.
15. The mean GCL ++ thickness in the inferior quadrant was 101.77±2.26 in the PCOS group and 101.7±2.38 in the control group and thickness in the superior quadrant was 99.98±2.40 in the PCOS group and 100.06±2.4 in the control group. The difference was statistically insignificant.
16. The outer retinal layer thickness in the PCOS group was 181.82±4.13 and in the control group was 181.79±4.14.
17. 41.82% patients in the PCOS group had a BMI ranging from >22-27 kg/m2, whereas 32.73% patients in the control group had a BMI ranging from 18-22. The mean BMI in the PCOS group was 25.17±3.50 kg/m2 and the mean BMI in the control group was 24.27±4.01 kg/m2. Even though it was higher in the PCOS group, the difference was statistically insignificant.
18. After stratification according to BMI, the superior RNFL thickness was found to be significantly thicker in PCOS patients with BMI>27 kg/m^2 as compared to controls with BMI > 27 kg/m^2
19. Patients with BMI>27 kg/m^2 have significantly thicker RNFL as compared to controls with BMI>27kg/m^2.

LIMITATIONS

1. Our study was limited by a small sample size.
2. Since the OCT machine used in our study was a spectral domain OCT, we could not measure the choroidal thickness.
3. We only stratified our patients according to BMI and not insulin resistance. Insulin resistance is a better measure of the metabolic status of the patient.
4. The outer retinal thickness was calculated manually rather than by a machine software.

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ANNEXURES

ANNEXURE I

ETHICAL CLEARANCE CERTIFICATE

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2020/2064 **Date: 01/01/2020**

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: **AIIMS/IEC/2019-20/956**

Project title: **"A study of retinal changes in women with Polycystic Ovarian Syndrome"**

Nature of Project: **Research Project**

Submitted as: **M.D. Dissertation**

Student Name: **Dr.Sakshi Shiromani**

Guide: **Dr.Kavita R. Bhatnagar**

Co-Guide: **Dr.Pratibha Singh & Dr.Suwarna Suman**

This is to inform that members of Institutional Ethics Committee (Annexure attached) met on **23-12-2019** and after through consideration accorded its approval on above project. Further, should any other methodology be used, would require separate authorization.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

On behalf of Ethics Committee, I wish you success in your research.

Dr. Pravesh Sharma
Member secretary
Institutional Ethics Committee
AIIMS,Jodhpur

Enclose:
1. Annexure 1

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Basni Phase-2, Jodhpur, Rajasthan-342005, Website: www.aiimsjodhpur.edu.in, **Phone:** 0291-2740741 Extn. 3109
Email: ethicscommittee@aiimsjodhpur.edu.in

Annexure 1

Institutional Ethics Committee
All India Institution of Medical Sciences, Jodhpur

Meeting of Institutional Ethics committee held on **23-12-2019 at 10:00** AM at Committee Room, Admin Block AIIMS Jodhpur.

Following members were participated in the meeting:-

S/No.	Name of Member	Qualification	Role/Designation in Ethics Committee
1.	Dr. F.S.K Barar	MBBS, MD (Pharmacology)	**Chairman**
2.	Justice N.N Mathur	LLB	Legal Expert
3.	Dr. Varsha Sharma	M.A (Sociology)	Social Scientist
4.	Mr. B.S.Yadav	B.Sc., M.Sc. (Physics), B.Ed.	Lay Person
5.	Dr. K.R.Haldiya	MD (General Medicine)	Clinician
6.	Dr. Arvind Mathur	MBBS, MS (General Medicine)	Clinician
7.	Dr. Surajit Ghatak	MBBS, MS (Anatomy)	Basic Medical Scientist
8.	Dr. Vijaya Lakshmi Nag	MBBS, MD (Microbiology)	Basic Medical Scientist
9.	Dr. Sneha Ambwani	MBBS, MD (Pharmacology)	Basic Medical Scientist
10.	Dr. Kuldeep Singh	MBBS, MD (Paediatric), DM (General Medicine)	Clinician
11.	Dr. Abhinav Dixit	MBBS, MD (Physiology), DNB (Physiology)	Basic Medical Scientist
12.	Dr. Pradeep Kumar Bhatia	MBBS, MD (Anaesthesiology)	Clinician
13.	Dr. Tanuj Kanchan	MBBS, MD (Forensic Medicine)	Basic Medical Scientist
14.	Dr. Pankaj Bhardwaj	MBBS, MD (CM&FM)	Clinician
15.	Dr. Praveen Sharma	M.Sc., Ph.D. (Biochemistry)	Member Secretary

Dr. Praveen Sharma
Member Secretary
Institutional Ethics Committee
AIIMS,Jodhpur

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ANNEXURE II

DATA COLLECTION SHEET

Group 1(Study Group) € **Group 2(Comparison Group) □**

DATE:

NAME:

AGE:

REGISTRATION NUMBER:

ADDRESS:

CONTACT NUMBER:

LAST MENSTRUAL PERIOD (LMP):

AGE AT MENARCHE:

PRIMARY COMPLAINTS: DURATION:

PAST HISTORY:

PERSONAL HISTORY:

FAMILY HISTORY:

OCULAR EXAMINATION:

S.NO		RIGHT EYE	LEFT EYE
1	VISUAL ACUITY (UNAIDED) Distance Near		
2	VISUAL ACUITY (BEST CORRECTED)		
3	REFRACTION		
4	IOP(mm Hg)		

5	CCT(µm)		
6	SCHIRMER'S TEST(mm)		
7	OCULAR SURFACE STAINING SCORE(grading)		
8	TEAR FILM BREAK-UP TIME(s)		
9	MEIBOMIAN GLAND DYSFUNCTION(grading)		

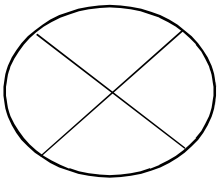
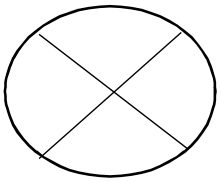
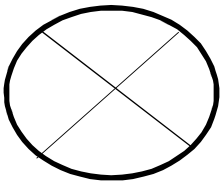
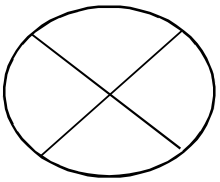
ANTERIOR SEGMENT EVALUATION:

RIGHT EYE	LEFT EYE

FUNDUS EXAMINATION

RIGHT EYE	LEFT EYE

OCT FINDINGS:

S.NO		RIGHT EYE	LEFT EYE
1	DISC RNFL(µm)		
2	MACULAR RNFL(µm)		
3	TOTAL MACULAR THICKNESS(µm)		
4	GCL+(µm)	SUPERIOR INFERIOR	SUPERIOR INFERIOR
5	GCL++(µm)	SUPERIOR INFERIOR	SUPERIOR INFERIOR

ANNEXURE III

All India Institute of Medical Sciences

Jodhpur, Rajasthan

Informed Consent Form

Title of Thesis/Dissertation: A study of retinal changes in women with Polycystic Ovarian Syndrome.

