"OCULAR ASSOCIATIONS OF METABOLIC SYNDROME AT TERTIARY HEALTH CARE CENTRE -A CROSS SECTIONAL STUDY"

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LIST OF ABBREVIATIONS

WHO	World Health Organization
EGIR	European Group for the Study of Insulin Resistance
NCEP ATP III	National Cholesterol Education Program—Third Adult Treatment Panel
HTN	Hypertension
DM	Diabetes Mellitus
MetS	Metabolic syndrome
PSC	Posterior subcapsular cataract
ARMD	Age-related macular degeneration
CRAO	Central retinal artery occlusion
CRVO	Central retinal vein occlusion
BRVO	Branch retinal vein occlusion
DED	Dry eye disease
DR	Diabetic retinopathy
CNP	Cranial nerve palsy
POAG	Primary open angle glaucoma
PACG	Primary angle-closure glaucoma
NTG/LTG	Normal or low tension glaucoma
CCT	Central corneal thickness
NS	Nuclear sclerosis
PXF	Pseudoexfoliation
CC	Cortical cataract
PCO	Posterior capsule opacification

SMC	Senile Mature Cataract
WNL	Within normal limits
IOP	Intraocular pressure
NVI	Neovascularisation of Iris
NVE	Neovascularisation Elsewhere
NVD	Neovascularisation of Disc
NPDR	Non-proliferative diabetic retinopathy
ADED	Advanced diabetic eye disease
DME	Diabetic macular edema
CNVM	Choroidal Neovascular Membranes
CDR	Cup Disc Ratio
CWS	Cotton Wool spots
IRMA	Intraretinal microvascular abnormalities
NRR	Neuro Retinal Rim
CF	Counting Fingers
HMCF	Hand movements close to face
FFAs	Free fatty acids
CRP	C-reactive protein
IOP	Intra-ocular Pressure
RAS	Renin-angiotensinogen system
JPHC	Japan Public Health Center
AMD	Age-related macular degeneration

ABSTRACT

Introduction:

The increased prevalence of metabolic syndrome is becoming a significant public health challenge. It is a known significant risk factor for development of cardiovascular diseases, cerebrovascular diseases and diabetes mellitus type 2. Association of metabolic syndrome to age related cataract, glaucoma, macular degeneration and intraocular pressure has been emphasized in several studies. The present study was carried out to assess the ocular manifestations in metabolic syndrome

Methodology:

The current study was the hospital based prospective cross sectional study of Ocular associations of metabolic syndrome conducted among 20-80 years old patients attending at KLES Dr. Prabhakar kore hospital and medical research Centre, Belagavi from Aug 2022- Jul 2023. The study subjects were enrolled in study by convenient sampling method who fulfilled inclusion & exclusion criteria after obtaining the informed consent. All subjects underwent detailed and thorough clinical history & ocular examination. Abdominal obesity by measuring waist circumference & waist to hip ratio. Serum lipid measurements using Fasting samples, to analyse Total Cholesterol, Plasma triglycerides, Plasma high density lipoprotein (HDL) cholesterol. Blood pressure measurement using Sphygmomanometer. Fasting plasma glucose was also measured.

Results:

Total 102 study subjects were enrolled in this study. The mean age of subject was 55.85 ± 11.08 years. About 61 (59.8%) were males and 41 (40.2%) were females. About 77 (75.49%) subjects had diminution of vision in their right eye while 71

(69.61%) had diminution of vision in their left eye. The mean duration of diminution of vision was 12.1 ± 9.93 months. Regarding hypertension, the mean duration was 27.15 ± 28.41 months. The mean duration of diabetes mellitus was 4.47 ± 4.17 years. The most common ocular manifestation was cataract followed by Diabetic retinopathy. The mean of right eye IOP 16.46 ± 4.91 mmHg. The mean IOP of left eye 15.74 ± 4.69 mmHg. The mean SBP was156.71 ± 13.46 mmHg. The mean DBP was 88.02 ± 6.45 mmHg. Ocular manifestations exhibit a significantly higher mean age compared to those without ocular manifestations($p < 0.001$). Both systolic blood pressure (SBP) and diastolic blood pressure (DBP) are significantly elevated in subjects with ocular manifestations in comparison to those without.

Conclusion: The findings of this study concluded that patients with age between 45 to 65 years were more at risk of developing ocular manifestation in metabolic syndrome. Amongst the study subjects selected it was found that cataract was the most common ocular manifestation followed by diabetic & hypertensive retinopathy. Where as Glaucoma & ARMD were diagnosed in equal prevalence followed by lid Xanthoma and central retinal vein occlusion.

Key words : Metabolic syndrome, Ocular manifestation, Cataract, Diabetic retinopathy, Hypertensive retinopathy

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INTRODUCTION

In 1920s, Kylin described metabolic syndrome as a cluster of conditions like hyperglycaemia, hypertension, and gout.[1] Two decades later, adiposity was associated with metabolic conditions like cardiovascular diseases and diabetes.[2] Metabolic syndrome was once known as "Syndrome X" until its 1988 popularisation by Reaven.[3] When it comes to the specifics, the three most popular definitions put out by the WHO, the European Group for the Study of Insulin Resistance (EGIR), and the National Cholesterol Education Program—Third Adult Treatment Panel (NCEP ATP III) are very similar. However, you might find differences in the clinical criteria used to identify these components. They emphasize on four core components: dyslipidaemia, obesity, hypertension, and insulin resistance.[4] Pathogenesis of metabolic syndrome is complex and cannot be elucidated completely; however, two potential causative factors central obesity and insulin resistance appear to stand out. Altered cellular pathways associated with metabolic syndrome contributing to elevated oxidative stress and cellular senescence can lead to end organ damage.[5] Several other factors like genetics, pro-inflammatory state, ageing, hormonal dysregulation and inactive lifestyle can be associated with metabolic syndrome.[6]

In terms of public health, the increasing incidence of metabolic syndrome is a big concern.[7] Nearly a quarter of the world's population has metabolic syndrome, says the International Diabetes Federation.[8] Diabetes mellitus type 2, cardiovascular disease, and cerebrovascular disease are all known to be significantly increased by it.[8] It has been shown in multiple research that metabolic syndrome is associated with age-related cataract, glaucoma, macular degeneration, and intraocular pressure.[9]

Individual components of this syndrome have been long term linked with development of multiple eye diseases.[7] "The ocular diseases like diabetic retinopathy, glaucoma and cataract that are known to cause vision loss have been associated with diabetes and hypertension.[10] Retinopathy, cataracts, intraocular pressure, and dry eye illness are all linked to metabolic syndrome, according to research published in 2020 by Lima Fontes M et al.[10,11] Wu KY et al in 2022, found a positive link of association between ocular hypertension and central corneal thickness with metabolic syndrome in Olmsted country.[12] In their 2016 study, Poh et al. detailed the growing body of data connecting certain metabolic syndrome risk factors to ocular diseases, such as glaucoma and ARMD, respectively.[7] Chopra et al in 2012 found a link between metabolic syndrome and central retinal artery occlusion that potentially could lead to vision loss. However, the evidence of association was found to be weak. Inflammation of the small and larger vessels of eye and dysfunction of endothelium has also been positively linked with metabolic syndrome.[13]

No studies have been conducted in a tertiary care hospital environment to assess correlations between ocular symptoms and metabolic syndrome in Indian population. Finding the growing body of information linking metabolic syndrome to ocular disorders would aid in reducing the likelihood of developing these conditions and preventing damage that might result in irreversible vision loss. Studying ocular symptoms of metabolic syndrome was, hence, the driving force behind our investigation. In addition to oculomotor nerve palsy, cataracts, primary open angle glaucoma, hypertensive retinopathy, diabetic retinopathy, Lipemia retinalis, age-related maculopathy, central retinal artery occlusion and central retinal vein occlusion, the study aims to determine whether these conditions are linked to metabolic syndrome.

OBJECTIVES

1) To assess the ocular manifestations in metabolic syndrome.

REVIEW OF LITERATURE

Central obesity, insulin resistance, hypertriglyceridemia, hypercholesterolemia, hypertension, and decreased high-density lipoprotein (HDL)-cholesterol concentrations are the hallmarks of metabolic syndrome (MetS), also referred to as syndrome X.[15, 14] It is acknowledged as a worldwide health risk associated with contemporary lifestyles because of the elevated risk of cardiovascular disease and other eye conditions such diabetic retinopathy, cataract, age-related macular degeneration, glaucoma, and dry eye syndrome. MetS prevalence is similar to type 2 diabetes and obesity prevalence. MetS is linked to a higher risk of cardiovascular diseases and is found in about 85% of T2DM patients. [16]

Pathophysiology

Among the processes that are thought to play a major role in the development of Metabolic Syndrome are insulin resistance, chronic inflammation, and neurohormonal activation.

- Insulin Resistance: The pancreatic beta cells release insulin when blood sugar levels are too high. This hormone increases the liver's, muscles', and adipose tissues' absorption of glucose while blocking lipolysis and hepatic gluconeogenesis. Insulin is less able to control lipolysis when adipose tissues develop insulin resistance. Because of changes to the insulin signalling cascade in multiple organs, this raises blood free fatty acids (FFAs) and subsequently insulin resistance.[17]

- Chronic inflammation: The high levels of numerous inflammatory markers (IL-6, C-reactive protein, and TNFα) may be explained by the pro-inflammatory state ultimately caused by the multiple pathogenic pathways that lead to the development of MetS.[18]
- Neurohormonal activation: The renin-angiotensinogen system is triggered. Adipose tissue stimulates the angiotensin-converting enzyme, which results in the production of the peptide angiotensin II (Ang II). Obesity and insulin resistance were found to be associated with elevated plasma Ang II levels.[19]

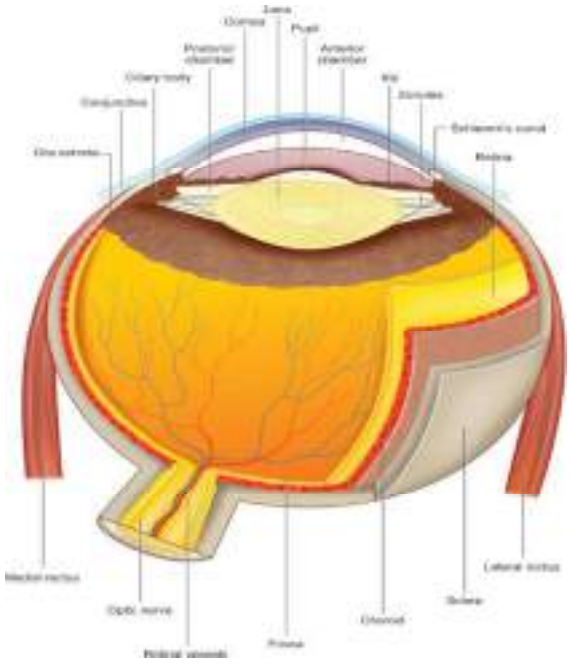


Fig 1: Anatomy of the eye

Anatomy of Eye

To understand the ocular structures and the related diseases cased by metabolic syndrome, it is very important to know the anatomy of eye. A specialised sensory organ situated within the bone orbit is the eye. There are three layers to the

eyeball: the fibrous sclera and cornea, the vascular uvea, and the nervous retina. The retina is the most important layer when it comes to processing information from the outside world. The back of the eye is home to the optic nerve (CN II), which carries visual information from the retina to the brain. Adipose tissue encircles the eyeball as it rests inside the orbit. Each eye has a thin, flexible tissue covering that is known as the lid. These function as shutters to protect the eyes from damaging light and debris. It is surrounded by a fine fascial coating called the Tenon's capsule. The sclera is a thin, opaque membrane that covers the posterior portion of the eye. The anterior bulbar conjunctiva and Tenon's capsule both cover the sclera's outer surface. There may be a suprachoroidal area between its inner surface and the choroid. Episclera, scleral stroma and lamina fusca are the three distinctive layers of sclera. The anterior continuous sclera and thin, avascular cornea make up the front one-sixth of the eyeball. In anatomy, the limbus is the transitional zone between the conjunctivocorneal and corneoscleral junctions, which is located around the circumcornea. A 2 mm broad surgical limbus separates the transparent cornea from the opaque sclera around the eye. The primary vascular layer of the eye is uvea. It is comprised of three interconnected sections. Their order is as follows: choroid, ciliary body, and iris, from back to front. Two smooth muscles, the sphincter pupillae and the dilater pupillae, give the iris its contractile ability. A small hole, known as the pupil, is located anterior to the iris. The creation of aqueous occurs in the ciliary body, which is the anterior projection of the choroid at ora serrata. In glaucoma and in maintaining intraocular pressure, the dynamics of aqueous humour play a pivotal role. Pars plana describes the smooth back of the ciliary body and pars plicata describes the front, the corona ciliaris.

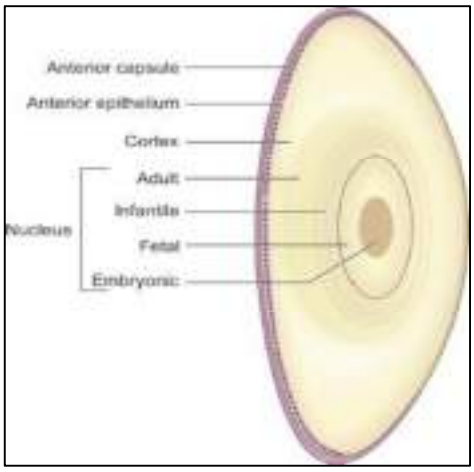


Fig 2: Structure of crystalline lens.

Inside each eye are two components called the vitreous body and the lens that work together to cause refraction. Parts of the eye's refractive medium include the vitreous body, lens, cornea, and aqueous humour. Situated midway between the vitreous and iris in the patellar fossa, the lens is a clear, biconvex crystalline structure that is nerve-free. The three distinct parts are the lens capsule, the anterior lens epithelium, and the lens substance or fibres. The anterior and posterior chambers, which hold the aqueous humour, are visible in the eye's cross-section. The intersection of the iris and cornea is located in the anterior chamber of the eyeball. Between the lens and the iris is a small, slit-shaped hollow that is known as the posterior chamber.

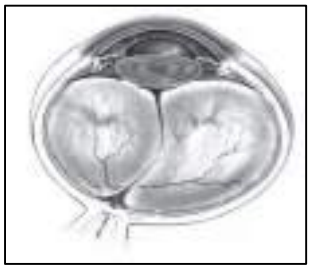


Fig 3: Vitreous Humour

A hydrophilic gel, vitreous humour is see-through and colourless. It provides structural support for the eye and aids in visual functions. The lens and ciliary body form the anterior boundary of the vitreous cavity, while the retina forms the posterior boundary. It may help prevent cataracts and keep the lens transparent by reducing the damage that reactive oxygen species do to the lens's proteins.[20]

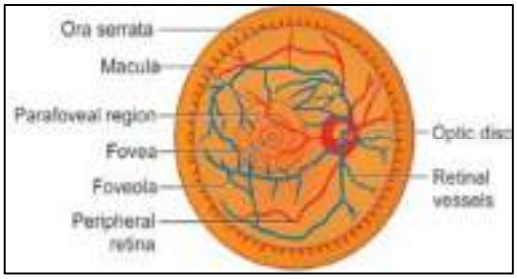


Fig 4: Anatomy of Retina

The choroid is the area of the eyeball's vascular coat that is located most posteriorly. It is absent on the posterior pole of the eye, where the optic nerve leaves the eyeball, and it extends from the optic disc to the ora serrata.

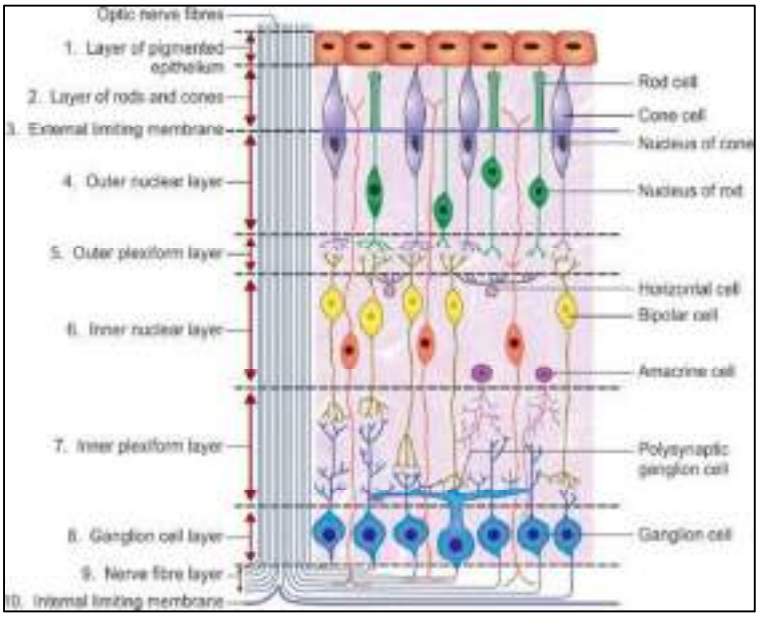


Fig 5: Retinal layers

1. Pigment epithelium of the retina
2. Rod and cone layer
3. The outer limiting membrane
4. The outer nuclear layer
5. The outer plexiform layer
6. The inner nuclear layer
7. The inner plexiform layer
8. Layer of ganglion cells
9. Layer of nerve fibres
10. The internal limiting membrane

RETINAL BLOOD SUPPLY :-

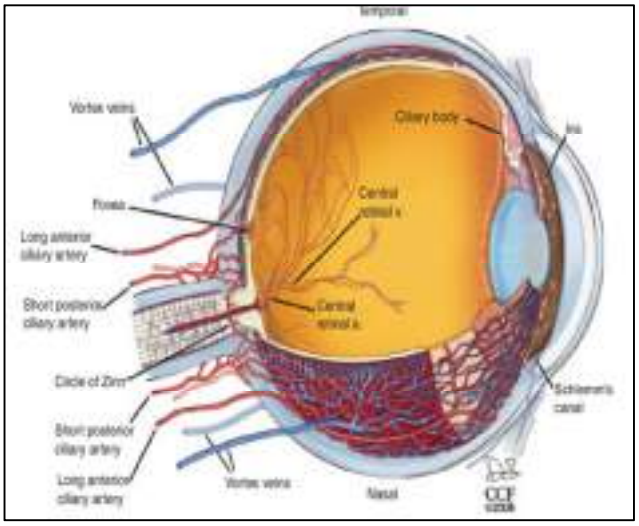


Fig 6: Blood supply of retina

The choriocapillaris supplies nourishment to the pigment epithelium, outer nuclear layer, rod and cone layer, corneal lining, and external limiting membrane, among other layers of the eye. The six inner layers of the retina that receive blood and oxygen from a central retinal artery are the limiting membrane, nerve fiber layer,

inner plexiform layer, inner ganglion cell layer, and inner nuclear layer. The choriocapillaris and the central retinal artery make up the two layers that make up the plexiform outer layer.