Name of PG Student: Dr.Sakshi Shiromani Tel. No. 9711299706/_____

Patient/Volunteer Identification No._____

I, _____

D/o_____ R/o give my full, free, voluntary consent to be a part of the study "A study of retinal changes in women with Polycystic Ovarian Syndrome", the procedure and nature of which has been explained to me in my own language to my full satisfaction. I confirm that I have had the opportunity to ask questions. I understand that my participation is voluntary and am aware of my right to opt out of the study at any time without giving any reason. I understand that the information collected about me and any of my medical records may be looked at by responsible individual from Department of Ophthalmology, ALL INDIA INSTITUTE OF MEDICAL SCIENCES (AIIMS) or from regulatory authorities. I give permission for these individuals to have access to my records.

Signature/Left thumb impression

This to certify that the above consent has been obtained in my presence.

Date: _____ Place: _____

Signature of PG Student

Witness 1	Witness 2
Signature	Signature
Name: _____	Name: _____
Address: _____	Address: _____
Phone no_____	Phone no_____

ANNEXURE IV

अखिल भारतीय चिकित्सा विज्ञान संस्थान

जोधपुर, राजस्थान

सूचित सहमति प्रपत्र

थीसिस/निबंध का शीर्षक: पॉलीसिस्टिक ओवेरियन सिंड्रोम वाली महिलाओं में रेटिना में बदलाव का अध्ययन।

पीजी छात्रा का नाम: डॉ. साक्षी शिरोमणि

दूरभाष। संख्या 9711299706 /

रोगी / स्वयंसेवी की पहचान._____

मैं, _____पुत्री_____अध्ययन का एक हिस्सा बनने के लिए मेरी पूर्ण, स्वतंत्र, स्वैच्छिक सहमति व्यक्त करती हूँ। थीसिस / निबंध का शीर्षक "पॉलीसिस्टिक ओवेरियन सिंड्रोम वाली महिलाओं में रेटिना में बदलाव का अध्ययन"

जिस प्रक्रिया और प्रकृति को मुझे अपनी पूरी संतुष्टि के लिए अपनी भाषा में समझाया गया है मैं पुष्टि करती हूं कि मुझे प्रश्न पूछने का अवसर मिला है।

मैं समझती हूं कि मेरी भागीदारी स्वैच्छिक है और मुझे किसी भी कारण दिए बिना किसी भी समय अध्ययन से बाहर निकलने के मेरे अधिकार की जानकारी है।

मैं समझती हूं कि मेरे और मेरे मेडिकल रिकॉर्ड के बारे में एकत्रित की गई जानकारी को नेत्र विज्ञान विभाग, अखिल भारतीय चिकित्सा विज्ञान संस्थान से जिम्मेदार व्यक्ति द्वारा देखा जा सकता है। मैं इन व्यक्तियों को अपने अभिलेखों तक पहुंच के लिए अनुमति देती हूं।

हस्ताक्षर / बाएं अंगूठे का छाप

यह प्रमाणित करने के लिए कि मेरी उपस्थिति में उपरोक्त सहमति प्राप्त की गई है।

तारीख : _____स्थान: _____

पीजी छात्र के हस्ताक्षर

1. साक्षी 1	2. साक्षी 2
हस्ताक्षर :	हस्ताक्षर:
नाम: _____	नाम: _____
पता:_____	पता: _____
फ़ोन नंबर:_____	फ़ोन नंबर:_____

ANNEXURE V

PATIENT INFORMATION SHEET

Title of Thesis/Dissertation: A study of retinal changes in women with Polycystic Ovarian Syndrome.

You are invited to take part in this research study. Before you decide whether or not to take part it is important for you to understand why the research is being done and what will it involve. Please take your time to read the information and then decide. Queries if any will be addressed .This study aims to compare Optical Coherence Tomography based Retinal Nerve Fibre Layer thickness and Ganglion Cell Layer thickness at the posterior pole, and total macular thickness in women with Polycystic Ovarian Syndrome vs healthy reproductive age group females.

1) Why have I been chosen to take part in the study?

You have been chosen to take part in the study because you are a known case of polycystic ovarian syndrome. You will be evaluated for different parameters as specified in the title of the study apart from a basic ophthalmological examination. In case you do not belong to the study group, you have been chosen for the study because you are a healthy reproductive age female and you belong to the comparison group.

2) What is the purpose of the study?

The purpose of the study is to carry out a basic ophthalmological examination in PCOS patients. Basic anterior segment parameters including the IOP, CCT, Schirmer's Test, ocular surface staining and tear break up time will be done. A dilated fundus examination will be done. The posterior segment pictures will be taken on an OCT machine and compared with healthy reproductive age group females. The main aim is to find out a significant difference, if any, and devise preventive strategies for visual impairment in these patients.

3) Do I have to take part in the study?

It is up-to you to decide whether or not to take part in the study. In case you decide to take part, you will be given the information sheet and will be asked to sign the consent form.

If you decide to take part, you can still withdraw your consent anytime in the study without giving any reasons.

4) What will happen to me if I take part in the research?

This study is a cross sectional study which means that it is a onetime screening. You will be subjected to a history taking and examination. The examination will involve measuring your IOP, CCT, Schirmer's Test, ocular surface staining and tear break up time. You will be assessed for Meibomian Gland Dysfunction. A dilated fundus examination will be done .You will then be examined on a slit lamp to evaluate your anterior segment. This will be followed by Ocular Coherence Tomography Imaging where the thickness of your nerve fibre layer of retina around the disc and macula will be evaluated. In addition to this, the ganglion cell layer and inner plexiform layer thickness will also be evaluated. All these procedures are non-invasive.

5) What do I have to do?