The principal blood vessel that provides blood to a fovea is the choriocapillaris. The superior and inferior temporal branches of the central retinal artery give blood to the macular region. The cilioretinal artery, which supplies blood to the macula, can occasionally be seen inside the temporal margin of the disc. When a central retinal artery blockage is present, it helps to preserve center vision.

Structures of the eye most commonly affected in metabolic syndrome:

- Lids
- Cornea
- Angles of anterior chamber
- Lens
- Uvea
- Vitreous
- Retina
- Optic disc

Metabolic syndrome and retinal microvascular changes

Common risk factors for retinopathy and associated microvascular diseases include diabetes and hypertension. Furthermore, MetS is associated with endothelial dysfunction in both large and small vessels, inflammation, and atherosclerosis in major arteries.[20]

Tien yin wong et al. conducted a cross-sectional study in 2004 to look into the relationship between metabolic syndrome and retinal microvascular abnormalities. [21] There were 11,265 participants in the research, ranging in age from 49 to 73. Microaneurysms, retinal haemorrhages, arteriovenous nicking, and focal arteriolar constriction are examples of retinal microvascular symptoms. To identify these, a standardised technique was used to examine retinal photographs. Retinopathy, arteriovenous nicking, focal arteriolar constriction, generalized retinal arteriolar narrowing, and generalized retinal venular dilatation were reported to be more common in those with metabolic syndrome. Even yet, there were associations with venular dilatation, localized arteriolar constriction, or generalized arteriolar narrowing in those without diabetes or hypertension.

As to the 2009 report of Saito et al. on the Japan Public Health Centre-based Prospective (JPHC) Study.[22] 12,412 males and 21,639 females, aged 40-69 years, who did not have a history of cancer or cardiovascular disease (CVD) had baseline assessments of metabolic risk factors. Metabolic syndrome patients exhibited smaller retinal artery diameters and larger retinal venule diameters, findings that were in agreement with those of Tien yin wong et al. In 2012, researchers from Japan (Zhao et al. [23]) found comparable outcomes.

Metabolic syndrome and cataract

An essential part of the eye's refractive system is the lens. With an estimated 17 million victims in 2002, cataract was the leading cause of blindness globally, according to the World Health Organisation.[21] The informal definition of a cataract is an optical defect in the lens large enough to cause light to disperse noticeably. The process of cataract development has long been thought to include the denaturation,

coagulation, agglutination, or precipitation of soluble lens proteins. Half of the world's blindness and 33% of visual impairment are caused by it, making it a huge public health concern. The most common form of cataract that develops over time is called "age-related cataract," and it strikes men and women equally after the age of 50. Although the illness often affects both eyes equally, it nearly invariably manifests in one eye first. Pre-senile cataract is a disorder in which cataractous alterations resembling senile cataract appear before the age of fifty. Diabetes mellitus is one of the most common causes of pre-senile cataract. It has long been recognized that diabetes and hyperglycaemia raise the risk of cataract development.[22]

The primary phase of cataract formation is the accumulation of protein or yellow-brown pigment clumps in the lens that reduce light transmission to the retina at the back of the eye. The breakdown of lens proteins due to ageing is the most prevalent cause, while conditions like diabetes and high blood pressure may hasten this process. If the lens's ability to remove reactive oxygen species decreases or oxidative stress increases, the lens may become more opaque.[23]

Cataracts may develop in hyperglycaemic patients due to oxidative stress, increased nonenzymatic glycation of lens proteins, and activation of the polyol pathway, which results in sorbitol buildup.[24] Sorbitol is produced from glucose by the enzyme aldose reductase. Polyol dehydrogenase transforms sorbitan into fructose, a glycolysis substrate that is not as ideal. Sorbitol and fructose both have the ability to raise osmotic pressure, which might be useful for controlling the lens's volume.

Two kinds of cataracts are linked to diabetes:

Fig 7: Cataract

1. Diabetics often experience the onset and rapid progression of senile cataracts at a young age.

2. "Snowflake cataract" and "snowstorm cataract" are alternative names for the same kind of diabetic cataract. This rare condition, which typically strikes young people, is caused by osmotic overhydration of the lens. As sorbitol accumulates during glucose metabolism by NADPH+ dependent aldose reductase, osmotic overhydration of the lens occurs. An enormous amount of fluid vacuoles build up beneath the anterior and posterior capsules prior to the appearance of bilateral snowflake-like white opacities in the cortex.[25]

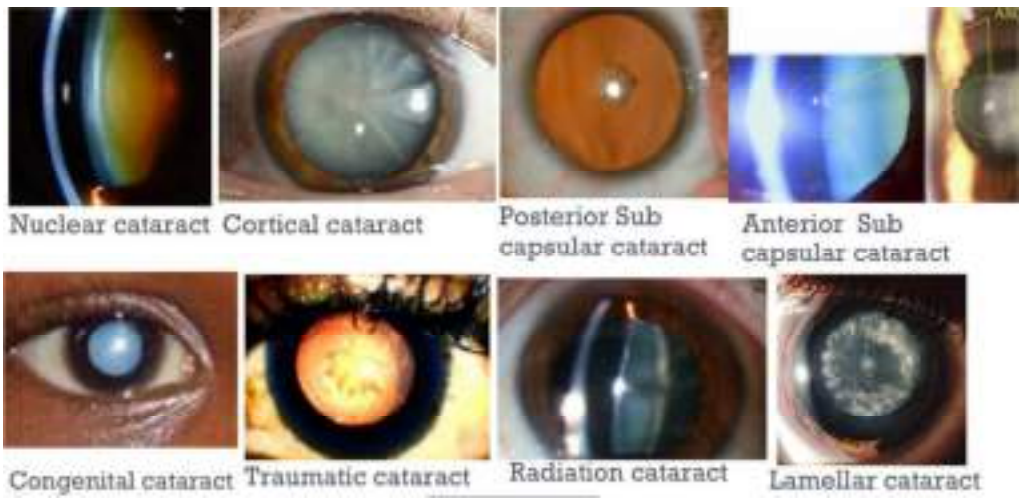


Fig 8: Different types of cataract

Types of cataracts:

- Nuclear cataracts
- Cortical cataracts
- Posterior subcapsular cataracts
- Anterior subcapsular cataracts
- Congenital cataracts
- Traumatic cataracts
- Radiation cataracts
- Lamellar or zonular cataracts

Clinical features:

1. Glare
2. Uniocular polyopia
3. Coloured halos
4. Early stages of cataract can cause blurred or distorted vision, as well as cloudy or partially cloudy vision.
5. Deterioration of vision

An increased risk of backward subcapsular, nuclear, and cortical cataracts is associated with a higher body mass index. Obesity has been linked to cataract through endothelial dysfunction, inflammation, and oxidative stress.[26] Cataracts have been linked to inflammatory markers such as intracellular adhesion molecule-1, C-reactive protein, and interleukin-6.[27] There is conflicting evidence linking hypertension to cataracts. Preliminary data from animal research suggests that changes in the extracellular fluid volume, ciliary body status, inadequate ion transport at the lens epithelium, and modifications in the lens capsule's protein structures could all play a role in the development of cataracts.[28]

A correlation between MetS and cataract has been seen in the majority of observational studies. Cataract prevalence increased with rising MetS component numbers in both men and women, according to the Singapore Malay Eye Study, which surveyed 3,280 Malay individuals between the ages of 40 and 80. The three primary components of MetS—diabetes and hypertension—were all significantly correlated with cataract in this research. A cataract was four times as likely to occur in those who also had diabetes and high blood pressure. Serum lipids, HDL, and body mass index were not shown to be associated with cataracts in this study. Metabolic syndrome was positively correlated with all subtypes of cortical cataract.[29]

The Blue Mountains Eye study, which tracked 3654 senior citizens in Australia for ten years, discovered that MetS elevated the prevalence of all cataract subtypes, including posterior subcapsular cataract (PSC), cortical, and nuclear.[30] Ghaem Maralani et al. discovered that at 5 years, cortical and posterior subcapsular cataracts were more common in the same group of people with MetS alterations. [31] In a similar vein, Paunksnis et al. found that MetS was associated with cataracts in a European survey of middle-aged men and women.[32] Cataracts are more common in MetS patients, according to Bojarskiene et al. despite the fact that this association was only statistically significant in females.[33]

Metabolic syndrome and glaucoma

Definition: The disease known as glaucoma is actually a group of related conditions. The optic disc takes on a certain appearance and develops a pattern of permanent visual field abnormalities due to progressive optic neuropathy. Elevated intraocular pressure is often, but not always, a symptom of glaucoma.[34]

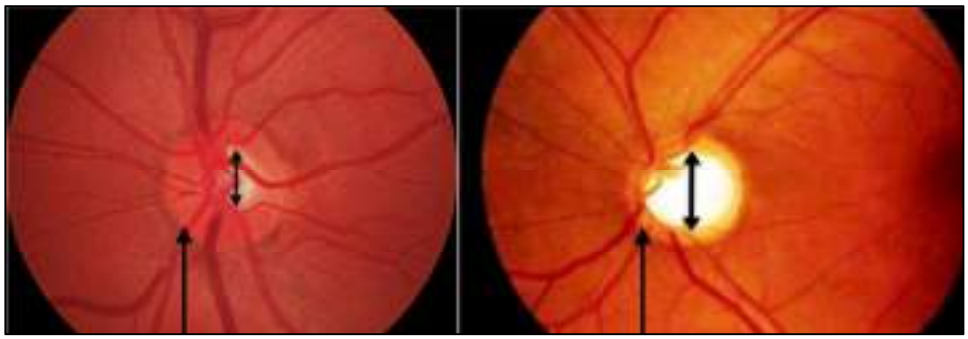


Fig 9: Normal optic nerve head and Glaucomatous cupping

Aqueous humor dynamics are crucial to the pathogenesis of glaucoma. It mostly affects ocular structures like the ciliary body, anterior chamber angle, and aqueous outflow system.[35]

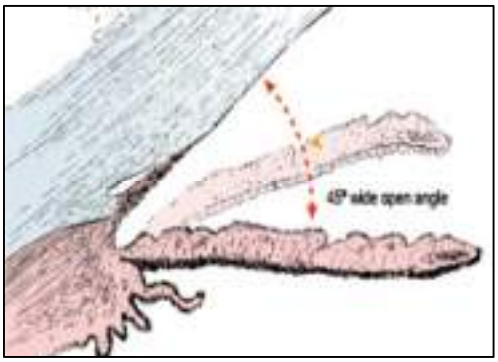


Fig 10: Angle of anterior chamber

It advances over time and is the primary cause of permanent blindness worldwide.[36] Intraocular pressure (IOP) is the most prevalent risk factor for glaucoma, while there are other ones as well. For this reason, situations in which the IOP is consistently high but glaucomatous damage is absent are referred to as "ocular hypertension." Disc cupping and other abnormalities of the visual field are indicative of normal or low tension glaucoma (NTG/LTG), a condition when the intraocular pressure (IOP) is normal or low.[37]

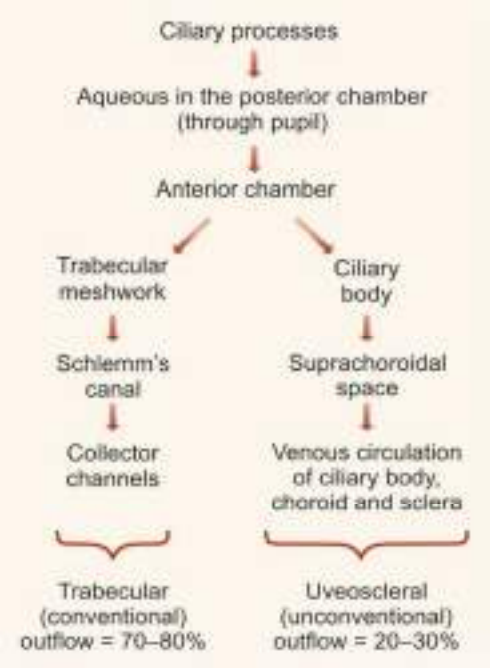


Fig 11: Aqueous humour drainage

Aqueous Humour Drainage

Water humour passes through the pupil and moves from the rear chamber into the front chamber, meeting some physiological resistance along route.

Two pathways allow the water to exit the anterior chamber:

1. Trabecular (conventional) outflow
    A. Passive filter mechanisms
    B. Aqueous outflow active pump mechanism
2. Uveoscleral (unconventional) outflow

Classification:

A. Congenital/developmental glaucoma

1. Primary congenital glaucoma

2. Developmental glaucoma

B. Primary adult glaucoma

1. Primary open-angle glaucoma (POAG)

In this kind of primary glaucoma, the elevation of intraocular pressure has no apparent ocular or systemic origin. It is typically characterised by:

- Slowly progressive raised intraocular pressure (>21 mm Hg recorded on at least few occasions) associated with,
- Open normal appearing anterior chamber angle
- Characteristic optic disc cupping
- Specific visual field defects

2. Primary angle-closure glaucoma (PACG)

In primary angle closure disease, the peripheral iris presses against the trabecular meshwork (TM), further narrowing the anterior chamber and obstructing the passage of aqueous outflow.

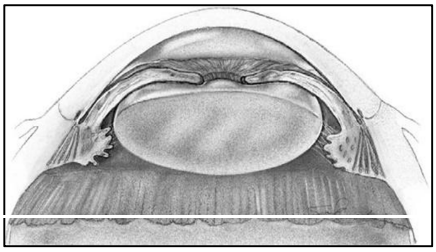


Fig 12: Primary angle closure glaucoma

3. Primary mixed mechanism glaucoma

C. Secondary glaucoma

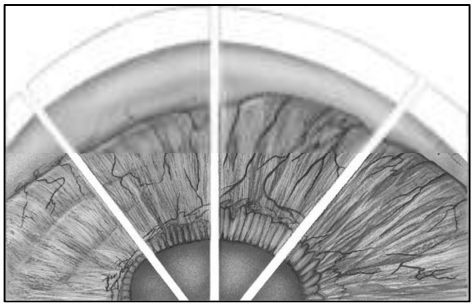


Fig 13: Neovascular glaucoma

An elevated intraocular pressure can be caused by a variety of ocular or systemic illnesses. That is why the symptoms might be either caused by the main illness or by the consequences of increased intraocular pressure. Eg. Primary open-angle glaucoma.

The force that the contents of the eyeball exert on the eyeball's outer layers is known as intraocular pressure (IOP). With an average pressure of 15.5 ±2.57 mm Hg, the normal intraocular pressure (IOP) stays within the normal range of 10.5 to 20.5 mm Hg because of the dynamic equilibrium between the generation of aqueous humour, its outflow, and the pressure in the episcleral veins.In primary angle closure disease, the peripheral iris presses against the trabecular meshwork (TM), further narrowing the anterior chamber and obstructing the passage of aqueous outflow.[38]

Systemic blood pressure is correlated with intraocular pressure, according to many research. When blood pressure fluctuates significantly, intraocular pressure (IOP) changes just slightly. According to Bulpitt and colleagues, a 2 mmHg increase in intraocular pressure (IOP) would necessitate a 100 mmHg rise in systemic blood pressure. In a normal heart, the intraocular pressure (IOP) changes by 1-3 mm Hg with each cardiac cycle. The extent of this intraocular pressure fluctuation is related to both the change in artery pressure and the height of the ocular pressure. There is a weak correlation between systemic hypertension and glaucoma; most of the impact is due to changes in perfusion pressure or other vascular effects, not elevated intraocular pressure.[39]

Increased intraocular pressure (IOP) is linked to increases in episcleral venous pressure (EVP), which may be caused by either systemic or localised factors. When episcleral venous pressure rises, intraocular pressure (IOP) often follows suit within a similar range.

At this time, it is unclear how MetS is linked to IOP. Some pathophysiological linkages, including aquaporins, endocannabinoid overactivity, and sympathetic activation, have been uncovered in recent studies. Sympathetic hyperstimulation is

linked to conditions like as obesity, high blood pressure, and insulin resistance.[40] Obesity, dyslipidaemia, and hyperglycaemia are among conditions that may arise when the endocannabinoid system is overactive. Among the MetS components, diabetes has the potential to raise intraocular pressure (IOP) or harm the blood vessels that feed the optic nerve. Corneal stiffness due to glycation-induced collagen cross-linking and autonomic dysfunction in diabetes both contribute to elevated intraocular pressure (IOP).Dyslipidemia and glaucoma are not clearly linked.