You will have to sign an informed consent form and read the patient information sheet provided to you. You will have to cooperate for IOP, CCT, Schirmer's Test, ocular surface staining, Tear Break Up Time, assessment for Meibomian Gland Dysfunction, remaining anterior segment examination; and posterior segment examination and imaging on OCT machine. This is a cross sectional study, so no follow up from your side will be required.

6) What are the possible benefits of taking part in the study?

PCOS can cause changes in the anterior and posterior segment of the eye, which many a times go unnoticed. Your anterior and posterior segment parameters will be evaluated and you will be screened for abnormalities in all those parameters. Moreover, if any significant findings are found after evaluation, you will be subjected to preventive strategies and you will be a candidate for early treatment, if required.

7) What are the possible side effects of taking part in the study?

There are no additional side effects of taking part in the study.

8) Will my data be kept confidential?

Your medical records and demographic data will be disclosed only to the researcher, treating physician and concerned authorities.

ANNEXURE VI

रोगी सूचना पत्रक

थीसिस / निबंध का शीर्षक : पॉलीसिस्टिक ओवेरियन सिंड्रोम वाली महिलाओं में रेटिना में बदलाव का अध्ययन ।

आपको इस शोध अध्ययन में भाग लेने के लिए आमंत्रित किया जाता है।भाग लेना है या नहीं, यह तय करने से पहले यह आपके लिए समझना महत्वपूर्ण है कि शोध क्यों किया जा रहा है और इसमें क्या शामिल होगा। कृपया जानकारी पढ़ने और वि र तय करने के लिए अपना समय लें। किसी भी प्रश्न को संबोधित किया जाएगा। इस अध्ययन का उद्देश्य पीछे के पोल पर रेटिनल नर्व ा ाइबर लेयर मोटाई पर आधारित ऑप्टिकल कॉइरेंस ोमोग्राफी, गैंग्लियन सेल लेयर की मोटाई और पॉलीसिस्टिक ओवेरियन सिंड्रोम बनाम स्वस्थ प्रजनन आयु समूह महिलाओं के साथ महिलाओं में कुल मैक्युलर मोटाई की तुलना करना है।

1) अध्ययन में भाग लेने के लिए मुझे क्यों चुना गया है?

आपको अध्ययन में भाग लेने के लिए चुना गया है क्योंकि आप पॉलीसिस्टिक डिम्बग्रंथि सिंड्रोम के एक ज्ञात मामले हैं। आपको एक बुनियादी नेत्र विज्ञान परीक्षा के अलावा अध्ययन के शीर्षक में निर्दिष्ट विभिन्न मापदंडों के लिए मूल्यांकन किया जाएगा। यदि आप अध्ययन समूह से संबंधित नहीं हैं, तो आपको अध्ययन के लिए चुना गया है क्योंकि आप एक स्वस्थ प्रजनन आयु की महिला हैं और आप तुलना समूह से संबंधित हैं।

2) अध्ययन का उद्देश्य क्या है?

अध्ययन का उद्देश्य पीसीओएस रोगियों में एक बुनियादी नेत्र परीक्षा करना है। एक ं डस परीक्षा होगी| पीछे के खंड के चित्र ओ. सी. ी मशीन पर लिए जाएंगे और उनकी तुलना स्वस्थ प्रजनन आयु समूह की महिलाओं के साथ की जाएगी। आईओपी, सीसीटी और शिमर टेस्ट, आंसू फिल्म की शिथिलता सहित बुनियादी पूर्वकाल खंड पैरामीटर भी किए जाएंगे। मुख्य उद्देश्य इन रोगियों में दृश्य हानि के लिए एक महत्वपूर्ण अंतर, यदि कोई हो, और निवारक रणनीतियों का पता लगाना है।

3) क्या मुझे अध्ययन में हिस्सा लेना जरूरी है?

यह तय करना है कि आपको भाग लेना है या नहीं। यदि आप भाग लेने का निर्णय लेते हैं तो आपको सूचना पत्र दिया जाएगा और सहमति पत्र पर हस्ताक्षर करने के लिए कहा जाएगा। यदि आप भाग लेने

क□निर्णय लेते हैं तो आप बिन□किसी कर□ण के अध्ययन में कभी भी अपनी सहमति व□ास ले सकते हैं।

4) यदि मैं अध्ययन में भ□ा लेत□हूं तो मेरे स□ा क्य□होग□?

यह अध्ययन एक क्रॉस सेक्शनल अध्ययन है जिसक□अर्थ है कि यह एक ब□ार की स्क्रीनिंग है। आप एक इतिह□ास लेने और परीक्ष□के अधीन होंगे। परीक्ष□में आपके आईओपी, सीसीट□ी और शिमर ट□ेस्ट, आंसू फि□ल्म की शिथिलत□शा□मिल होंगे। फि□र आपको अपने पूर्वक□ल खंड क□संक्षेप में मूल्यांक□न करने के लिए एक स्लि□ लैंप पर जां□च की जाए□गी। आपको मीबोमियन ग्लैंड डिस□ंक्शन के लिए मूल्यांक□न किय□जाए□ग□ एक पतल□ं डस परीक्ष□होगी| इसके बाद□ एक इमेजिंग होती है, जहां□डिस्क और मैक्युल□के चारों ओर रेटि□न□की आपकी तंत्रिक□□ □इबर परत की मो□ाई क□मूल्यांक□न किय□ जाए□ग□ इसके अलाव□, न□ीग्रन्थि सेल परत और आंतरिक परत की मो□ाई क□भी मूल्यांक□न किय□ जाए□ग□ ये सभी प्रक्रियाएं गैर-आक्र□मक हैं।

5) मुझे क्य□करन□होग□?

आपको आईओपी, सीसीट□ी और शिमर के ट□ेस्ट और आंसू फिल्म की शिथिलता, पोस्टीरियर सेगमें□ इमेजिंग के लिए सहयोग करन□होग□ आपको एक सूचित सहमति □ ॉर्म पर हस्त□ार करन□होग□और आपको प्रद□ा की गई रोगी सूचन□पत्र को पढ़न□होग□ यह एक क्रॉस सेक्शनल अध्ययन है, इसलिए आपकी ओर से किसी भी अनुवर्ती कार्र□वाई की आवश्यकत□नहीं होगी।

6) अध्ययन में भ□ा लेने के संभ□ावित ल□ा क्य□हैं?

पीसीओएस आंख के पूर्वकाल और पीछे के खंड में परिवर्तन का कारण बन सकता है, जो कई बार किसी का ध्यान नहीं जाता है। आपके पूर्वक□ल और पीछे के खंड म□ादंडों क□मूल्यांक□न किय□जाए□ग□ और आपको उन सभी म□ादंडों में अस□ा□मान्यत□ओं के लिए स्क्रीन किय□जाए□ग□

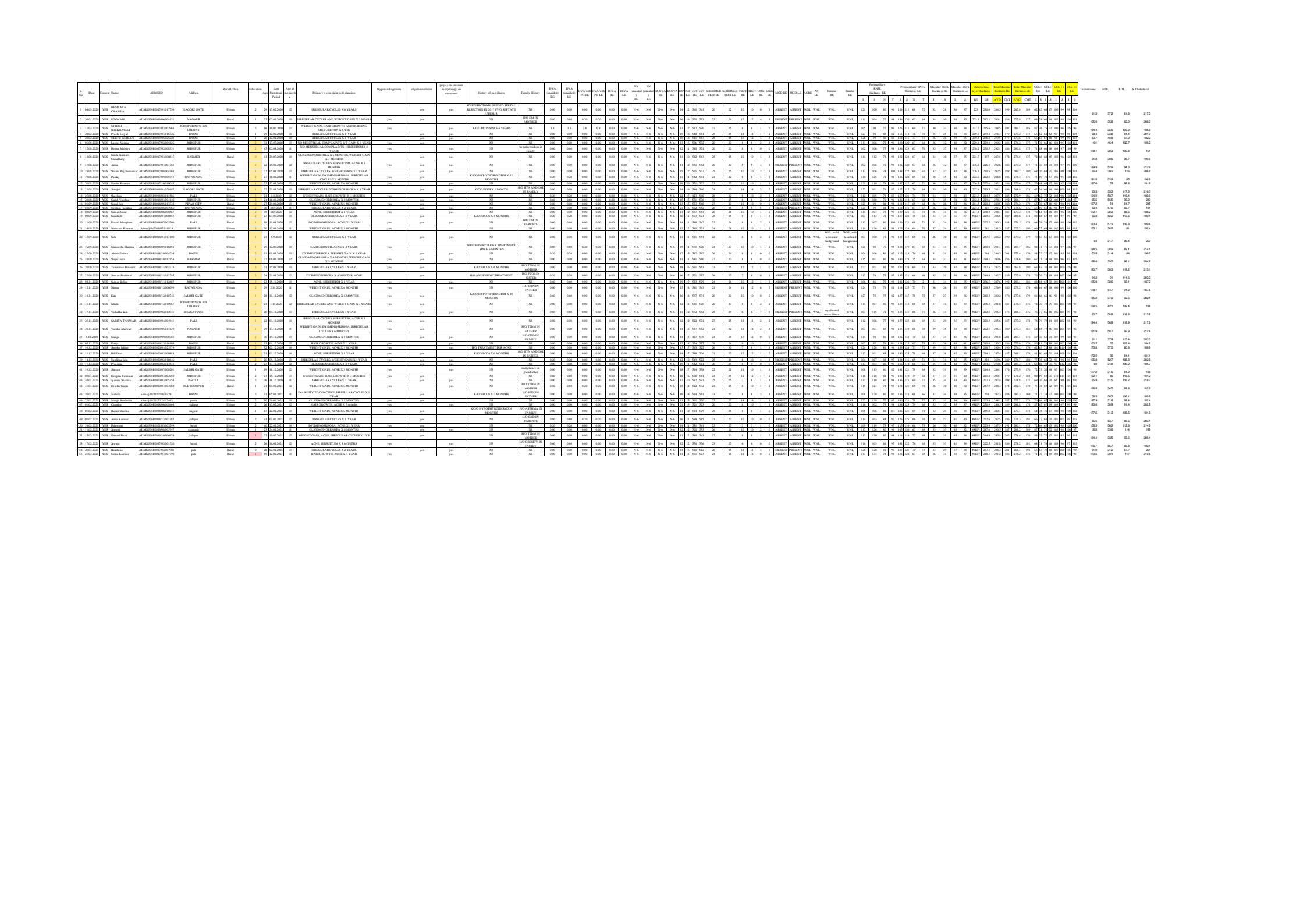
इसके अलावा, यदि अध्ययन के बाद कोई महत्वपूर्ण निष्कर्ष मिलता है, तो आपको निवारक रणनीतियों के अधीन किया जाएगा और यदि आवश्यक हो, तो आप प्रारंभिक उपचार के लिए एक उम्मीदवार होंगे।

7) अध्ययन में भ□ा लेने के संभ□ावित दुष्प्रभ□ाव क्य□हैं?

अध्ययन में भ□ा लेने के कोई भी अतिरिक्त दुष्प्रभ□ाव नहीं हैं।

8) क्या मेरा डेटा गोपनीय रखा जाएगा?

आपके मेडिकल रिकॉर्ड और जनसांख्यिकीय डेटा का केवल शोधकर्ता, चिकित्सक और संबंधित अधिकारियों के सामने खुलासा किया जाएगा।