Researchers Chang et al. found that individuals with MetS had substantially greater intraocular pressure (IOP) compared to those without the condition in a 2004 analysis of clinical data from 1112 patients receiving health checks. [41] An average rise of 0.33 mm Hg in intraocular pressure (IOP) was linked to each extra MetS component. Their results jived with those of a 2005 study by Oh et al. on Koreans.[42]

Primary open angle glaucoma incidence was compared in 2019 by Jung et al. between nonobese individuals with metabolic illness and metabolically fit obese patients.[43] In the research, 4970 individuals, or 1.3% of the overall sample size, had POAG. POAG was more common in those with high blood pressure, total cholesterol, and fasting glucose levels. Individuals with a body mass index (BMI) higher than 30 kg/m^2 were more likely to have POAG than people with a normal BMI. A higher number of MetS components was similarly linked to an increased risk of POAG. adults with metabolic disease or non-metabolic illness had a higher probability of developing POAG (adjusted hazard ratio [HR], 1.574; 95% CI, 1.449-1.711; adjusted HR, 1.521; 95% CI, 1.405-1.645; adjusted HR, 1.019; 95% CI, 0.907-1.144) in comparison to obese adults with metabolic health.

A case-control study conducted by Kim et al. on 18,240 South Koreans did not find a significant connection between MetS and NTG (Normal tension glaucoma). He discovered that NTG is linked to hypertension and decreased glucose tolerance.[44]

Metabolic syndrome and Third nerve palsy

Anatomic course of cranial nerve III

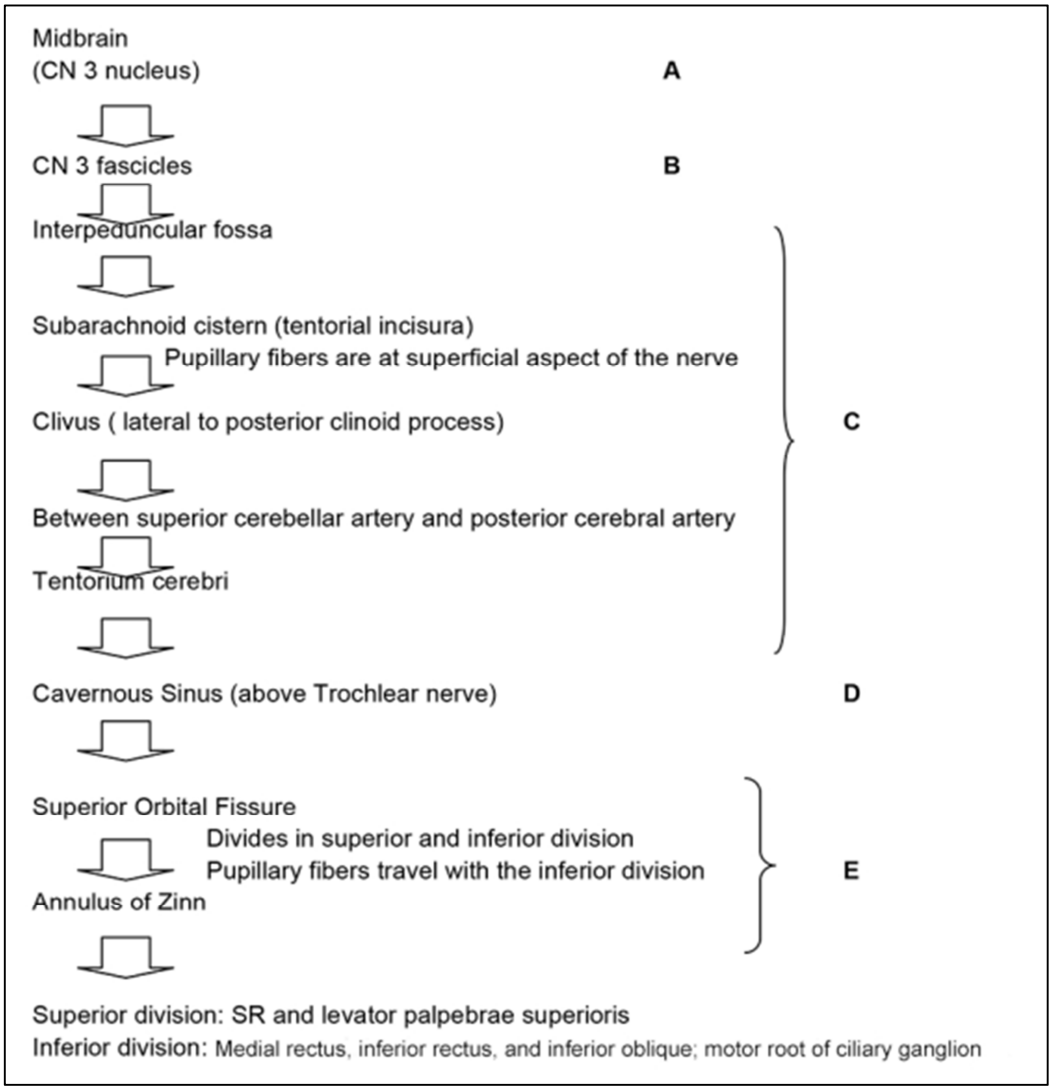


Fig 14: Anatomic course of 3rd cranial nerve

The ciliary muscles, sphincter pupillae, superior, middle, inferior recti, and inferior oblique extraocular muscles, as well as the levator palpebrae superioris of the upper eyelid, are all supplied by the outer parasympathetic fibres of the oculomotor nerve. The inner somatic fibres of the nerve make up its second main component.

Oculomotor nerve palsy may result from trauma, vascular ischemia, intracranial tumours, haemorrhage or congenital disorders. The bulk of cases with acquired nerve palsy are caused by systemic factors, the most prevalent of which are diabetes mellitus and hypertension. These factors also produce ischemic alterations in the nerve.[45]

Acquired lesions of the third nerve at different levels have diverse causes and symptoms: [46]

- Supranuclear lesions: Lesions at the le pathway cause conjugate paresis of botl
- Nuclear lesions: Vascular diseases, den
- Fascicular lesions: The etiology is simil
- Basilar portion: In this region, isolated t to aneurysms, diabetes mellitus[33] and e
- Intracavernous portion: any lesion in th palsies of the cranial nerve IV, cranial V. The common etiology is diabetes, pit fistula.
- Intraorbital portion: Trauma, tumors an

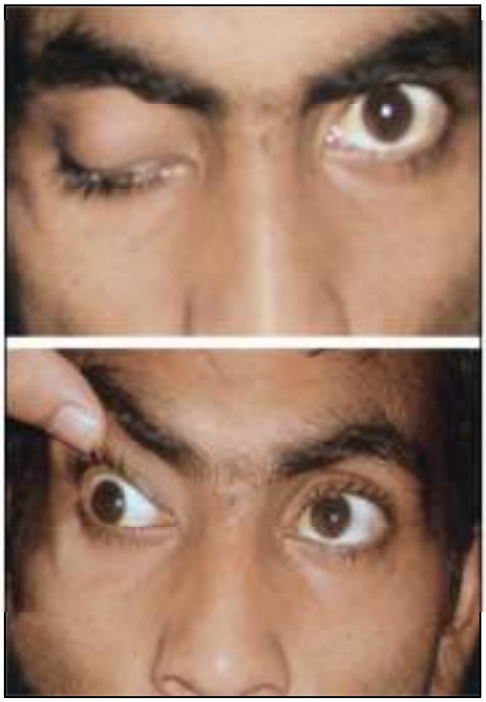


Fig 15: 3rd Cranial nerve palsy

Clinical Features

- Ptosis: Since the levator palpebrae superioris muscle is paralysed
- Ocular deviation: Down and out position.
- Pupil: In compressive third-nerve palsy, the paralysis of the sphincter pupillae causes pupils to become fixed and dilated. Another sign of ciliary muscle paralysis is an inability to accommodate. with contrast, with ischemic lesions, accommodation is unaffected and the pupil is left intact.
- Diplopia: The damaged eye's deviation causes the picture to fall on an extrafoveal spot, causing this to happen.

Since the pupillary fibres are located on the periphery of the nervous system and get more collateral blood flow than the main trunk, they are less likely to be affected by ischemia in CN III palsy that does not include the pupil. Because of this, atherosclerosis, diabetes mellitus, and systemic hypertension are common in patients, and migraine pupil is not always involved.

Ischemia, compression, or inflammation are all possible causes of whole oculomotor nerve palsy that does not impact the pupil. The majority of CN III palsies, whether whole or partial, that do not affect the pupil are caused by an ischemic process. following the first four weeks, these patients start to feel better, and by the twelve weeks following the insult, they have completely recovered. After six months of stability, individuals who still have some vision loss may be candidates for strabismus surgery or prisms. When this occurs, correcting the patient's primary and reading positions is the major focus of strabismus surgery.[47]

In order to ascertain if metabolic syndrome (MetS) is connected to the onset of third, fourth, and sixth cranial nerve palsy (CNP), Daye Diana Choi et al.undertook research in 2021. [48] The National Health Insurance Service (NHIS) of South Korea provided the 4,067,842 individuals whose ages ranged from 20 to 90 years old, whose data was used in the analysis. CNP was more common in persons with MetS (n = 851,004) than in those without it (n = 3,216,838). As the number of MetS components rose, the frequency of CNPs reduced as well. In large-scale cohort studies involving populations, it has been proposed that MetS and its constituent parts could be the cause of CNP.

Metabolic syndrome and diabetic retinopathy

Changes in the retina seen in individuals with diabetes mellitus are called diabetic retinopathy. Diabetic retinopathy has become more common as people with diabetes live longer. Many people go blind as a result of this. A significant factor in the onset and advancement of DR is chronic hyperglycaemia, which damages tissues. A person's susceptibility to the effects of hyperglycaemia depends on a number of clinical factors, such as their hypertension and dyslipidaemia, as well as their genetic makeup.[49]

Some have proposed that oxidative stress mediates the interconnected biochemical and molecular processes of DR pathogenesis that are produced by hyperglycaemia. The generation of superoxide starts a self-sustaining cycle in which additional reactive oxygen species (ROS) are produced as a result of metabolic failure.[50] 'When intracellular ROS levels are too high, they alter gene expression in a way that damages cells permanently. One of the main causes of the vascular anomalies and VEFG expression that are characteristic of DR is chronic low-grade

inflammation, which in turn causes capillary blockage and hypoxia.[51] Diabetic retinopathy risk factors include ethnicity, smoking, pregnancy, dyslipidaemia, uncontrolled and chronic diabetes, and uncontrolled hypertension.

Risk factors

1. Duration of diabetes

- After 10 years, 20% of type I and 25% of type II diabetics develop retinopathy.
- After 20 years, 90% of type I and 60% of type II diabetics develop retinopathy.
- After 30 years, 95% of both type I and type II diabetics develop retinopathy.

2. Sex- Incidence is more in females than males (4:3).
3. Poor metabolic control is less important than duration, but is nevertheless relevant to the development and progression of DR.
4. Heredity. It is transmitted as a recessive trait. The effect of heredity is more on the proliferative retinopathy.
5. Pregnancy may accelerate diabetic retinopathy.
6. Hypertension, when associated, may also accentuate diabetic retinopathy.
7. Other risk factors include smoking, obesity, anaemia and hyperlipidaemia.

Pathogenesis

When diabetes mellitus is not under control, hyperglycaemia sets in, and DR develops from there. Diabetic retinopathy is characterised by microangiopathy, which is caused by hyperglycaemia and affects the pre-capillary arterioles, capillaries, and venules of the retina.

Some of the ways in which microangiopathy can be caused by hyperglycaemia are:

1. Cellular damage.

2. Haematological and biochemical changes induced by hyperglycaemia

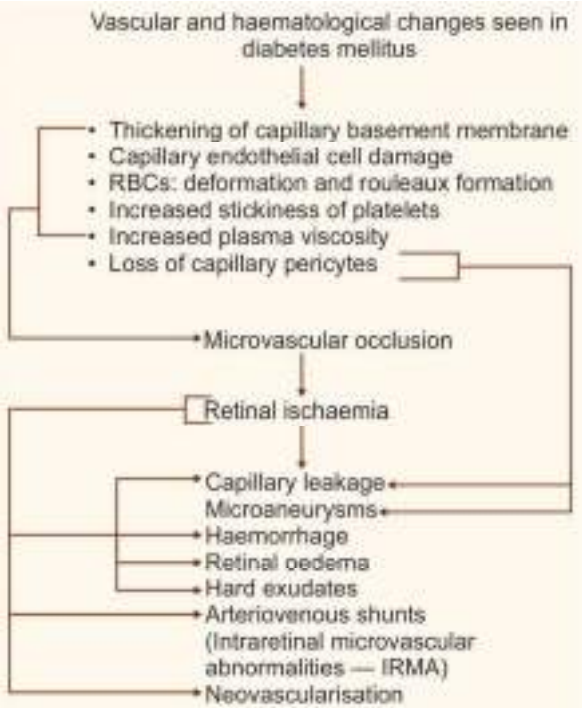


Fig 16: Vascular and hematological changes in Diabetes mellitus

Classification of Diabetic Retinopathy

There are several ways that diabetic retinopathy might be categorised. The following is the currently used categorization:

I. Non-proliferative diabetic retinopathy (NPDR)

- Mild NPDR
- Moderate NPDR
- Severe NPDR
- Very severe NPDR

II. Proliferative diabetic retinopathy (PDR)

III. Diabetic maculopathy

IV. Advanced diabetic eye disease (ADED)

Classification of NPDR by ETDRS study:

1. Mild NPDR

- There needs to be one microaneurysm.

2. Microaneurysms or intraretinal haemorrhage in two or three quadrants with moderate NPDR.

- Early-stage internal retinal microvascular abnormalities (IRMA) and the presence of either soft or hard exudates are both possible.

3.Severe NPDR- Any one of the following (4-2-1 Rule):

- There are severe retinal haemorrhages and four microaneurysms.
- Venous beads in two quadrants.
- Changes to an intraretinal microvascular abnormality (IRMA) region.

4.Very severe NPDR- Any two of the following things (4–2-1):

- Four corners have microaneurysms, and the retina has significant haemorrhages.
- Changes to a single location of intraretinal microvascular abnormalities (IRMA).

- Two areas of venous beading.

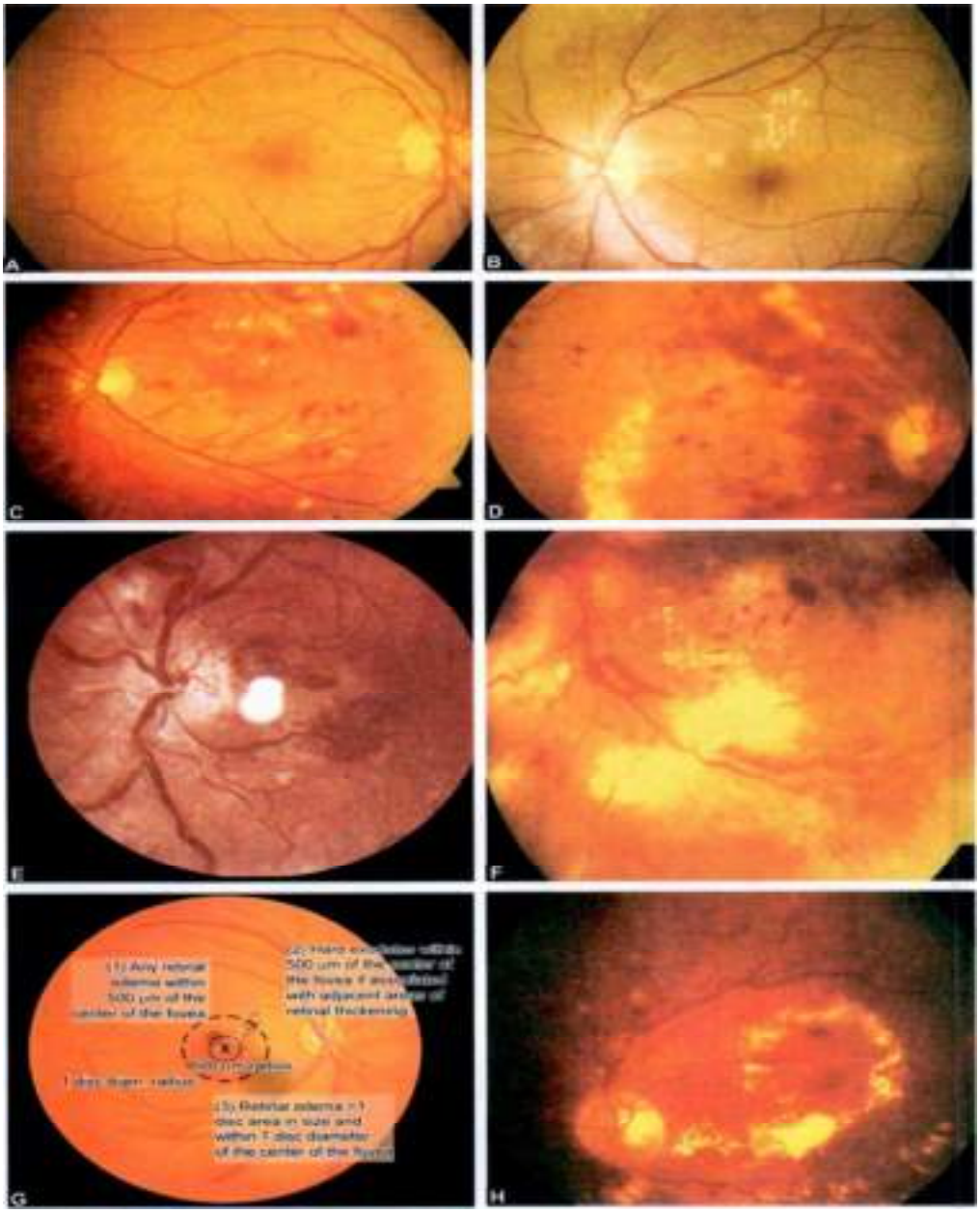


Fig 17: Diabetic retinopathy: A-mild NPDR; B-moderate NPDR;C- severe NPDR; D-very severe NPDR;E- early PDR;F- high-risk PDR;G-Criteria of CSME; H-focal exudative diabetic maculopathy

Researchers Keenan et al. examined retinopathy and metabolic syndrome in 2009 in addition to diabetes.[52] A cross-sectional study with 8,205 participants over 40 years of age was carried out; 6,582 of those individuals were not diabetics. Retinopathy affected 3.5% of people without diabetes and 5.4% of the general population. Research findings were no longer associated with metabolic syndrome or retinopathy (OR, 2.23; 95% CI, 1.69 to 2.95), when diabetes was taken into account. While metabolic syndrome was not associated with retinopathy (OR, 1.23; 95% CI, 0.77 to 1.99), high blood pressure was (OR, 1.61; 95% CI, 1.09 to 2.37) in the non-diabetic group.