S. No.	Date	Consent	Name	AIIMS ID	Address	Rural/Urban	Education	Age	Last Menstrual Period	Age at menarche	Primary's complaint with duration	History of past illness	Family History
1	04.03.2020	YES	Saraswati Prajapat	AIIMS/JDH/2018/05/019515	Ratanada	Urban	2	24	01.03.2020	12	refractory error, no menstrual complaints	NS	NS
2	30.01.2020	YES	Bhawana Choudhary	AIIMS/JDH/2015/06/005465	Pali	Rural	0	19	12.01.2020	12	refractory error, no menstrual complaints	NS	NS
3	11.03.2020	YES	Laxmi Soni	AIIMS/JDH/2020/07/001365	Basni	Urban	3	31	25.02.2020	13	headache, no menstrual complaints	K/C/O HYPOTHYROIDISM X 24 MONTHS	NS
4	20.02.2020	YES	Satyawati Kessani	AIIMS/JDH/2020/08/000742	Old Jodhpur	Urban	0	36	13.02.2020	11	headache, no menstrual complaints	NS	F/H/O T2DM
5	20.02.2020	YES	TAMNA BEGAM	AIIMS/JDH/2020/08/004043	Nai Sadak	Urban	3	42	15.07.2020	14	refractory error, no menstrual complaints	NS	NS
6	06.08.2020	YES	ANTAR DEVI	AIIMS/JDH/2020/08/003893	Paota	Urban	1	33	02.08.2020	13	refractory error, no menstrual complaints	NS	F/H/O HTN
7	12.08.2020	YES	Sushila	AIIMS/JDH/2019/06/013702	Basni	Urban	2	35	11.08.2020	11	headache, no menstrual complaints	NS	NS
8	14.08.2020	YES	SAROJA S	AIIMS/JDH/2020/06/006434		Urban	1	28	29.07.2020	14	refractory error, no menstrual complaints	NS	NS
9	17.08.2020	YES	Geeta Patel	AIIMS/JDH/2020/07/005795	Ratanada	Urban	2	26	14.08.2020	13	refractory error, no menstrual complaints	NS	NS
10	18.08.2020	YES	Yashasvi	AIIMS/JDH/2020/08/006331	Barmer	Rural	0	41	03.08.2020	12	headache, no menstrual complaints	K/C/O HYPOTHYROIDISM X 18 MONTHS	F/H/O T2DM
11	19.08.2020	YES	BABITA	AIIMS/JDH/2020/09/005386	Basni	Urban	1	43	11.08.2020	12	refractory error, no menstrual complaints	NS	F/H/O APPENDECTOMY
12	20.08.2020	YES	POOJA KANWAR	AIIMS/JDH/2020/10/004378	Ratanada	Urban	2	39	27.07.2020	12	refractory error, no menstrual complaints	NS	NS
13	22.08.2020	YES	RINNI	AIIMS/JDH/2020/10/009460	Jodhpur	Urban	0	21	16.08.2020	13	allergic conjunctivitis, no menstrual complaints	NS	NS
14	25.08.2020	YES	RATNA RAM	AIIMS/JDH/2020/12/000731	Jodhpur	Urban	2	20	17.08.2020	11	headache, no menstrual complaints	NS	NS
15	28.08.2020	YES	Tina	AIIMS/JDH/2021/02/002277	Basni	Urban	2	29	20.02.2020	14	headache, no menstrual complaints	NS	F/H/O MIGRAINE
16	01.09.2020	YES	Neha Solanki	AIIMS/JDH/2021/02/002562	Jodhpur	Urban	1	25	19.08.2020	13	refractory error, no menstrual complaints	NS	NS
17	03.09.2020	YES	Sunita Dave	AIIMS/JDH/2017/02/000183		Urban	2	20	27.08.2020	11	headache, no menstrual complaints	NS	F/H/O CAD
18	08.09.2020	YES	Shanti Devi	AIIMS/JDH/2017/02/004766	Basni	Urban	3	32	01.08.2020	11	chalazion, no menstrual complaints	NS	NS
19	09.09.2020	YES	Komal Sharma	AIIMS/JDH/2017/08/000563		Urban	1	37	01.09.2020	14	refractory error, no menstrual complaints	NS	NS
20	11.09.2020	YES	Pooja Choudhary	AIIMS/JDH/2018/06/001347	Jodhpur	Urban	3	43	02.08.2020	12	refractory error, no menstrual complaints	NS	NS
21	14.09.2020	YES	Bhagwati	AIIMS/JDH/2020/12/008512	Ratanada	Urban	2	34	18.08.2020	12	allergic conjunctivitis, no menstrual complaints	h/o skin allergy X 2 years	F/H/O KIDNEY DISEASE
22	15.09.2020	YES	JAIDA BANO	AIIMS/JDH/2021/01/010421	Nagaur	Rural	0	36	10.09.2020	14	refractory error, no menstrual complaints	NS	NS
23	16.09.2020	YES	CHHOTI	AIIMS/JDH/2021/01/011908	Jodhpur	Urban	1	29		14	headache, no menstrual complaints	NS	NS
24	17.09.2020	YES	LAXMI KUMARI	AIIMS/JDH/2021/01/017010	Jodhpur	Urban	1	27	28.08.2020	13	headache, no menstrual complaints	NS	NS
25	19.09.2020	YES	Kamla Devi	AIIMS/JDH/2021/02/007047		Urban	2	42	09.09.2020	12	allergic conjunctivitis, no menstrual complaints	h/o allergic rhinitis X 1 year	NS
26	20.09.2020	YES	MANJU VISHNOI	AIIMS/JDH/2021/03/003990	Basni	Urban	1	44	16.09.2020	13	allergic conjunctivitis, no menstrual complaints	NS	F/H/O T2DM
27	22.09.2020	YES	NASREEN BANOO	AIIMS/JDH/2021/03/011544		Urban	3	39	21.09.2020	13	refractory error, no menstrual complaints	NS	NS