Hendrik A. van Leiden et al. studied 233 people with normal or impaired glucose metabolism, ages 50 to 74, to determine the association between smoking, age, sex, hypertension, BMI, waist-hip ratio, serum lipid levels, and glycosylated haemoglobin with the occurrence of retinopathy. [53] The cumulative incidence of glucose metabolism was 7.3% for people with normal glucose metabolism, 13.6% for those with impaired glucose metabolism, and 17.5% for those with diabetes. Age, sex, BMI, smoking, serum triglyceride, total HDL, and non-HDL cholesterol levels were not associated with retinopathy (P>.05 for all); instead, glycemia, hypertension, and abdominal obesity were revealed to be the predictors of retinopathy in the general population.

Abdul-Ghani et al. (2016) discovered a notably higher incidence of microvascular-related issues among diabetic patients with MetS (46.6% vs. 26.8%, P =.0005) in a study of Jewish individuals with type 2 diabetes. The study comprised 145 patients without the syndrome and 270 people with MetS based on NCEP-ATP III criteria. [54]

In a 2016 multicentric study, DR and MetS were correlated with either the NCEP-ATP III criteria (1.41 times) or the IDF criteria (1.49 times) in 7859 Italian type 2 diabetes. This study found a connection between MetS and DR in 638 individuals with type 1 diabetes, however it was not close to statistical significance.[55]

Costa et al. discovered in 2004 that among 548 Europeans with diabetes who met the WHO criteria for MetS, the prevalence of retinopathy was higher (44% vs. 20%).[56]

Patients with MetS showed a lower prevalence of DR (16.9% vs. 21.3%) than patients without the disease, according to a cross-sectional study involving 1414 diabetic patients from South India. DR was more common in people with MetS who had had diabetes for less than ten years, as well as in women who had had the disease for eleven to twenty years.[57]

Retinopathy was more prevalent in those with MetS in a 2018 research of 1986 Asian patients with type 2 diabetes, as assessed by NCEP-ATP III (37.9% in T2D+MetS vs. 28.6% T2D without MetS P<001).[58]

Zhou et al. (2018) conducted a meta-analysis incorporating twelve observational studies that investigated the correlation between MetS and diabetic retinopathy. Researchers were unable to find a link between MetS and DR in those with type 1 or type 2 diabetes. Furthermore, there was no evidence linking retinopathy to any specific MetS component. Among the variables taken into account were triglyceride levels, good cholesterol, waist-to-hip ratio, and hypertension.[59]

Metabolic syndrome and Hypertensive retinopathy

Among the several eye problems that can arise from hypertension are retinopathy, optic neuropathy, choroidopathy, and obstruction of important retinal arteries, such as the central retinal vein, branch retinal artery, and central retinal artery.

Fundus alterations in hypertensive retinopathy are symptoms of systemic hypertension.

One aspect of the clinical presentation of hypertensive retinopathy is altered hypertension.

- Optic neuropathy
- Choroidopathy
- Retinopathy

The American College of Cardiology/American Heart Association (ACC/AHA) suggested the following definitions for high blood pressure in 2017.[60]

Category	Systolic (SBP)	Diastolic (DBP)
Elevated blood pressure	120-129 mmHg	< 80 mmHg
Stage 1 hypertension	130-139 mmHg	80-89 mmHg
Stage 2 hypertension	≥ 140 mmHg	≥ 90 mmHg

Pathophysiology

The degree to which hypertension is controlled determines the phases of hypertensive retinopathy, which can be categorised as vasoconstrictive, sclerotic, and exudative.

- Vasoconstrictive Phase: Retinal arteriole constriction and vasospasm limit flow as a result of local autoregulatory processes brought about by higher luminal pressures.
- Sclerotic Phase: As the arteriolar [61] decreases, changes occur in the AV crossing, and silver and copper wire are implemented, the endothelial wall layers experience intimal thickening, medial hyperplasia, and hyaline deterioration.
- Exudative Phase: A breached blood-brain barrier that permits plasma and blood to escape is indicated by retinal haemorrhages, hard exudates, retinal ischemia, and necrosis of smooth muscle.

Clinical types

- Chronic hypertensive retinopathy
    1. Hypertension with involutionary (senile) sclerosis
    2. Chronic hypertension with compensatory arteriolar sclerosis
- Malignant or acute hypertensive retinopathy
    1. Acute hypertensive retinopathy
    2. Acute hypertensive choroidopathy
    3. Acute hypertensive optic neuropathy

Staging of Hypertensive Retinopathy

Keith and Wagner classification

- Grade I. Vein concealment and the arteriolar light reflex are both mildly attenuated, but the attenuation of the arteriolar branches is disproportionately high.
- Grade II. Deflection of veins at arteriovenous crossings, together with considerable generalised constriction and localised attenuation of arterioles, is known as Salu's sign.
- Grade III. Varieties show right-angle deflection, grade II alterations including copper wiring of arterioles, bonnet sign, gunn sign, and banking of veins distal to arteriovenous crossings. Additionally, there are cotton-wool patches, hard exudates, and flame-shaped haemorrhages.
- Grade IV. All grade III alterations, in addition to arteriole silver-wiring and papilledema

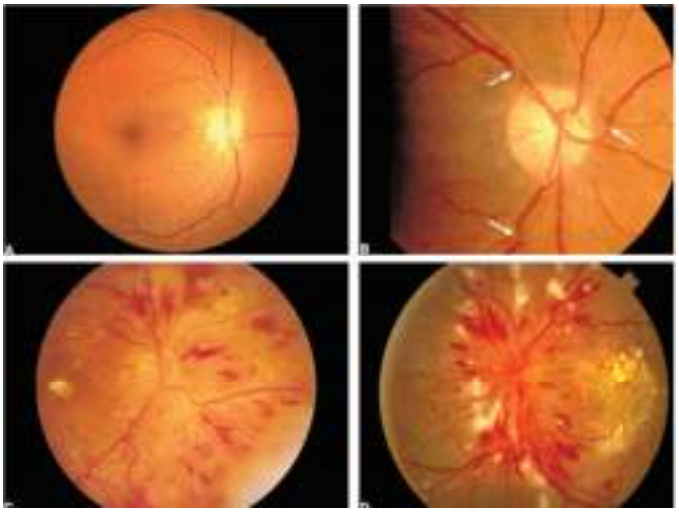


Fig 18: Hypertensive retinopathy: A, grade I; B, grade II; C; grade III; D, grade IV

Scheie classification

- Stage 0. No visible retinal abnormalities
- Stage 1. Diffuse arteriolar narrowing; no focal constriction
- Stage 2. Arteriolar constriction is more noticeable when there is a focused narrowing.
- Stage 3. Focal and diffuse narrowing, with retinal haemorrhages
- Stage 4. Retinal oedema, hard exudates, optic disc edema

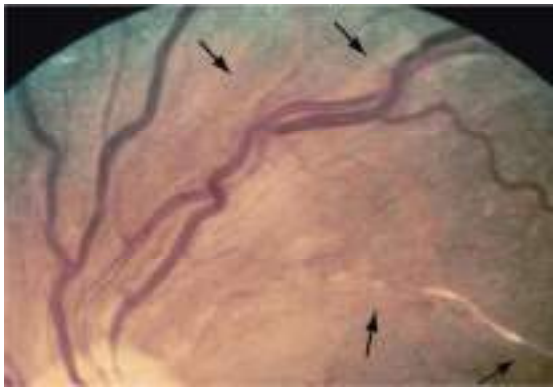


Fig 19: copper-wiring, arteriovenous nicking and silver-wiring seen in hypertensive retinopathy. [61]

Modified Scheie Classification of Hypertensive Retinopathy :

- Grade 0: No changes
- Grade 1: Barely detectable arterial narrowing
- Grade 2: Obvious arterial narrowing with focal irregularities
- Grade 3: Grade 2 plus retinal hemorrhages, exudates, cotton wool spots, or retinal edema
- Grade 4: Grade 3 plus papilledema

The differential diagnosis for hypertensive retinopathy includes radiation retinopathy, ocular ischemic syndrome, anaemia and other blood dyscrasias, and retinal vein blockage.

Metabolic syndrome and retinal microvascular changes

Diabetes and hypertension are frequently linked to retinopathy and other microvascular disorders. Moreover, MetS is associated with endothelial dysfunction affecting both large and small vessels, inflammation, and atherosclerosis affecting major arteries.[62]

In 2004, Tien Yin Wong et al. carried out a cross-sectional investigation to look at the connection between retinal microvascular anomalies and metabolic syndrome. [63] The 11,265 study participants ranged in age from 49 to 73. Retinal images were assessed for retinal microvascular indicators, including arteriovenous nicking, microaneurysms, retinal haemorrhages, and localized arteriolar constriction, using a standardized procedure. A higher incidence of retinopathy, localized arteriolar constriction, arteriovenous nicking, generalized retinal arteriolar narrowing, and generalized retinal venular dilatation was observed to be correlated with type 2 diabetes. Associations for venular dilatation, localized arteriolar narrowing, generalized arteriolar narrowing, and arteriovenous nicking were observed even in individuals without diabetes or hypertension.

In his 2009 research, Saito et al. provided a detailed description of the Japan Public Health center-based Prospective (JPHC) study, which evaluated metabolic risk factors at baseline in 21,639 females and 12,412 males aged 40 to 69 without a history of cancer or cardiovascular disease (CVD).[64] Patients with metabolic syndrome

showed greater retinal venule diameters and lower retinal artery diameters, which was consistent with Tien yin wong et al.'s findings.

In 2012, Zhao et al. observed strikingly identical outcomes in Japanese people.[65]

Metabolic syndrome and central retinal artery occlusion

The ciliary arteries travel through the choriocapillaris to supply blood to the outer retina, while the central retinal artery supplies blood to the inner retina. The ciliary artery receives its primary branch from the ophthalmic artery and thereafter serves the anterior region via the rectus muscles. When it comes to eye diseases, CRAO is among the most serious and pressing issues. It happens when a material inside the optic nerve blocks blood flow to the central retina. Sudden, painless blindness is a telltale sign of retinal artery blockage.[66]When blood flow to the inner retinal layers is insufficient, the layers of nerve fibres and ganglion cells bulge.

Aetiology

- Emboli
- Atherosclerosis-related thrombosis
- Vascular wall inflammation
- Angio spasm
- Raised intraocular pressure
- Thrombophilic disorders
- Systemic hypotension
- Cardiac causes include arrhythmia and mitral valve prolapse.

- Rarer causes include hypercoagulation diseases (e.g., oral contraceptives, polycythaemia, antiphospholipid syndrome, hyperhomocysteinaemia, and sickling hemoglobinopathies) and ocular migraine.

Clinical features

Central retinal artery occlusion (CRAO)

- Visual acuity markedly reduced
- Relative afferent pupillary defect (RAPD) will be present.

Fundus examination shows:

- Marked narrowing of retinal arteries and mild narrowing of retinal veins.
- Retina becomes milky white due to ischaemic oedema. In eyes with cilioretinal artery part of macula remains normal in colour
- Cherry-red spot is seen in the center of macula due to vascular choroid shining through the thin retina in foveal region, in contrast to the surrounding pale retina
- Cattle tracking, i.e., segmentation of blood column is seen in the retinal veins.
- Atrophic changes. In most cases retinal oedema resolves over a period of 4–6 weeks and atrophic changes in the form of grossly attenuated thread like arteries atrophic appearing retina and consecutive optic atrophy occur in long standing cases

Retinal oedema encircles the fovea, with the exception of that particular region of the posterior pole, because of the multilayer nature of the inner retina. The surrounding fovea is hazy and oedematous retina, with a "cherry red spot" shaped underlying choroid with intact retinal pigment epithelium (RPE) standing out. The most frequent causes of central retinal artery occlusion are vasculitis, giant cell arteritis, polyarteritis nodosa, sickle cell disease, and carotid and cardiac emboli.

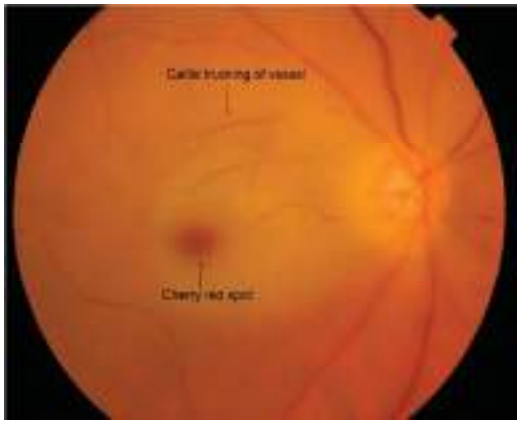


Fig 20: Fundus finding of CRAO

Potential risk factors for the development of chronic obstructive pulmonary disease (CRAO) include arteriosclerosis, persistent atrial fibrillation, congestive cardiac failure, cerebrovascular accident, systemic hypertension, myocardial infarction, diabetes mellitus, and rheumatic heart disease.

According to the case study by Kosanović-Jaković N et al. a 52-year-old man experienced painless loss of vision in his right eye (no feeling of light) in 2005. The lab results, which showed an increased erythrocyte sedimentation rate of 105 mm/h and an elevated C-reactive protein level of 22 mg/L, were in line with the fundoscopy-confirmed symptoms of CRAO. Antiphospholipid syndrome, collagen vascular disorders, hypercoagulable state, and vascular disease were excluded with specific laboratory testing and fluorescein angiography.[67]

A 64-year-old man's case of severe left-eye blindness that came on suddenly, without pain, was described in another report published in 2010. Indirect

ophthalmoscopy showed signs compatible with chronic retinopathy of the eye, and laboratory tests showed hyperglycaemia, hyperuricemia, hypertriglyceridemia, hypercholesterolemia, and a high C-reactive protein level of 21 mg/L. Other systemic illnesses were ruled out by fluorescein angiography and immunological tests.[68]

Central retinal vein occlusion

Both systemic and local variables linked to ageing increase the risk of retinal vein thrombosis. It ranks just behind DR as the most frequent retinal vascular disease. The adventitial sheath, arteriovenous thickening, and compression of a venule at an arteriovenous crossing are the hallmarks of occlusion of a branch retinal vein. Thrombosis, turbulent flow, and the death of endothelial cells are the results. Atherosclerotic alterations in the artery may cause central retinal vein blockage because the sheaths of the two vessels meet at sites posterior to the lamina cribrosa.

Among those living in industrialised nations, 5.20 per 1000 have retinal vein occlusions, with 0.8 per 1000 experiencing central retinal vein occlusions.[69] There are two forms of RVO: branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO). Based on whether the veins are perfused or not, there are two subtypes of central retinal vein blockage: ischemic and non-ischemic. Some of the variables that might lead to this condition include ageing, open-angle glaucoma, diabetes, high cholesterol, and systemic arterial hypertension.

Aetiology

- Thrombosis in the venous lumen is secondary to pressure from an atherosclerotic retinal artery that shares an adventitia with the vein.
- Common risk factors include hypertension and diabetes mellitus.
- Cryoglobulinemia, leukaemia, multiple myeloma, hyperlipidaemia, polycythaemia, and hyper viscosity of the blood are all conditions characterised by abnormally thick blood.
- Arteriosclerosis, syphilis, and systemic lupus erythematosus can all cause peripheral or central periphery-based phlebitis of the retina.
- Increased pressure within the eye. Patients suffering from primary open-angle glaucoma are more likely to experience central retinal vein blockage.
- Ocular tumours, cellulitis, erysipelas, and cavernous sinus thrombosis are examples of local causes.

Classification

1. Critical vein occlusion in the retina (CRVO).
2. It might be venous stasis retinopathy, which is non-ischemic, or haemorrhagic retinopathy, which is ischaemic.
3. The condition known as branch retinal vein occlusion (BRVO)

Non-ischaemic CRVO

Symptoms:

- Vision loss occurs suddenly and painlessly in one eye.
- The degree to which VA is compromised varies with the severity.
- Low or non-existent relative afferent pupillary deficit (RAPD).

Fundus:

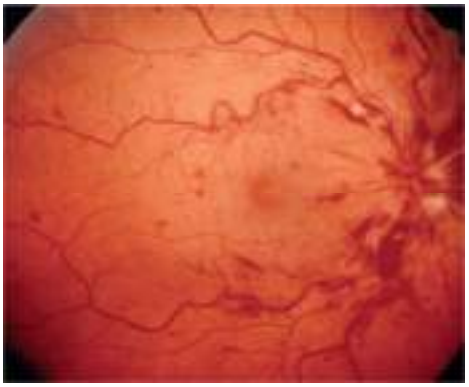


Fig 21: Non ischemic CRVO

Signs are present in every quadrant: ● Cotton-wool spots; optic disc and macular oedema; haemorrhages (dot, blot, and flame); tortuosity and dilated veins, dots, and flames in the central retina. ● A perivenular pattern of patchy retinal whitening is observed at the posterior pole in younger individuals with non-ischemic CRVO.

- Among the numerous anomalies are conditions like vascular disease, sclerosis, epiretinal gliosis, macular pigmentary alterations, atrophic changes, and collateral vessels in the optic disc and surrounding regions.
- Visual impairment is most commonly caused by secondary atrophy and chronic macular oedema.
- Optociliary shunts and retinochoroidal collaterals are disc collaterals.