28	02.11.2020	YES	Karishma Udani	AIIMS/JDH/2017/04/004890	Jodhpur	Urban	2	22	25.10.2020	14	headache, no menstrual complaints	NS	F/H/O T2DM & HTN
29	12.11.2020	YES	Meera Soni	AIIMS/JDH/2020/06/001187	Ratanada	Urban	1	21	13.10.2020	11	headache, no menstrual complaints	NS	NS
30	14.11.2020	YES	DISHA PARMAR	AIIMS/JDH/2020/09/005391	Jodhpur	Urban	1	30	02.11.2020	12	refractory error, no menstrual complaints	NS	NS
31	16.11.2020	YES	Kamla	AIIMS/JDH/2014/08/003387	Basni	Urban	3	40	22.10.2020	12	refractory error, no menstrual complaints	NS	NS
32	17.11.2020	YES	Bhanwari Devi	AIIMS/JDH/2015/10/001231	Jodhpur	Urban	2	42	14.11.2020	14	allergic conjunctivitis, no menstrual complaints	K/C/O HYPOTHYROIDISM X 7 MONTHS	NS
33	25.11.2020	YES	Sangeeta Singal	AIIMS/JDH/2017/09/001480	Sardarpura	Urban	2	38	22.11.2020	14	refractory error, no menstrual complaints	NS	NS
34	30.11.2020	YES	Murti Devi	AIIMS/JDH/2017/09/012997	Jodhpur	Urban	1	20	19.11.2020	11	refractory error, no menstrual complaints	NS	NS
35	4.12.2020	YES	Shanti	AIIMS/JDH/2018/09/014733		Urban	2	19	18.11.2020	13	allergic conjunctivitis, no menstrual complaints	NS	NS
36	05.12.2020	YES	Geeta Devi Lomror	AIIMS/JDH/2019/11/007148	Ratanada	Urban	2	28	15.11.2020	11	headache, no menstrual complaints	NS	NS
37	10.12.2020	YES	Saroj Kunwar	AIIMS/JDH/2020/06/005425	Jodhpur	Urban	1	26	09.11.2020	14	headache, no menstrual complaints	k/c/o migraine X 2 years	F/H/O T2DM & HTN
38	11.12.2020	YES	SRISHTI	AIIMS/JDH/2020/07/000591	Jodhpur	Urban	2	19	17.11.2020	14	allergic conjunctivitis, no menstrual complaints	NS	NS
39	14.12.2020	YES	Suaa	AIIMS/JDH/2020/09/002507	Basni	Urban	2	30	26.11.2020	12	allergic conjunctivitis, no menstrual complaints	NS	F/H/O T2DM
40	17.12.2020	YES	Prem Devi	AIIMS/JDH/2020/09/010801	Basni	Rural	0	36	05.12.2020	12	refractory error, no menstrual complaints	NS	NS
41	19.12.2020	YES	VIMLA	AIIMS/JDH/2020/09/011739		Urban	3	42	03.12.2020	12	refractory error, no menstrual complaints	NS	NS
42	03.01.2021	YES	Keshu	AIIMS/JDH/2020/11/005956	Jodhpur	Urban	1	33	23.12.2020	11	headache, no menstrual complaints	NS	F/H/O HTN
43	10.01.2021	YES	Amma Devi	AIIMS/JDH/2020/12/000131	Pali	Rural	0	35	22.12.2020	11	headache, no menstrual complaints	NS	F/H/O GALL BLADDER DISEASE
44	15.01.2021	YES	Meenakshi Meena	AIIMS/JDH/2017/03/001949	jodhpur	Urban	3	28	25.12.2020	12	allergic conjunctivitis, no menstrual complaints	NS	F/H/O T2DM
45	20.01.2021	YES	Sumitra Panchariya	AIIMS/JDH/2017/03/011969	Basni	Urban	1	26	19.01.2021	11	allergic conjunctivitis, no menstrual complaints	NS	NS
46	21.01.2021	YES	Gurmeet Kaur	AIIMS/JDH/2018/08/000107	Jodhpur	Urban	2	44	12.01.2021	13	refractory error, no menstrual complaints	K/C/O HYPOTHYROIDISM X 9 MONTHS	NS
47	24.01.2021	YES	Priyanka Haritwal	AIIMS/JDH/2019/07/000044	Jodhpur	Urban	1	34	18.01.2021	11	allergic conjunctivitis, no menstrual complaints	NS	NS
48	02.02.2021	YES	Saroj Choudhary	AIIMS/JDH/2019/08/000820	Jodhpur	Urban	3	37	22.01.2021	11	headache, no menstrual complaints	NS	F/H/O CAD
49	04.02.2021	YES	Shobha Dadhich...	AIIMS/JDH/2019/08/002909	Ratanada	Urban	2	30	09.01.2021	14	refractory error, no menstrual complaints	NS	NS
50	06.02.2021	YES	Fula Devi	AIIMS/JDH/2019/12/008658	Jodhpur	Urban	1	28	18.01.2021	12	refractory error, no menstrual complaints	NS	NS
51	07.02.2021	YES	Vidha Devi	AIIMS/JDH/2020/01/019539	Jodhpur	Urban	2	43	01.02.2021	12	allergic conjunctivitis, no menstrual complaints	NS	F/H/O T2DM
52	10.02.2021	YES	Naurta Devi	AIIMS/JDH/2020/01/026679	Pipar City	Rural	0	45	05.02.2021	14	refractory error, no menstrual complaints	NS	F/H/O T2DM
53	12.02.2021	YES	Ladudi	AIIMS/JDH/2020/02/014551	Air Force Area	Urban	2	25	03.02.2021	14	headache, no menstrual complaints	NS	NS
54	14.02.2021	YES	Kamla Devi	AIIMS/JDH/2020/03/000350	Ratanada	Urban	1	36	10.02.2021	13	chalazion, no menstrual complaints	K/C/O HYPOTHYROIDISM X 16 MONTHS	NS
55	15.02.2021	YES	BHANWARI	AIIMS/JDH/2020/07/002743	Basni	Urban	2	33	24.01.2021	12	allergic conjunctivitis, no menstrual complaints	NS	NS