Pathophysiology:

Thrombosis is caused by three primary things: hypercoagulability, endothelial injury, and venous stasis.

Ischaemic central retinal vein occlusion

Symptoms include capillary closure, retinal hypoxia, and significantly reduced perfusion to the retina. Most cases of visual impairment are caused by macular ischaemia and non-vascular glaucoma.

Symptoms:

- Visual impairment that is both sudden and severe, yet painless, and affects just one eye. Neovascular glaucoma may sometimes appear with redness, photophobia, and discomfort.
- Macular ischaemia is a leading cause of severe VA and a very bad prognosis.
- RAPD is present.
- NVI- About half of the eyes may develop rubeosis iridis, which is sometimes referred to as "hundred-day glaucoma" and can lead to neovascular glaucoma if left untreated.

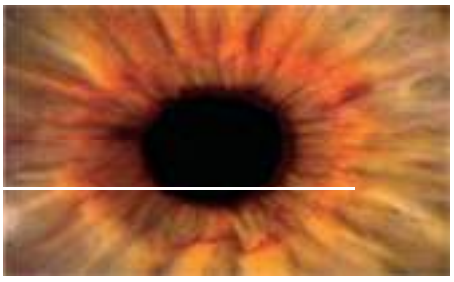


Fig 22: Neovascularization of iris

Fig 23: Neovascularization of angle

- Gonioscopy- When neovascularization does not occur along the edge of the pupil, it is possible for angle neovascularization to develop.

Fundus:

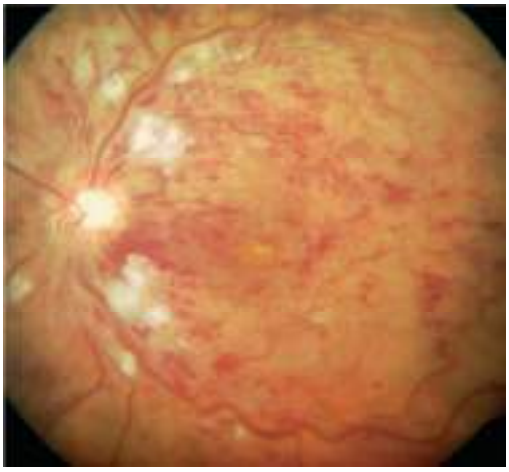


Fig 24: Ischemic CRVO

- Frequent signs and symptoms include engorgement of all branches of the central retinal vein, severe tortuosity, and flame-shaped haemorrhages affecting the posterior and peripheral retina.
- Optic disc swelling and hyperaemia are typically present.
- Alterations to the macula's retina and RPE, including as atrophy, hyperplasia, an epiretinal membrane, and persistent CMO, are possible.
- Exudative age-related macular degeneration-like subretinal fibrosis might form.
- There is considerable vitreous haemorrhage and retinal neovascularization.
- Optic disc collaterals.

Branch retinal vein occlusion :

Diagnosis

- The position of the blockage determines the symptoms and VA. Metamorphopsia and abrupt, painless blurring of vision may occur if the macula is affected. Symptoms of peripheral occlusion are not always obvious.
- The incidence of neovascular glaucoma (NVG) and iris neovascularization (NVI) differs significantly between CRVO and BRVO.

Fundus

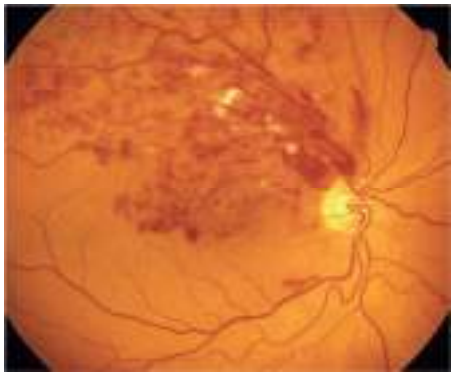


Fig 25: Branch retinal vein occlusion

- The retinal area drained by the thrombosed vein exhibits flame-shaped and dot-and-blot hemorrhages, together with dilatation and tortuosity of the afflicted venous segment.
- Retinal oedema and cotton-wool spots are possible.

- The most typical area to be damaged is the superotemporal quadrant.
- In most cases, the initial symptoms go away within 6-12 months, but the condition is still associated with venous sheathing, sclerosis, and recurrent bleeding.
- Retinal neovascularization is a possibility.

- Neovascularization may lead to tractional retinal detachment, recurrent vitreous and preretinal haemorrhage, and other complications.
- Chronic macular oedema.

Metabolic syndrome and central retinal vein occlusion

In 2020, Dong Hui Li examined the connection between the occurrence of retinal vein occlusion (RVO) and the metabolic syndrome (METS). 23,153,600 people who had never had RVO before took part in a retrospective cohort study. The subjects ranged in age from 47.64 to 13.51 years. Within this group, 6,398,071 individuals (27.6%) had a diagnosis of METS, 11,747,439 (50.7%) were male, and 11,406,161 (49.3%) were female. RVO occurred in 1000 person-years at an overall frequency of 0.947. According to the research, there was an increased risk of acquiring RVO and METS for each diagnostic criterion. One particularly significant determinant for the development of RVO appears to be elevated blood pressure.[70]

Age-related macular degeneration

Age-related macular degeneration (AMD) is an eye disorder that impairs central vision. This disease is brought on by damage to the macula, which is in charge of sharp, forward-looking vision, and can happen with age. The macula, a light-sensitive region near the rear of the eye, is a component of the retina.

Dry ARMD and wet ARMD are the two main forms of ARMD.

The most common form of AMD, called dry/atrophic AMD, moves at a snail's pace. The macula grows thinner as we become older. Dry AMD progresses via three distinct phases: early, medium, and late. There is currently no treatment for late-stage dry AMD.

A less common form of late AMD, wet AMD (sometimes called advanced neovascular AMD) usually causes vision loss to progress more rapidly. Wet AMD may progress from any stage of dry AMD, although it invariably occurs in the later stages.

Clinical features:

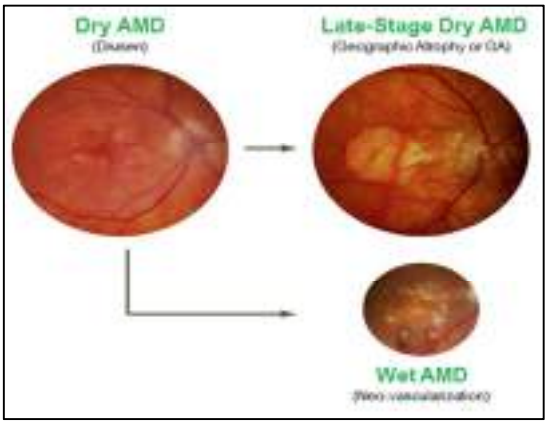


Fig 26: Stages of ARMD

- Early dry AMD doesn't cause any symptoms.
- Patients with intermediate-stage dry AMD may have minor central vision blurriness or have difficulty seeing in dim light.
- Many patients have blurred centre vision and wavy or crooked straight lines in late AMD (whether dry or wet type). This hazy region could grow or turn into solid black dots as time passes.

Metabolic syndrome and age-related macular degeneration

These fundus photos illustrate the cross-sectional link that the Age-Related Eye Disease Study identified between higher body mass index and more advanced

age-related macular degeneration (AMD).[71] Hyperleptinemia brought on by obesity raises systemic oxidative stress, which is recognized to be a major factor in the development of AMD.

Researchers Haleh Ghaem Maralani et al. looked at the link between MetS and AMD in 2015. This study found no association between MetS and early-stage AMD.However, incidence of late ARMD was higher among those younger than 70 years old who had MetS. The same research also found that lipid levels, obesity, and high blood glucose levels were connected with the development of AMD at different stages.[72]

Howard et al.[73] discovered that overweight nonsmoking women were more likely to have early and late AMD when they used body mass index (BMI) and waist circumference as markers.

In a cross-sectional study by Erke et al. which included people in Norway between the ages of 65 and 87, it was only in women that a link between obesity, hypertension, and late AMD was seen.[74] On the other hand, a research of 21,287 people from Europe by Adams et al. showed inconsistent associations between obesity and AMD. Actually, in women, early AMD was inversely correlated with all obesity markers.[75]

Moon et al., conducted a retrospective investigation on 10,449 Korean adults and discovered a link between hyperlipidaemia and AMD's early onset. [76] In a research by Tomany et al., the same component was linked to incident geographic atrophy; however, the inverse was true for incident neovascular AMD.[77]

Diagnostic test for metabolic syndrome:

Classification systems for metabolic syndrome: ATP III NCEP and IDF			
Risk factors		ATP III NCEP (any 3 of 5 features)	IDF (large waist + 2 features)
Waist circumference	Men	>102 cm (40 in)	>94 cm (37 in)
	Women	>88 cm (35 in)	>80 cm (35 in)
Triglycerides		>1.7 mmol/L (150 mg/dL)	≥1.7 mmol/L (150 mg/dL)
HDL cholesterol	Men	<1.03 mmol/L (40 mg/dL)	<1.03 mmol/L (40 mg/dL)
	Women	<1.29 mmol/L (50 mg/dL)	<1.29 mmol/L (50 mg/dL)
Blood pressure		>130/85 mmHg	>130/85 mmHg
Fasting glucose		≥6.1 mmol/L (110 mg/dL)	≥5.6 mmol/L (100 mg/dL)

ATP III NCEP= Adult Treatment Panel 3 National Cholesterol Education Programme; IDF= International Diabetes Federation

Fig 27: Diagnostic criteria for metabolic syndrome

Waist hip ratio assessment:

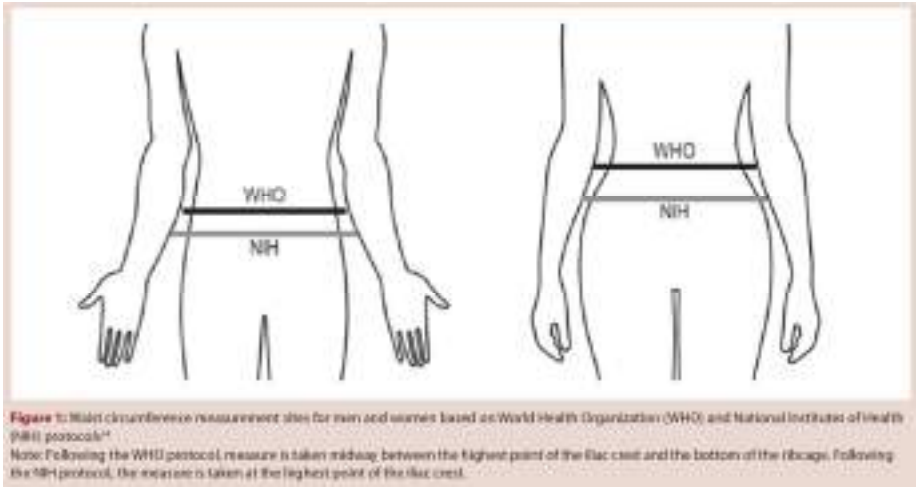


Figure 1: Waist circumference measurement sites for men and women based on World Health Organization (WHO) and National Institutes of Health (NIH) protocols[14]
Note: Following the WHO protocol, measure is taken midway between the highest point of the iliac crest and the bottom of the ribcage. Following the NIH protocol, the measure is taken at the highest point of the iliac crest.

Fig 28: Waist to hip ratio measurement

Risk	Female	Male
Low	0.80 or below	0.95 or below
Moderate	0.81-0.85	0.96-1.0
High	0.8 or higher	1.0 or higher

MATERIAL & METHODS

Participants in the trial, whose ages ranged from twenty to eighty, were seen at the KLES Dr. Prabhakar Kore Hospital and Medical Research Centre in Belagavi from August 2022 to July 2023. The hospital served as the site for the prospective cross-sectional study.

The formula utilized to determine sample size is

$$n = \frac{p(100 - p)Z^2}{d^2}$$

Z denotes the necessary degree of confidence, n the necessary sample size, p the percentage of a state or condition that occurs, and d the percentage of the maximum error.

We assume that, 50% of them will have cataract among subjects with metabolic syndrome.

With percentage of maximum error as 10% at 95% confidence level sample size is given by,

$$n = \frac{50 \times (100 - 50) \times (1.96)^2}{10^2}$$

$$n = 96.04 \approx 96$$

A minimum of 96 people must be surveyed in order to achieve a 95% confidence level and a 10% margin of error.

The accuracy improves as the size of the sample grows.

Inclusion criteria :

Three out of the five components should be between the ages of 20 and 80 for this particular situation.

1. In this research, a big waist was defined as a man's or woman's waist circumference of more than 102 cm or 88 cm, respectively.

2. Hypertriglyceridemia is defined as blood triglyceride levels of 150 mg/dL (1.69 mM) or above.
3. For men, a low HDL cholesterol level is 40 mg/dL (1.04 mM) while for women, it is 50 mg/dL (1.29 mM).
4. Blood pressure is considered high when the diastolic measurement is 85 mm Hg or the systolic reading is 130 mm Hg.
5. A fasting glucose concentration of 110 mg/dL (6.1 mM) or above is considered high glucose.

Exclusion Criteria:

1. Patients with any other co-morbidities, other than obesity associated

2. People with only obesity without any associated syndrome such as diabetes or hypertension or dyslipidaemia.

3. People with Congenital ocular deformities such as cloudiness of cornea, irregularly shaped pupil, opacities in the lens.

Data collection procedure :

The study subjects were enrolled in study by convenient sampling method who fulfilled inclusion criteria after obtaining the informed consent at KLEs Dr. Prabhakar Kore hospital, Belagavi with age group above 20 years with metabolic syndrome, their details and thorough clinical history was obtained.

A) Age related cataractous changes associated with metabolic syndrome are

- Nuclear cataract
- Cortical cataract
- Posterior subcapsular opacities

B) Primary open angle glaucoma

- Raised IOP

C) Retinal microvasculature changes because of diabetes mellitus, non proliferative and proliferative diabetic retinopathy such as

- Microaneurysms,
- Retinal hemorrhages,
- Hard exudates,
- Cotton wool spots,
- Retinal venular abnormalities (venous bleeding and tortuosity),
- Intraretinal micro-vascular abnormalities, and
- New blood vessels.

D) Hypertensive retinopathy changes such as

- Narrowing of the retinal arteries
- Focal narrowing of the retinal arteries
- Arterio-venous nipping
- Retinal hemorrhages
- Hard exudates
- Cotton wool spots
- Swelling of the optic nerve head
- Macular star

E) Lipemia retinalis changes such as

- Retinal artery and vein occlusions
- Ischemic optic neuropathy

F) Central retinal artery occlusion changes such as

- Sudden, painless blindness
- Cherry red spot in fundus

G) Age related Maculopathy changes such as

- Drusens near the macula (multiple white spots)
- In advanced dry ARMD, an extensive region of the retina thins and loses function, creating a condition known as macula atrophy.
- Advanced wet age-related macular degeneration is characterised by macula haemorrhage and scarring.
- Choroidal neovascularization

Oculomotor palsy and recurrent lid entropion are both conditions that have been linked to obesity.

The clinical signs and symptoms caused in metabolic syndrome are assessed by a questionnaire

- All subjects underwent ocular examination to check for any anterior and posterior segment pathologies.
- Visual acuity was checked by using Snellen chart, Detailed fundoscopy with both Indirect Ophthalmoscope with 20 D Lens and Slit lamp Bio microscopy with 90 D Lens.
- Measuring waist circumference at the umbilicus (belly button), the natural waist (the space between the bottom rib and the top of the hip bone), or the midsection's narrowest point can be used to determine abdominal obesity. Moreover, the waist-to-hip ratio is computed by first measuring the hip at the widest point on the buttocks, then dividing the result by the hip measurement.
- Serum lipid measurements using Fasting samples, to analyse Total Cholesterol, Plasma triglycerides
- Plasma HDL cholesterol levels
- Sphygmomanometer readings for blood pressure
- Fasting plasma glucose

Operational definition :

1. A waist circumference of more than 102 cm for men and 88 cm for women was considered wide in this study.
2. Blood triglyceride levels above 150 mg/dL, or 1.69 mm, are considered hypertriglyceridemia.

3. HDL cholesterol is deemed low at 40 mg/dL (1.04 mM) for men and 50 mg/dL (1.29 mM) for women.
4. If a participant's blood pressure was considered high—defined as a systolic reading of 130 mm Hg or a diastolic reading of 85 mm Hg—they were required to fast for eight hours. A hyperglycemia of 110 millimeters per (6.1 mM) is deemed serious.

Statistical analysis:

R version 4.3.2 statistical tools and Microsoft Excel were used for data analysis. frequency tables that present categorical variables. Continuous variables presented in the form of Mean ± SD / Median (Min, Max). A chi-square test is used to examine if category variables are related. The QQ plot and the Shapiro-Wilk test are used to determine whether a variable is normal. Parametric tests are performed when the data has a normal distribution. Non-parametric tests are employed in the other case. To compare the mean of the variables across ocular manifestation, apply the two sample t test or Welch's t test. Mann Whitney To compare the distribution of variables over ocular manifestation, utilize the U test. A P-value of 0.05 or less was regarded as statistically significant.