S. No.	DVA (unaided) RE	DVA (unaided) LE	DVA with PH RE	DVA with PH LE	BCVA RE	BCVA LE	NV (unaided) RE	NV (unaided) LE	BCNVA RE	BCNVA LE	IOP RE	IOP LE	CCT RE	CCT LE	SCHIRMER TEST RE	SCHIRMER TEST LE	TBUT RE	TBUT LE	OSS S RE	OSS S LE	MGD RE	MGD LE	AS RE	AS LE	Fundus RE	Fundus LE
1	0.20	0.20	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	14	13	560	561	20	22	10	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
2	0.60	0.60	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	12	12	520	533	25	26	12	12	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
3	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	15	11	512	530	27	25	8	8	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
4	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	18	11	540	544	25	25	14	14	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
5	0.20	0.20	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	18	12	541	543	25	25	13	12	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
6	0.60	0.60	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	12	11	536	532	20	20	8	8	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
7	0.20	0.20	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	15	11	540	521	20	20	8	8	5	6	PRESENT	PRESENT	WNL	WNL	WNL	WNL
8	0.80	0.80	0.20	0.20	0.00	0.00	N-6	N-6	N-6	N-6	19	15	542	543	25	25	10	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
9	1.1	1.3	0.8	0.8	0.00	0.00	N-6	N-6	N-6	N-6	11	11	551	552	20	20	5	5	1	1	ABSENT	ABSENT	WNL	WNL	WNL	WNL
10	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	15	16	521	522	25	25	10	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
11	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	12	17	542	541	21	22	8	8	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
12	0.80	0.80	0.20	0.20	0.00	0.00	N-6	N-6	N-6	N-6	11	12	521	522	25	25	10	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
13	1.1	1.1	0.8	0.8	0.00	0.00	N-6	N-6	N-6	N-6	18	17	546	540	24	20	14	14	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
14	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	16	14	423	540	28	20	8	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
15	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	16	18	551	536	30	25	8	8	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
16	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	13	11	533	540	27	20	10	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
17	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	15	15	562	542	26	25	5	5	1	1	ABSENT	ABSENT	WNL	WNL	WNL	WNL
18	0.80	0.80	0.20	0.20	0.00	0.00	N-6	N-6	N-6	N-6	15	12	537	551	20	21	10	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
19	0.20	0.20	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	13	11	563	521	25	25	8	8	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
20	0.60	0.60	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	12	18	548	542	25	24	8	8	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
21	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	11	16	540	521	24	28	10	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
22	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	11	10	541	554	22	30	8	8	0	0	ABSENT	ABSENT	WNL	WNL	WNL, mild tesselated background	WNL, mild tesselated background
23	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	15	14	531	520	24	27	10	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
24	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	13	12	542	512	26	26	8	8	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
25	0.60	0.60	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	12	15	541	540	32	20	8	8	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
26	0.20	0.20	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	11	18	561	563	23	25	12	12	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
27	0.20	0.20	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	11	18	521	532	26	25	7	8	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
28	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	12	12	513	529	24	26	10	12	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
29	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	11	15	541	543	21	24	11	12	4	5	PRESENT	PRESENT	WNL	WNL	WNL	WNL
30	0.20	0.20	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	11	19	537	531	20	20	10	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
31	0.60	0.60	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	15	12	541	520	20	23	8	8	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
32	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	11	16	552	542	25	24	6	6	5	7	PRESENT	PRESENT	WNL	WNL	myelinated nerve fibres	WNL
33	0.80	0.80	0.20	0.20	0.00	0.00	N-6	N-6	N-6	N-6	16	18	522	521	27	25	11	11	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
34	1.1	1.3	0.8	0.8	0.00	0.00	N-6	N-6	N-6	N-6	17	20	547	542	21	22	11	14	4	6	PRESENT	PRESENT	WNL	WNL	WNL	WNL
35	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	12	14	427	535	24	24	13	12	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
36	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	15	16	554	537	28	24	9	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
37	0.20	0.20	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	17	13	563	522	26	30	7	8	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
38	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	14	15	538	556	21	25	12	12	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
39	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	11	15	549	522	25	24	8	10	1	1	ABSENT	ABSENT	WNL	WNL	WNL	WNL
40	0.20	0.20	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	15	13	542	511	20	24	8	9	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
41	0.80	0.80	0.20	0.20	0.00	0.00	N-6	N-6	N-6	N-6	12	12	514	538	22	21	11	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
42	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	11	11	560	564	24	25	12	12	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
43	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	18	11	532	531	25	25	7	8	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
44	0.60	0.60	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	16	15	522	532	24	25	8	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
45	0.20	0.20	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	11	14	514	541	23	22	8	8	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
46	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	14	16	542	543	25	25	10	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
47	0.80	0.80	0.20	0.20	0.00	0.00	N-6	N-6	N-6	N-6	14	17	551	552	20	20	5	5	1	1	ABSENT	ABSENT	WNL	WNL	WNL	WNL
48	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	16	18	521	522	25	25	10	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
49	0.20	0.20	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	13	15	542	541	21	22	8	8	5	4	PRESENT	PRESENT	WNL	WNL	WNL	WNL
50	0.60	0.60	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	15	14	521	522	25	25	10	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
51	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	15	12	546	540	24	20	14	14	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
52	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	13	15	423	540	28	20	8	10	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
53	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	12	18	551	536	30	25	8	8	0	0	ABSENT	ABSENT	WNL	WNL	WNL	WNL
54	0.00	0.00	0.00	0.00	0.00	0.00	N-6	N-6	N-6	N-6	11	18	533	540	27	20	10	10	3	5	PRESENT	PRESENT	WNL	WNL	WNL	WNL
55	1.1	1.1	0.8	0.8	0.00	0.00	N-6	N-6	N-6	N-6	11	12	562	542	26	25	5	5	1	1	ABSENT	ABSENT	WNL	WNL	WNL	WNL

S. No.	Peripapillary RNFL thickness RE				Peripapillary RNFL thickness LE				Macular RNFL thickness RE		Macular RNFL thickness LE		Outer retinal layer thickness		Total Macular thickness RE		Total Macular thickness LE		GCL+ RE		GCL+ LE		GCL ++ RE		GCL ++ LE	
	I	S	N	T	I	S	N	T	I	S	I	S	RE	LE	AVG	CMT	AVG	CMT	I	S	I	S	I	S	I	S
1	121	100	80	96	126	111	68	72	32	28	36	37	284.5	267.8	285	199	268	189	62	65	66	67	100	99	98	104
2	111	104	72	98	136	120	65	68	34	30	38	35	290.1	277.9	290	184	278	177	69	78	66	66	102	98	104	101
3	105	99	77	99	125	111	69	71	30	33	30	34	288.5	289.1	289	191	289	185	87	76	75	72	100	96	105	96
4	123	98	85	82	113	114	76	70	35	25	38	34	278.3	273.2	278	179	273	173	65	62	64	62	99	98	98	105
5	126	99	86	83	114	115	77	71	36	26	39	35	279.5	277.6	280	177	278	178	66	63	67	68	98	99	99	104
6	113	106	72	96	138	120	67	68	36	32	40	32	290.2	276.2	290	186	276	177	71	70	66	66	104	95	104	101
7	102	106	77	98	136	123	65	70	35	37	34	37	292.1	280.8	292	186	281	175	71	68	66	68	104	97	110	99
8	111	112	78	98	132	124	67	68	34	30	37	35	283.5	276.5	284	172	277	175	72	68	68	65	102	96	102	101
9	102	106	72	98	136	120	67	68	36	32	40	37	292.6	279.2	293	186	279	177	71	70	69	70	104	97	99	100
10	113	106	74	100	138	122	69	67	32	32	42	38	292.5	289.7	293	188	290	180	68	20	69	71	105	99	109	101
11	110	125	72	98	136	122	65	68	38	35	44	32	288.8	276.4	289	186	276	175	71	69	70	67	106	95	102	102
12	121	110	74	99	137	122	67	71	36	29	41	37	292.1	275.6	292	186	276	175	70	68	68	67	101	97	103	101
13	122	101	79	82	127	112	76	68	33	30	38	40	291.1	268.8	291	199	269	178	62	76	66	66	100	100	98	105
14	112	105	71	83	137	121	74	70	34	33	30	43	287.5	272.9	288	185	273	186	69	62	75	72	102	98	102	101
15	106	100	76	96	126	112	67	68	31	25	38	32	278.3	286.1	278	192	286	174	87	63	64	62	100	97	106	97
16	121	99	84	98	114	115	65	68	36	26	32	36	280.5	274.2	281	180	274	179	65	70	67	68	99	98	99	104
17	124	99	84	98	114	115	67	67	36	32	40	34	291.2	278.6	291	178	279	176	63	69	65	66	98	99	98	103
18	114	107	71	97	139	121	77	72	35	31	36	36	298.1	277.2	298	187	277	178	70	64	67	68	101	96	105	100
19	103	113	72	99	137	123	78	68	34	34	35	37	286.5	281.8	287	189	282	174	88	66	67	69	103	97	99	99
20	112	107	80	100	126	121	68	71	32	24	36	34	280.3	279.5	280	188	280	178	64	79	76	67	100	98	100	102
21	114	126	83	99	125	124	64	70	37	24	42	39	281.5	277.2	282	187	277	190	66	77	68	69	102	101	99	103
22	107	100	72	96	115	115	65	72	26	30	40	32	286.2	279.2	286	190	279	179	70	63	65	63	102	98	103	100
23	121	98	79	95	138	119	67	69	33	34	41	35	291.1	289.7	291	186	290	186	88	71	71	73	104	97	106	97
24	104	106	81	97	115	118	76	69	31	31	43	34	284.5	275.4	285	201	275	176	88	72	72	67	101	95	99	101
25	115	101	80	96	140	123	75	63	34	32	41	31	290.6	278.6	291	185	279	180	67	71	74	68	105	96	97	105
26	122	101	81	95	127	124	69	73	33	29	37	38	287.5	267.8	288	200	268	190	63	63	70	69	101	100	105	99
27	112	78	73	97	135	121	66	69	35	31	39	36	292.7	277.9	293	185	278	178	70	70	71	69	103	102	106	95
28	106	86	79	98	126	126	70	2	31	34	34	35	287.6	289.1	288	192	289	186	88	88	67	70	101	100	101	97
29	124	73	73	81	114	125	77	71	36	26	31	35	276.9	273.2	277	180	273	174	66	64	67	68	100	99	100	100
30	127	75	75	82	137	115	78	72	37	27	39	36	280.2	277.6	280	178	278	179	86	66	66	66	99	98	102	98
31	114	107	80	95	133	114	68	69	37	31	41	33	291.8	278.4	292	187	278	176	72	70	72	75	105	104	100	97
32	103	115	72	97	135	115	66	71	36	34	41	38	296.4	281.3	296	173	281	176	76	77	66	88	106	104	99	98
33	112	106	77	94	137	125	68	69	33	29	35	33	285.6	277.2	286	187	277	178	78	79	79	64	103	102	98	99
34	103	101	85	91	135	119	68	69	39	35	38	38	296.4	273.4	296	189	273	181	64	65	77	66	105	104	101	96
35	111	98	86	84	136	118	70	64	37	34	41	36	291.8	289.1	292	201	289	176	69	70	63	70	107	99	103	97
36	107	97	76	101	128	123	63	73	33	26	43	41	280.5	275.9	281	186	276	179	80	81	71	88	102	102	100	98
37	124	128	81	96	133	124	75	72	39	33	45	38	290.4	276.2	290	190	276	176	62	63	72	88	101	110	104	98
38	115	101	83	98	130	125	78	69	37	38	42	33	287.4	269.1	287	187	269	174	81	80	68	71	103	109	101	104
39	104	107	84	97	124	116	65	71	34	31	45	35	269.6	276.7	270	189	277	180	77	78	68	72	99	98	96	105
40	113	104	80	99	116	112	68	65	35	38	42	36	270.8	289.3	271	202	289	172	65	66	70	71	97	112	105	98
41	108	113	80	82	141	121	78	63	32	31	39	39	284.1	275.9	284	176	276	170	72	73	20	68	95	103	104	99
42	116	118	81	96	126	110	79	68	37	33	31	40	290.1	276.2	290	179	276	188	88	89	69	71	110	114	101	104
43	112	110	82	98	136	115	69	71	35	34	33	43	297.4	278.8	297	198	279	177	69	70	68	70	96	99	99	110
44	115	127	74	95	134	121	65	70	36	30	40	32	288.3	282.4	288	174	282	170	75	76	69	72	107	95	101	102
45	108	129	80	92	135	118	68	66	37	34	39	35	287.3	280.3	287	184	280	169	71	72	74	77	100	101	100	99
46	111	112	78	98	132	124	67	68	34	30	37	35	283.5	276.5	284	172	277	175	72	68	68	65	102	96	102	101
47	102	106	72	98	136	120	67	68	36	32	40	37	292.6	279.2	293	186	279	177	71	70	69	70	104	97	99	100
48	113	106	74	100	138	122	69	67	32	32	42	38	292.5	289.7	293	188	290	180	68	20	69	71	105	99	109	101
49	110	125	72	98	136	122	65	68	38	35	44	32	288.8	276.4	289	186	276	175	71	69	70	67	106	95	102	102
50	121	110	74	99	137	122	67	71	36	29	41	37	292.1	275.6	292	186	276	175	70	68	68	67	101	97	103	101
51	122	101	79	82	127	112	76	68	33	30	38	40	291.1	268.8	291	199	269	178	62	76	66	66	100	100	98	105
52	112	105	71	83	137	121	74	70	34	33	30	43	287.5	272.9	288	185	273	186	69	62	75	72	102	98	102	101
53	106	100	76	96	126	112	67	68	31	25	38	32	278.3	286.1	278	192	286	174	87	63	64	62	100	97	106	97
54	121	99	84	98	114	115	65	68	36	26	32	36	280.5	274.2	281	180	274	179	65	70	67	68	99	98	99	104
55	124	99	84	98	114	115	67	67	36	32	40	34	291.2	278.6	291	178	279	176	63	69	65	66	98	99	98	103

Visual acuity scales

Foot	Metre	Decimal	LogMAR
20/200	6/60	0.10	1.00
20/160	6/48	0.125	0.90
20/125	6/38	0.16	0.80
20/100	6/30	0.20	0.70
20/80	6/24	0.25	0.60
20/63	6/19	0.32	0.50
20/50	6/15	0.40	0.40
20/40	6/12	0.50	0.30
20/32	6/9.5	0.63	0.20
20/25	6/7.5	0.80	0.10
20/20	6/6	1.00	0.00
20/16	6/4.8	1.25	–0.10
20/12.5	6/3.8	1.60	–0.20
20/10	6/3	2.00	–0.30

Education Level	
Illiterate	0
Early childhood, primary or secondary	1
Bachelor's or Master's Level	2
Doctoral or equivalent Level	3