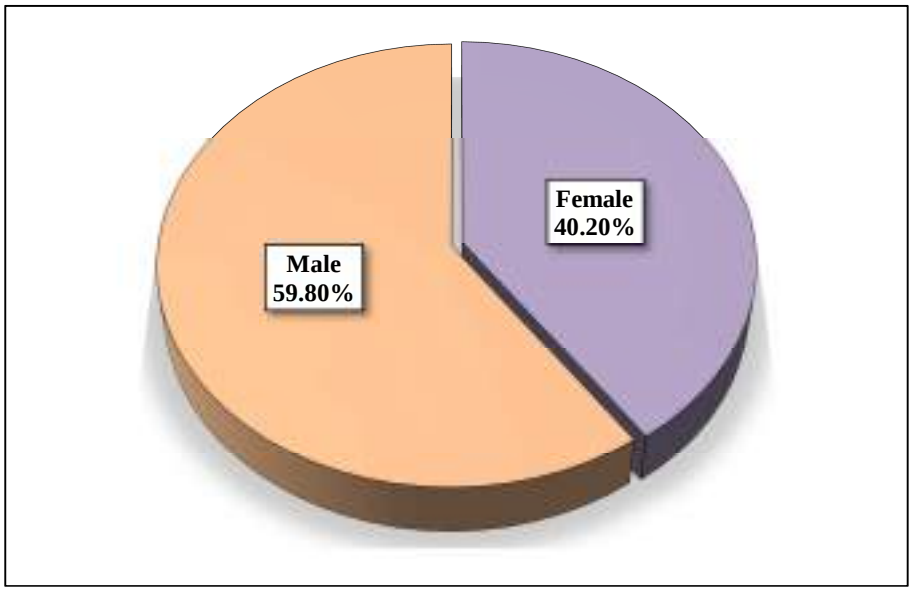
RESULTS

With an average age of 55.85 ± 11.08 years, the 102 participants whose ages are recorded in the data span from 20 to 80 years.

Table 1: Distribution of subjects according to Gender

Gender	**Frequency**	**Percentage**
Female	41	40.2
Male	61	59.8
Total	102	100.0

Out of 102 subjects, 61 (59.8%) were males and 41 (40.2%) were females. (Table 1)



Graph 1 : Distribution of subjects according to gender

Table 2: Distribution of subjects according to occupation.

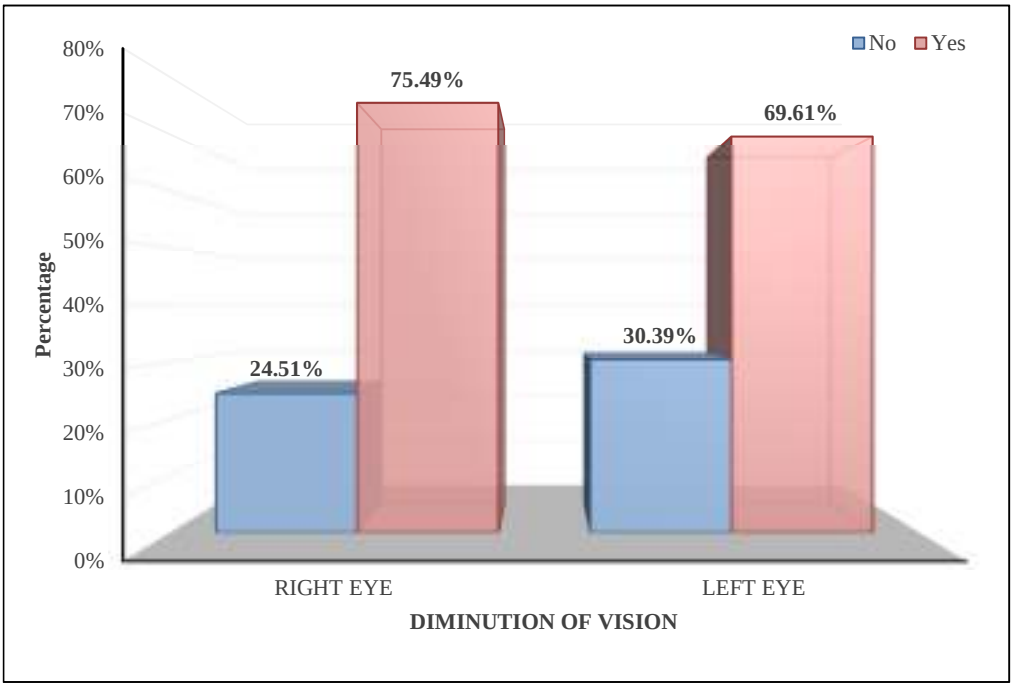
Occupation	Frequency	Percentage
Farmer	31	30.39
Housewife	29	28.43
Retired	11	10.78
Shop Owner	5	4.9
Teacher	5	4.9
Daily wage worker	4	3.92
Pvt Job	1	0.98
Banker	2	1.96
Driver	2	1.96
Carpenter	1	0.98
Clerk	1	0.98
Contractor	1	0.98
Guard	1	0.98
Gardener	2	1.96
Maid	1	0.98
Painter	1	0.98
Pvt Job	1	0.98
Shop keeper	1	0.98
Student	1	0.98
Washerman	1	0.98
None	1	0.98

Out of 102 subjects, 31 (30.39%) were farmers, 11 (10.78%) were retired and 29 (28.43%) were housewives. (Table 2)

Table 3: Distribution of subjects according to diminution of vision.

Diminution of vision	Right Eye	Left Eye
No	25 (24.51%)	31 (30.39%)
Yes	77 (75.49%)	71 (69.61%)

Out of 102 subjects, 77 (75.49%) had diminution of vision in their right eye while 71 (69.61%) had diminution of vision in their left eye. (Table 3)



Graph 2 : Distribution of subjects according to diminution of vision.

Table 4: Distribution of duration of diminution of vision, hypertension and DM.

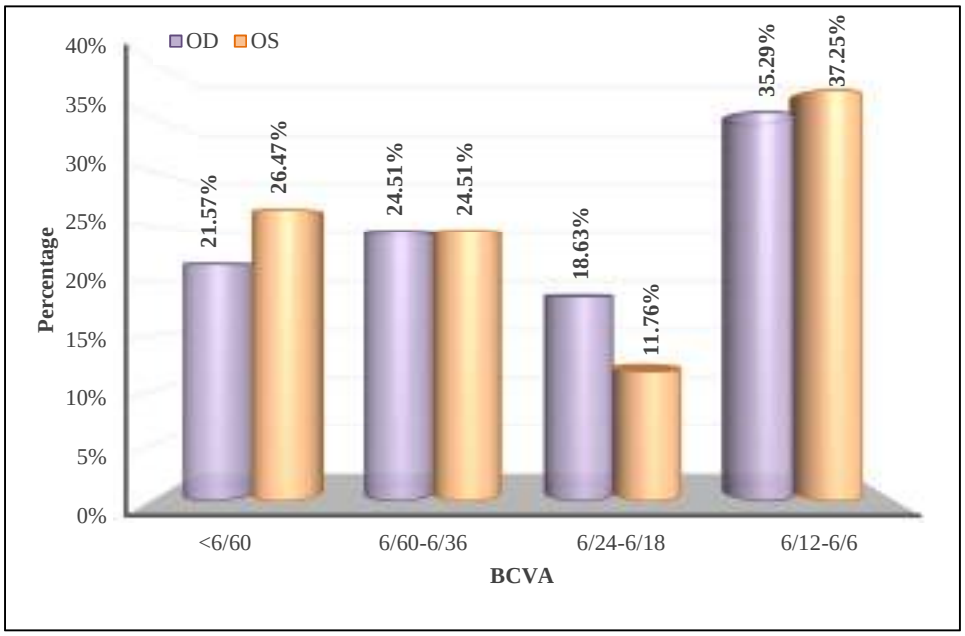
Variables	Mean ± SD	Median	Range
Duration of diminution of vision (months)	12.1 ± 9.93	12	0.07-48
Duration of hypertension (months)	27.15 ± 28.41	24	1-144
Duration of DM (years)	4.47 ± 4.17	3	0.3-20

The mean duration of diminution of vision was 12.1 ± 9.93 months and a median of 12 months, ranging from 0.07 to 48 months. Regarding hypertension, the mean duration was 27.15 ± 28.41 months and a median of 24 months, ranging from 1 to 144 months. The mean duration of diabetes mellitus was 4.47 ± 4.17 years and a median of 3 years, ranging from 0.33 to 20 years. (Table 4)

Table 5: Distribution of subjects according to BCVA.

BCVA	OD	OS
<6/60	22 (21.57%)	27 (26.47%)
6/60-6/36	25 (24.51%)	25 (24.51%)
6/24-6/18	19 (18.63%)	12 (11.76%)
6/12-6/6	36 (35.29%)	38 (37.25%)

It was observed that 22 (21.57%) and 27 (26.47%) subjects had BCVA less than 6/60 in right eyes and left eyes respectively. Additionally, 25 (24.51%) in right eye and 25 (24.51%) in left eye had BCVA falling within the 6/60-6/36 range. Furthermore, 19 (18.63%) in right eye and 12 (11.76%) in left eye had BCVA within the 6/24-6/18 range, while 36 (35.29%) in right eye and 38 (37.25%) in left eye had BCVA within the 6/12-6/6 range. (Table 5)



Graph 3 : Distribution of subjects according to BCVA.

Table 6: Distribution of subjects according to anterior segment manifestation.

Anterior segment	Right eye	Left eye
Cataract	72 (70.59%)	74 (72.55%)
Cataract + PXF	4 (3.92%)	3 (2.94%)
Cataract + Xanthoma	4 (3.92%)	3 (2.94%)
Clear	1 (0.98%)	1 (0.98%)
Pseudophakia	13 (12.75%)	11 (10.78%)
Cataract + NVI	0	1 (0.98%)
NVI, Hyphemia	0	1 (0.98%)
Normal anterior segment	7(6.86%)	7(6.86%)

Cataract in right eye was found in 72(70.59%) subject & in left eye 74(72.55%) subject. Cataract was associated with PXF affect 4(3.92%) right eye of subject & 3(2.94%) left eye of subject. Also Cataract with xanthoma affect 4(3.92%) right eye of subject & 3(2.94%) left eye of subject. Pseudophakia found in 13(12.75%) of right eye of subject & 11 (10.78%) left eye of subject. Normal anterior segment was found in 7(6.86%) subject on right side & in 7(6.86%) subject on left side. Only in one (0.98%) study subject found clear anterior segment. Cataract with NVI affect left eye of only one subject (0.98%) & NVI with Hyphemia found in left eye of only one subject (0.98%). (Table 6)

Table 7: Distribution of subjects according to IOP.

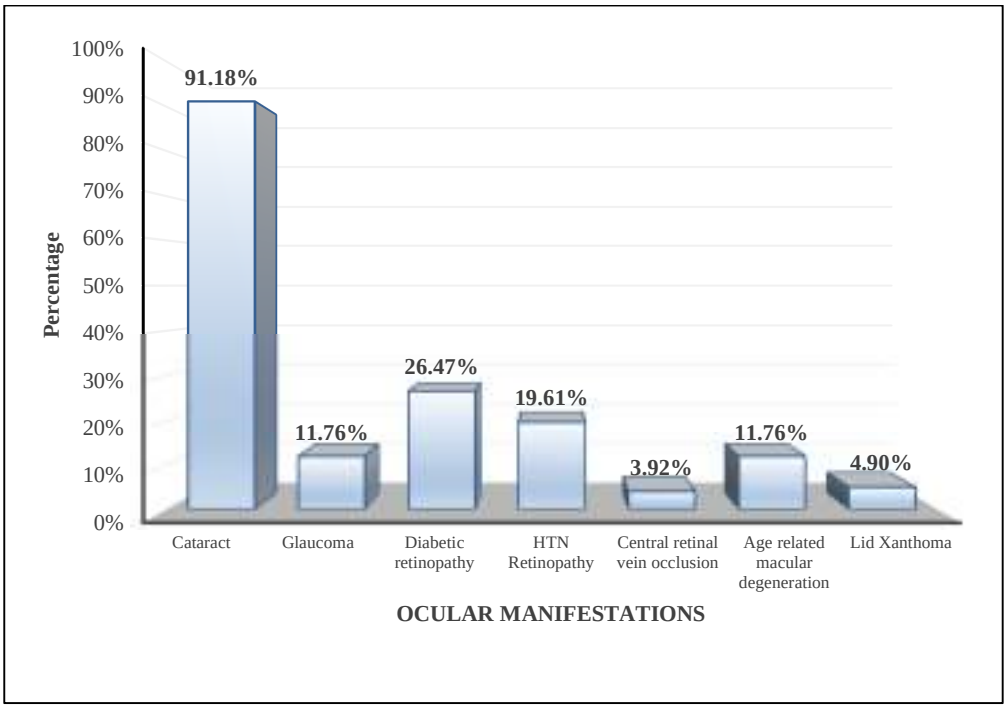
IOP (mmHg)	Right eye	Left eye
Mean ± S.D.	16.46 ± 4.91	15.74 ± 4.69
Median (Range)	16 (7.8 - 34.2)	15.6 (6 - 45)

The IOP of right eye ranged from 7.8 to 34.2 with mean IOP 16.46 ± 4.91 mmHg. The IOP of left eye ranged from 6 to 45 with mean IOP 15.74 ± 4.69 mmHg. (Table 7).

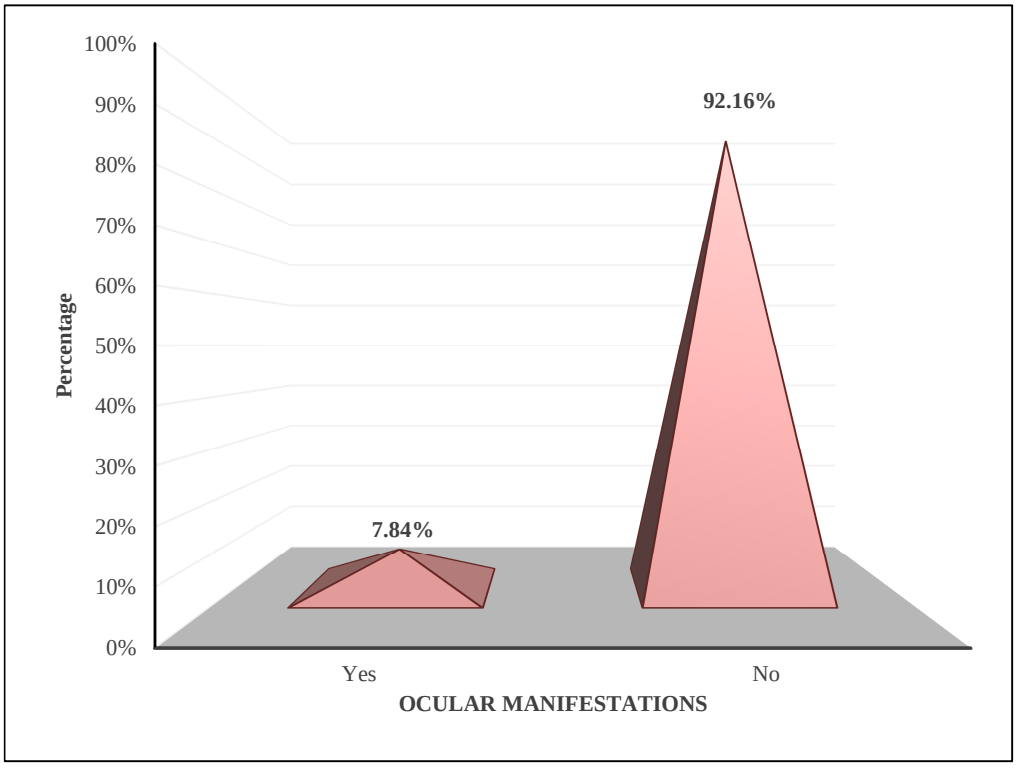
Table 8: Distribution of subjects according to different ocular manifestations.

Ocular manifestations	Sub Category	Number of subjects (%)
Cataract	No	9 (8.82%)
	Yes	93 (91.18%)
Glaucoma	No	90 (88.24%)
	Yes	12 (11.76%)
Diabetic retinopathy	No	75 (73.53%)
	Yes	27 (26.47%)
HTN Retinopathy	No	82 (80.39%)
	Yes	20 (19.61%)
Central retinal vein occlusion	No	98 (96.08%)
	Yes	4 (3.92%)
Age related macular degeneration	No	90 (88.24%)
	Yes	12 (11.76%)
Lid Xanthoma	No	97 (95.1%)
	Yes	5 (4.9%)

Among 102 subjects, 8 (7.84%) didn't have any ocular manifestations while 94 (92.16%) had one or the other ocular manifestations. About 93 (91.18%) had cataract, 12 (11.76%) had glaucoma, 27 (26.47%) had diabetic retinopathy, 20 (19.61%) had HTN retinopathy, 4 (3.92%) had central retinal vein occlusion, 12 (11.76%) had age related macular degeneration and 5 (4.9%) had lid Xanthoma. (Table 8)



Graph 4 : Distribution of subjects according to ocular manifestations.



Graph 5 : Distribution of subjects according to presence of ocular manifestations.

Table 9: Distribution of different variables.

Variables	Mean ± SD	Median (Range)
Waist Circumference (cm)	102.38 ± 6.18	103 (89 - 115)
Serum Triglycerides (mg%)	237.51 ± 60.76	234 (151 - 390)
HDL Cholesterol (mg%)	34.96 ± 5.85	34.5 (19 - 48)
SBP (mm of Hg)	156.71 ± 13.46	155 (138 - 190)
DBP (mm of Hg)	88.02 ± 6.45	90 (70 - 110)
Fasting Blood Sugar (mg%)	204.76 ± 61.9	187 (115 - 368)

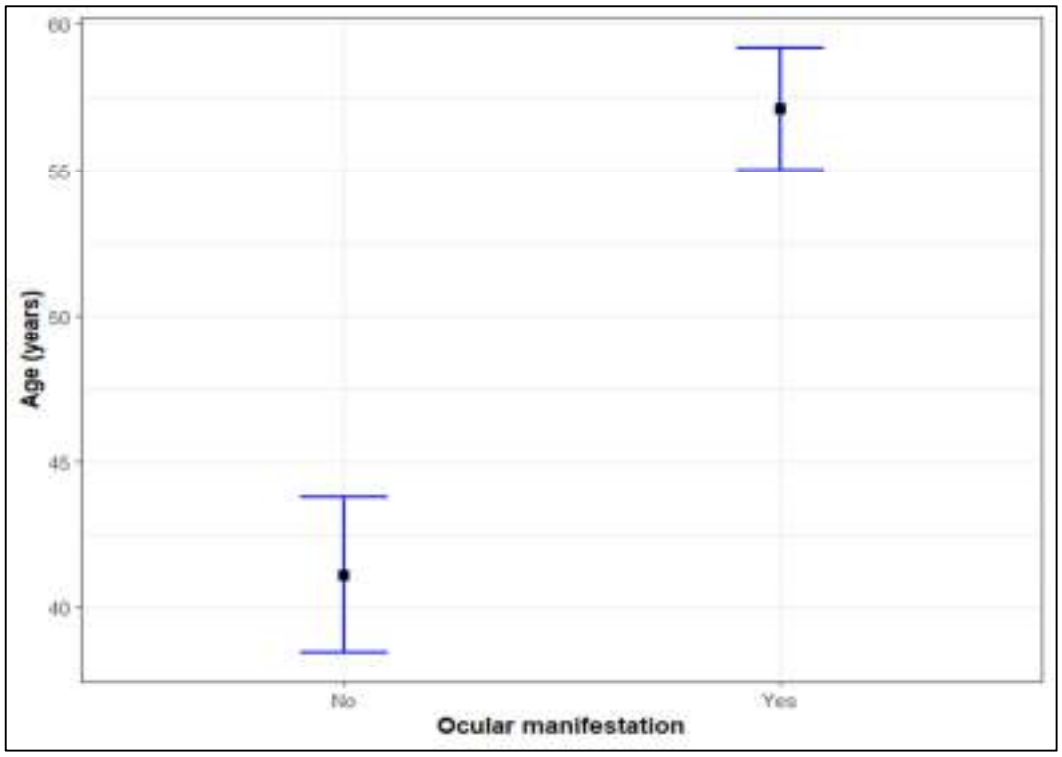
The waist circumference ranged from 89cm to 115 cm with mean of 102.38 ± 6.18 cm. The serum triglycerides ranged from 151 cm% to 390 mg% with mean of 237.51 ± 60.76 mg%. The HDL cholesterol ranged from 19 to 48 mg% with mean of 34.96 ± 5.85 mg%. The SBP ranged from 138 to 190 with mean of 156.71 ± 13.46 mmHg. The DBP ranged from 70 to 110 with mean of 88.02 ± 6.45 mmHg. The fasting blood sugar ranged from 115 to 368mg% with mean of 204.76 ± 61.9 mg%. (Table 9)

Table 10: Comparison of different variables with ocular manifestation.

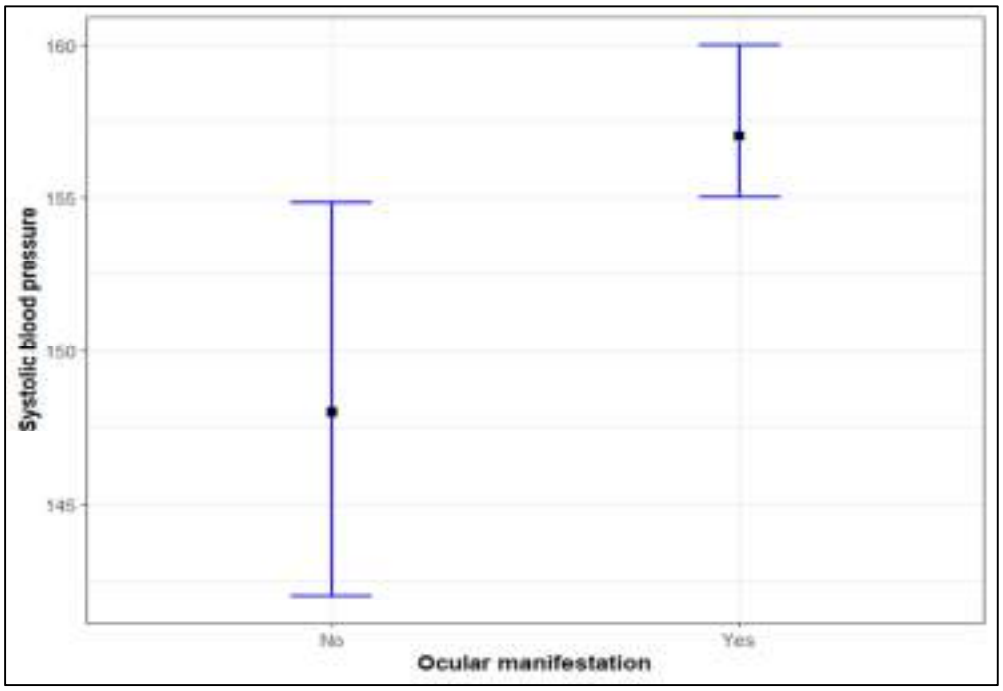
Variables	Sub Category	Ocular manifestation		p-value
		No	Yes	
Age (years)	Mean ± SD	41.12 ± 4.05	57.11 ± 10.58	**< 0.001^{WT}***
	Median (Range)	41 (35 - 46)	57 (29 - 80)	
Gender	Female	4 (50%)	37 (39.36%)	0.7231^{MC}
	Male	4 (50%)	57 (60.64%)	
Waist Circumference (cm)	Mean ± SD	98.75 ± 7.89	102.69 ± 5.96	0.0833^{t}
	Median (Range)	97 (89 - 111)	103 (89 - 115)	
Serum Triglycerides (mg%)	Mean ± SD	215.38 ± 36.85	239.39 ± 62.14	0.4291^{MW}
	Median (Range)	206.5 (180 - 290)	234 (151 - 390)	
HDL Cholesterol (mg%)	Mean ± SD	38.75 ± 5.31	34.64 ± 5.8	0.0558^{t}
	Median (Range)	39 (30 - 47)	34 (19 - 48)	
SBP (mm of Hg)	Mean ± SD	148 ± 10.9	157.45 ± 13.44	**0.0478^{MW}***
	Median (Range)	143 (140 - 170)	156 (138 - 190)	
DBP (mm of Hg)	Mean ± SD	84 ± 4.66	88.36 ± 6.49	**0.0304^{MW}***
	Median (Range)	84 (78 - 90)	90 (70 - 110)	
Fasting Blood Sugar (mg%)	Mean ± SD	172 ± 46.16	207.55 ± 62.46	0.0730^{MW}
	Median (Range)	154 (136 - 256)	187 (115 - 368)	

Abbreviation: t – Two sample t test, WT – Welch's t test, MW – Mann Whitney U test, * indicates statistical significance.

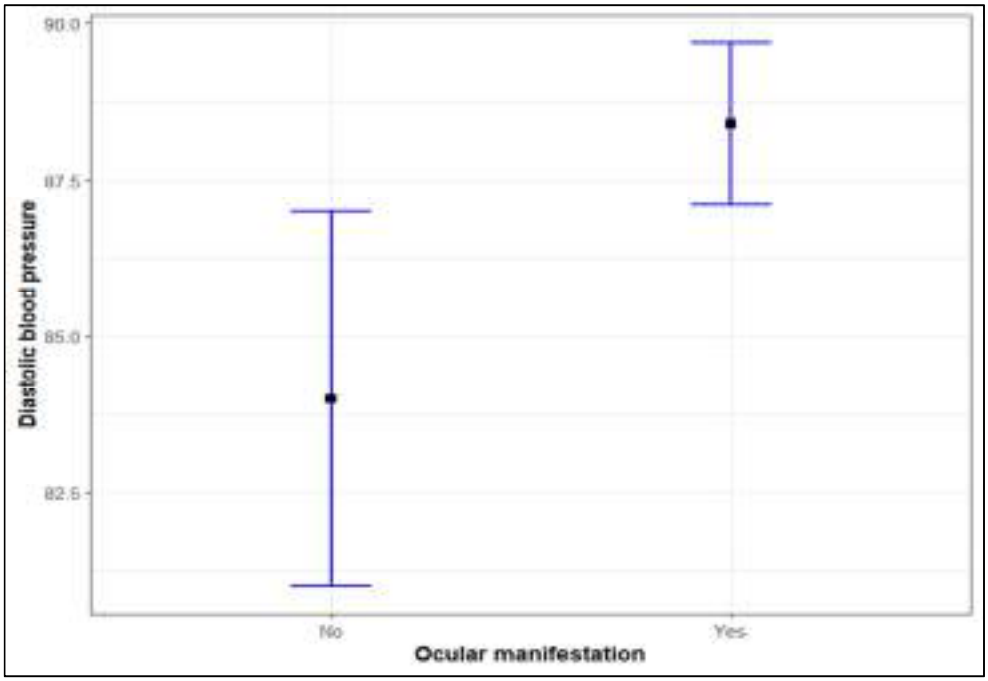
From Welch's t-test, it is observed that the subjects with ocular manifestations exhibit a significantly higher mean age compared to those without ocular manifestations (p-value < 0.001). Additionally, the Mann-Whitney U test reveals that both systolic blood pressure (SBP) and diastolic blood pressure (DBP) are significantly elevated in subjects with ocular manifestations in comparison to those without. Furthermore, there was increased waist circumference, serum triglycerides, and fasting blood sugar levels among those with ocular manifestations. However, these differences did not reach statistical significance. HDL cholesterol levels were lower in individuals with ocular manifestations. However, this difference lacked statistical significance. (Table 10)



Graph 6 : Mean plot of age over ocular manifestation.



Graph 7 : Mean plot of systolic blood pressure over ocular manifestation.



Graph 8 : Mean plot of diastolic blood pressure over ocular manifestation.

DISCUSSION

The aim of this study was to find out if patients (aged 20–80) who came to the KLES Dr. Prabhakar Kore Hospital and Medical Research Centre in Belagavi between 2022 and 2023 had ocular symptoms and metabolic syndrome. Understanding ocular symptoms in the context of metabolic syndrome was the goal of this investigation. By presuming a 50% prevalence of ocular manifestation, we were able to calculate the sample size. A sample size of 96 was determined.

Around the globe, metabolic syndrome is gaining significant attention as a major health concern. Its incidence has been rising steadily over the past few years. The International Diabetes Federation estimates that metabolic syndrome affects around 25% of the world's population. There is widespread agreement among definitions of metabolic syndrome that obesity, hypertension, dyslipidaemia, and hyperglycaemia are its main components. 11,265 people participated in a cross-sectional survey of the general public, which provided the data for this study. More US individuals with MetS than US patients without the syndrome experienced focal arteriolar constriction, lower retinal arteriolar diameters, larger retinal venular diameters, retinopathy, and arteriovenous nicking. These differences persisted even after accounting for variables like age, sex, race, education, alcohol consumption, and cigarette smoking.[63] It is commonly known that diabetes, hypertension, retinopathy, and other microvascular abnormalities are linked. Moreover, endothelial dysfunction in both big and small vessels, inflammation, and atherosclerosis affecting major arteries are linked to MetS.

In 2012, the same or comparable findings were reported in a study of Japanese participants by Zhao et al. Retinal venule diameters were larger and artery diameters were smaller in these individuals, according to Saito et al.[64]. Another Japanese investigation by Kawasaki et al.[78] also found something similar. They found that the incidence of dry eye was almost twice as high in metabolic syndrome patients as in controls.

Cataract

Among the ocular symptoms seen in our research of individuals with metabolic syndrome, cataract was the most prevalent. It accounted for a disproportionate share of cases of blindness in Asian countries.[79,80] Our research showed that ocular manifestation was significantly associated with older age. Cataracts and Met syndrome were linked in a study of middle-aged Europeans conducted by Paunksnis et al.[32]. Met syndrome was linked to an increased likelihood of needing cataract extraction in a hospital-based research conducted in Italy.[81] Subjects who were older had a much higher risk than those who were younger, according to our research. Ocular manifestation was also not associated with gender in this study's univariate logistic regression analysis. Contrary to our findings, Harikrishnan et al.[82] found that elderly persons (OR=1.16) and women (OR=1.84) had a greater risk of ocular manifestation during univariate and multivariate logistic regression analysis in their research in Kerala. Bojarskiene et al. observed a statistically significant increased risk of cataracts in women with MetS.[33].

It is believed that diabetic individuals account for up to 20% of all cataract treatments. [83] Cataract surgery is very popular because epidemiologic studies have shown that cataracts are the main cause of visual impairment in persons with older-onset diabetes.

Over the course of a decade, the Wisconsin study found that among patients with diabetes, 27% had cataract surgery for early onset and 44% for late onset.[86] The development of cataracts is an early complication of diabetes mellitus. Compared to non-diabetics, diabetics have a 2- to 5-fold higher chance of developing cataracts; diabetics under the age of 40 may have an even higher risk, 15 to 25 times higher. [87] Impaired fasting glucose (IFG), a pre-diabetic state, is linked to a higher risk of cortical cataract development.[88] In a research by Janghorbani and Amini, which monitored 3,888 people with type 2 diabetes for an average of 3.6 years after their first visit, a rate of cataract development of 33.1 per 1000 person-years of surveillance was found.[89] We also discovered a strong correlation between hypertension and eye symptoms in our research. Whether it was present alone or in conjunction with other Met syndrome components, Sabanayagam et al.[90] found a strong association between HTN and cataract. Cataracts of various kinds (nuclear, cortical, or posterior subcapsular) were linked to high blood pressure even in individuals without diabetes. He inferred that senile cataract in the Malay population is associated with the Met syndrome, which consists of high blood pressure and diabetes. These results highlight the significance of modifiable cataract risk. Certain studies on the relationship between hypertension and cataracts found that high systolic blood pressure was associated with the condition, but high diastolic blood pressure was not.[79] One of the Western studies that discovered a correlation between metabolic syndrome and all

three types of cataracts (nuclear, cortical, and posterior subcapsular) was the Blue Mountain Eye research, which involved an older cohort of Australians (Tan et al., 30).

Diabetic Retinopathy :

DR is the primary global cause of blindness in middle-aged working adults and the most common microvascular outcome in individuals with diabetes.[49,91] Diabetic retinopathy was the second most common ocular symptom, according to our research. Results from a 2016 study of Jewish individuals with type 2 diabetes showed that diabetic subjects with MetS had a significantly higher frequency of microvascular related difficulties than diabetic subjects without the syndrome (46.6% vs. 26.8%, P=.0005). The study comprised 270 individuals with a diagnosis of metastatic syndrome (MetS) based on NCEPATP III criteria, and 145 patients without the condition. This group includes the following conditions: retinopathy (9.6% vs. 4.1%, P=.046), neuropathy (10.4% vs. 7.5%, P=.38), leg ulcers (7.9% vs. 2.8%, P=.044), and microalbuminuria (41.5% vs. 23.9%, P=.013). Costa et al. found that retinopathy was more prevalent in those with MetS, as defined by WHO criteria, out of 548 European diabetics (44% vs. 20%).[56] " Researchers discovered an independent connection between DR and MetS diagnosed using either NCEP-ATP III criteria (1.41 times) or IDF criteria (1.49) in a multicentric Italian study conducted in 2016 that included 7859 type 2 diabetes patients. Furthermore, this study examined 638 individuals with type 1 diabetes and discovered a correlation between MetS and DR, albeit one that was not statistically significant.[55] Retinopathy was more common in patients with MetS, as defined by WHO criteria, according to a 2004 study by Costa et al., of 548 European diabetics (44% vs. 20%). 1414 diabetic patients from South India participated in a cross-sectional study, and it was discovered that the prevalence

of DR was 21.3% in patients without MetS and 16.9% in those with the condition. [56] A greater incidence of DR was seen in females with metabolic syndrome for less than 10 years and diabetes for 11–20 years.[57] When Finnish researchers looked at 85 type 2 diabetics in 2001, 85 of them had MetS (as defined by the World Health Organization), and they discovered no correlation between the two and diabetic retinopathy. Individuals with type 2 diabetes and metabolic syndrome were more likely to experience severe DR.[58]

The eye is only one of several organs that might be impacted by the systemic nature of diabetes mellitus. However, the onset and course of ocular problems in diabetes patients may be greatly affected by concurrent systemic illnesses. Retinopathy caused by diabetes may be prevented or slowed down with strict management of blood sugar and systemic hypertension.[93, 92] There are a number of factors that can affect the course of diabetic retinopathy. These include severe renal disease, macular exudation and moderate visual loss, elevated serum lipids, pregnancy, anaemia, and smoking. Excessive exercise in patients with advanced retinopathy can put them at risk of vitreous haemorrhage.[94]

Hypertensive retinopathy

It is well recognised that hypertension is linked to retinopathy and other microvascular alterations. Inflammation, atherosclerosis of the major arteries, and endothelial dysfunction of the big and small vessels are additional problems linked to metastatic syndrome.[18]

11,265 participants in a population-based cross-sectional survey made up the research sample. More US individuals with MetS than US patients without the

syndrome experienced focal arteriolar constriction, lower retinal arteriolar diameters, larger retinal venular diameters, retinopathy, and arteriovenous nicking. These differences persisted even after accounting for variables like age, sex, race, education, alcohol consumption, and cigarette smoking.[19] In 2012, Zhao et al.'s study from Japan yielded roughly similar results. According to Saito et al., these people had smaller artery sizes and greater retinal venule diameters. [64] The similar outcome was also found by Kawasaki et al. in their Japanese study.[74]

Glaucoma:

Among the eye conditions we examined, glaucoma ranked third in frequency. The average intraocular pressure (IOP) in the right eye was 16.46 ± 4.91 and in the left eye it was 15.74 ± 4.69. Systemic blood pressure is correlated with intraocular pressure, according to many research. Modest changes in intraocular pressure (IOP) accompany major shifts in blood pressure. Bulpitt and colleagues determined that a 100 mm Hg increase in systemic blood pressure would be necessary to elevate intraocular pressure (IOP) by 2 mm Hg. Only intraocular pressure (IOP) can be changed to change the risk of glaucoma. Both longitudinal and cross-sectional epidemiological research have consistently shown that increased intraocular pressure (IOP) is related with a number of cardiometabolic risk factors, including type 2 diabetes mellitus, hypertension, and concurrent atherosclerotic disease.[41,42] In a study conducted by Lee JS et al., clinical data from 1112 participants undergoing health checks were analyzed. [95] The results showed that people with metabolic syndrome had considerably greater intraocular pressure (IOP) than people without the condition. An average rise of 0.33 mm Hg in intraocular pressure was linked to each extra metabolic syndrome component. They confirmed the results in the Korean population

by Memarzadeh et al, Kim et al. discovered no statistically significant link between MetS and NTG (Normal tension glaucoma) in their case-control study of 18,240 South Koreans. [96] He discovered that NTG is linked to hypertension and decreased glucose tolerance.[44]

Age related macular degeneration:

In our study samples, 11.76 percent of the participants had age-related macular degeneration. Numerous studies have found strong evidence connecting obesity to AMD. According to the age-related eye disease study (AREDS), researchers observed an increasing prevalence of age-related macular degeneration (ARMD) in fundus photographs as participants' BMI increased.[97] AMD is the most common cause of significant and irreversible vision loss in people living in industrialized countries..[98]

There has only been one study investigating the relationship between MetS and AMD. A statistically significant correlation between MetS and early-stage ARMD could not be found in this investigation. On the other hand, MetS was linked to a higher risk of late-stage ARMD in individuals under 70. Additionally, the same study discovered that blood levels of fat, glucose, and cholesterol were independently linked to the development of AMD from early to late.[72] Howard et al. found that early and late AMD were more common in nonsmoking women who were obese, defined as having a high body mass index or waist circumference. [73] According to a Norwegian cross-sectional study, women 65–87 years old who were overweight or had high blood pressure had a higher chance of developing late-stage Alzheimer's disease (ADHD) (Erke et al., 1974). Conversely, Adams et al.'s study of 21,287 Europeans revealed erratic relationships between obesity and AMD. In fact, all obesity factors were inversely correlated with early AMD in women.[75]

Central retinal vein occlusion:

Retinal vein occlusion (RVO) is a prevalent retinal vascular disorder that affects people worldwide.[99–102] RVO is considered an artery disease; as the retinal arteries stiffen, it compresses the retinal vein, alters hemodynamic, and blocks the retinal circulation's venous return.[100-103] Major risk factors for RVO incidence include systemic vascular illnesses such as arterial hypertension, diabetes mellitus, atherosclerosis, cardiovascular disease, and thrombophilia.

In our study, about 3.92% study subject had central retinal vein occlusion. Metabolic syndrome has been linked to inflammation, endothelial dysfunction, and illnesses of both large and small vessels.[63] It is well-known that micro-vascular illnesses, such as retinal vascular diseases, are associated with systemic hypertension and diabetes.[11] In Japanese adults, the Kawasaki study found that retinopathy was more common in patients with Met syndrome than in those without the syndrome (odds ratio: 1.64, 95% CI: 1.02-2.64).[78] The risk of retinopathy and other micro-vascular alterations may be associated with Met Syndrome; thus, prospective studies are necessary to confirm this. Sudden blindness can be caused by anterior ischemic optic neuropathy.

Studies on the national population have demonstrated that METS and all of its diagnostic standards increase the likelihood of RVO occurring. Using NHIS claims data, our group has previously shown that a lower HDL cholesterol level is linked to an increased risk of RVO.[111] After controlling for hypertension, diabetes, and dyslipidaemia, the prior research calculated the risk of RVO based only on HDL cholesterol. This research expanded upon earlier results by examining METS and its five components in more detail, illuminating their relationship to RVO development.

Contrary to the current accepted definition of METS, earlier research on METS and RVO defined METS as a combination of hypertension, diabetes, and dyslipidemia.[112,113] Using a correct METS definition, our work is the first to demonstrate a link between METS and RVO. We also looked at the correlation between the number of fulfilled METS diagnostic criteria and the likelihood of RVO development; the BP criterion stood out as the most relevant. We also compared the results after looking at how METS affected different subgroups. This research has the potential to provide light on how to develop more effective and personalised treatment plans. The National Cholesterol Education Programme's Adult Treatment Panel III report states that METS requires more therapeutic attention.[114] Previous clinical research suggests that microvascular diseases like RVO could play a major role in METS.[115-117] People with METS or specific symptoms associated with it, including abdominal obesity, diabetes, dyslipidaemia, and hypertension, exhibit microcirculation abnormalities in skin and skeletal muscle structure and function, according to studies. [117,120,121]Our results are supported by these data, which show that RVO risk rises with METS presence and that each of the five METS diagnostic components raises RVO risk separately". This discovery highlights the significance of the role of each factor in microvascular disorders, such as RVO.

Eyelid Xanthoma :

Dyslipidaemia is often accompanied with xanthomas, which are common skin lesions that accumulate in certain areas, such as the buttocks, eyelids, trunk, extensor tendons of the wrists and elbows, Achilles tendon, and patellar tendon. [122] Patients with familial hyperlipidaemia type IIa are more likely to develop significant hypercholesterolemia, which has been linked to these skin lesions. [123]

A correlation between hypertriglyceridemia and eruptive xanthomas has been found in the literature. [124] total Clinicians should educate themselves on the characteristics of eruptive xanthoma in order to make an accurate early diagnosis, especially because research on the clinical courses of the disorder are available.[125–127] An essential sign of metabolic diseases, such as diabetes mellitus and dyslipidaemia, eruptive xanthomas appear with substantial hypertriglyceridemia. The skin on the back of the leg, the buttocks, the elbows, and the lower back is covered in clusters of papular eruptions that are between one and four millimetres in diameter.[128,129] Histopathology reveals the buildup of foamy cells caused by macrophage phagocytosis of residual lipoprotein.[129,130] The most common cause of eruptive xanthomas is hypertriglyceridemia; 8.5% of patients with a blood triglyceride level over 20 mmol/L (1772 mg/dl) develop this ailment, which goes away when the triglyceride level drops. [126,131] To avert the development of systemic atherosclerosis, it is necessary to treat hypertriglyceridemia and diabetic mellitus, which are believed to be important causes of eruptive xanthoma.[132] This form of skin lesion may be an indication of metabolic abnormalities; treating these illnesses can improve eruptions 11 and avoid cardiovascular events, so clinicians should be aware of this.[132]

CONCLUSION

A group of metabolic abnormalities known as metabolic syndrome (MetS) has just lately come to light as a modern health problem. It ranks high among the leading causes of heart disease. Our study found that people between the ages of 45 and 65 had a higher prevalence of ocular symptoms in metabolic syndrome. The most prevalent visual manifestation among the research individuals was cataract, followed by diabetic retinopathy and hypertensive retinopathy in that order. On the other hand, central retinal vein occlusion, lid xanthoma, age-related macular degeneration, and glaucoma were all detected in similar frequencies. Timely management of metabolic syndrome may prevent ocular manifestations. However, to confirm the casual relationship prospective interventional researches are required.

SUMMARY

The current study was the hospital based prospective cross sectional study of Ocular associations of metabolic syndrome conducted among 20-80 years old patients attending at KLES Dr. Prabhakar kore hospital and medical research Centre, Belagavi from Aug 2022- Jul 2023.

- Total 102 subjects enrolled in study after taking informed consent.
- The mean age of subject was 55.85 ± 11.08 years.
- About 61 (59.8%) were males and 41 (40.2%) were females. In present study, 31 (30.39%) were farmers, 11 (10.78%) were retired and 29 (28.43%) were housewives.
- In 77 (75.49%) subjects had diminution of vision in their right eye while 71 (69.61%) had diminution of vision in their left eye.
- The mean duration of diminution of vision was 12.1 ± 9.93 months. Regarding hypertension, the mean duration was 27.15 ± 28.41 months.
- The mean duration of diabetes mellitus was 4.47 ± 4.17 years.
- It was observed that 22 (21.57%) and 27 (26.47%) subjects had BCVA less than 6/60 in right eyes and left eyes respectively. Additionally, 25 (24.51%) in right eye and 25 (24.51%) in left eye had BCVA falling within the 6/60-6/36 range. Furthermore, 19 (18.63%) in right eye and 12 (11.76%) in left eye had BCVA within the 6/24-6/18 range, while 36 (35.29%) in right eye and 38 (37.25%) in left eye had BCVA within the 6/12-6/6 range.
- The most ocular manifestation was cataract followed by Diabetic retinopathy. The mean of right eye IOP 16.46 ± 4.91 mmHg.
- The mean IOP of left eye 15.74 ± 4.69 mmHg.

- The mean waist circumference 102.38 ± 6.18 cm.
- The mean serum triglycerides was 237.51 ± 60.76 mg%.
- The mean HDL cholesterol was 34.96 ± 5.85 mg%.
- The mean SBP was156.71 ± 13.46 mmHg.
- The mean DBP was 88.02 ± 6.45 mmHg.
- The mean fasting blood sugar was mean of 204.76 ± 61.9 mg%.
- Ocular manifestations exhibit a significantly higher mean age compared to those without ocular manifestations ($p < 0.001$). Both systolic blood pressure (SBP) and diastolic blood pressure (DBP) are significantly elevated in subjects with ocular manifestations in comparison to those without.

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ANNEXURES I - ETHICAL CLEARANCE

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to- be- University)
Accredited 'A+' Grade by NAAC in (3rd Cycle) Placed in Category 'A' by MHRD (GoI)
JNMC INSTITUTIONAL ETHICS COMMITTEE
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http://www.jnmc.edu
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Phone. (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref No.MDC/JNMCIEC/ 86 **Date: 27/09/2022**

To,

BK0121002

PG Student in Ophthalmology,
J. N. Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"OCULAR ASSOCIATIONS OF METABOLIC SYNDROME AT TERTIARY HEALTH CARE CENTRE- A CROSS SECTIONAL STUDY."** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee.

(Dr. Smita Sonoli)
Member Secretary
JNMC Institutional Ethics Committee
J.N.Medical College, Belagavi.

(Dr. Harsha Hegde)
Chairman,
JNMC Institutional Ethics Committee
J.N.Medical College, Belagavi

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ANNEXURE II – CONSENT FORM

Informed Consent Form

"Ocular associations of metabolic syndrome at Tertiary health care center -A cross sectional study"

Principal Investigator

Post graduate student

Department Of Ophthalmology,

Jawaharlal Nehru Medical College,

KAHER, Belagavi – 590010

Guide/Co Investigators:

Department of ophthalmology,

Jawaharlal Nehru Medical College,

KAHER, Belagavi – 590010

Objective: To assess the Ocular manifestations in metabolic syndrome aged 20-80 years

Introduction: The patient is being invited to participate in the study to assess the Ocular manifestations in metabolic syndrome subjects.

Explanation of procedure: If, you agree to be part of the research study, you will be asked the relevant history and will be subjected to relevant clinical examination and investigations.

Withdrawal from participation in the study: Participation in this study is voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study: You will/will not have nor get any benefits by participating in this study. The data gathered will help the population at large.

Possible risks from participating in the study: There are no risks involved in participating in this study.

Privacy and confidentiality: The information collected from you will be coded, to prevent any person from identifying you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You will not receive any payment for participating in this study.

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purposes and or presented to scientific groups. However, your identity will never be revealed.

Questions: In case of any questions with regard to this study, you are free to contact: "Principal investigator". If you have any question or complaints with regard to your right as study participant you may contact "Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052."

Legal rights: By signing this consent form, we are not waiving any of your legal rights.

CONSENT STATEMENT

I am making a voluntary decision to participate in the study **:** "Ocular associations of metabolic syndrome at Tertiary health care center, -A cross sectional study" My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature or left thumb impression of the participant:

Name of the witness:

Signature or left thumb impression of the witness:

Name of the investigator:

Signature of the investigator:

DATE:

PLACE:

ANNEXURE III- PROFORMA

PROFORMA

DATE: ☐☐ / ☐☐ / ☐☐☐☐

PATIENT'S/CONTROL'S NAME:

-

☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

AGE:_Years

SEX: (1-Male; 2-Female)

SR.No. _________

ADDRESS-____________________

CONTACT ☐☐☐☐☐☐☐☐☐☐

NUMBER:OP ☐☐☐☐☐☐☐☐

NUMBER:

IP NUMBER: ☐☐☐☐☐☐☐☐

DATE OF EXAMINATION: ☐/☐ ☐/☐ ☐☐☐☐

IS THE PATIENT/CONTROL ELIGIBLE FOR STUDY? (1-YES; 2-NO) ☐

HAS INFORMED CONSENT BEEN GIVEN? (1-YES; 2-NO ☐

CHIEF COMPLAINTS FOR THE CASE:

DIMINUTION OF VISION: 1- Present; 2- Absent ☐ ☐

RE

Duration:____Days/Months/Years

LE

Duration:____Days/Months/Years

HISTORY OF PRESENT ILLNESS:

1. DIMINUTION OF VISION 1- Gradual; 2- Sudden ☐

1- Progressive; 2- Static ☐

PAST HISTORY:

TRAUMA TO THE EYE: 1- Present; 2- Absent ☐

OCULAR SURGERY: 1- Present; 2- Absent ☐

Type of surgery: _____

Duration: months/years

HYPERTENSION: 1- Present; 2- Absent

Duration: months/years

DIABETES:
1- Type 1; 2- Type 2; 3- None

Duration: months/years

Medications:

History of Alcohol consumption: 1-Yes; 2-No

History of Acanthosis Nigricans 1-Yes; 2-No

History of Genetic disorders: 1- Yes; 2- No

History of Hirsutism: 1- Yes; 2- No

History of Hypothyroidism: 1- Yes; 2- No

History of Liver disease: 1- Yes; 2- No

History of Malignancy: 1- Yes; 2- No

History of Niacin use: 1- Yes; 2- No

History of Nicotinic acid use : 1- Yes; 2- No

History of Oral contraceptives: 1- Yes; 2- No

History of PCOD: 1- Yes; 2- No

History of SLE : 1- Yes; 2- No

History of Steroid use: 1- Yes; 2- No

Smoking/Tobacco addiction: 1-Present; 2-Absent

If Yes,

No. of years:_____Years

VISUAL ACUITY:

	RIGHT EYE	LEFT EYE
DISTANT		
PINHOLE		
NEAR		
AIDED		

OCULAR EXAMINATION

1. Adnexa (1- Normal; 2-Abnormal)		
2. Sclera (1- Normal; 2- Congested)		
3. Conjunctiva (1-normal; 2-conjunctival congestion; 3-ciliary congestion; 4-chemosis)		
4. Cornea (1- normal; 2-opacity; 3-vascularisation)		
5. Anterior chamber (1- normal depth; 2-shallow; 3-deep)		
6. Iris (1-normal, color & pattern; 2-Abnormal)		
7. Pupil: Size-_____in mm Shape- 1- Round & Regular; 2-AbnormalReaction: Direct (1. Present, 2. Absent) Indirect (1. Present, 2. Absent) Near reflex (1. Present, 2. Absent)		
8. Lens *Clarity- 1. Clear, 2. Opaque* *Cataract - (1), PCIOL - (2)* ***IOP**:*		

FUNDUS	RIGHT EYE	LEFT EYE
GLOW		
MEDIA		
DISC		
CUP: DISC RATIO		
BLOOD VESSELS		
BACKGROUND		
MACULA		

Body Weight:_____Kgs

Height:_____M

Body Mass Index: _____

Waist Circumference: _____

Waist: Hip: _____

Blood pressure:_____mm of Hg

Random blood sugar:_____mg/dl

HbA1c levels: _____

Lipid Profile: Done/Not Done
Hyperlipidemia/Hypercholesterolemia: _____
Triglycerides levels: _____

HDL levels: _____

LDL levels: _____

ECG: Done/Not Done
Renal Profile: Done/Not Done

NAME OF THE INVESTIGATOR:

SIGNATURE: .....

NAME OF THE GUIDE:

ANNEXURE IV: KEY TO MASTER CHART

Male	=	M
Female	=	F
Diabetes Mellitus	=	DM
Hypertension	=	HTN
Left Eye	=	LE
Right Eye	=	RE
Diminution of vision	=	DOV
Visual Acuity	=	VA
Senile Immature Cataract	=	SIMC
Senile Mature Cataract	=	SMC
Hypermature Cataract	=	HMC
Posterior supcapsular cataract	=	PSC
Posterior Polar Cataract	=	PPC
Metabolic syndrome	=	MetS
Age-related macular degeneration	=	ARMD
Central retinal artery occlusion	=	CRAO
Central retinal vein occlusion	=	CRVO
Branch retinal vein occlusion	=	BRVO
Diabetic retinopathy	=	DR
Primary open angle glaucoma	=	POAG
Primary angle-closure glaucoma	=	PACG
Normal tension glaucoma	=	NTG
Nuclear sclerosis	=	NS

Pseudoexfoliation	=	PXF
Cortical cataract	=	CC
Posterior capsule opacification	=	PCO
Within normal limits	=	WNL
Intraocular pressure	=	IOP
Neovascularisation of Iris	=	NVI
Neovascularisation Elsewhere	=	NVE
Neovascularisation of Disc	=	NVD
Non-proliferative diabetic retinopathy	=	NPDR
Diabetic macular edema	=	DME
Choroidal Neovascular Membranes	=	CNVM
Cup Disc Ratio	=	CDR
Cotton Wool spots	=	CWS
Intraretinal microvascular abnormalities	=	IRMA
Neuro Retinal Rim	=	NRR
Counting Fingers	=	CF
Hand movements close to face	=	HMCF

ANNEXURES V- MASTER CHART

no.	n years)	ss (Aadhar Card / Ratio	ss (Aadhar Card / Ratio	ct number	on	members in family	of family	pation of women	pation of husband	ation of women	ation of husband	economic class (B.G. P	on of marriage
1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
2	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
3	25-29	Rural	Non Slum	8552908691	Muslim	3	Nuclear	Semi skill	Clerical / Shop	Primary school c	High school cer	I-Upper Mi	6
4	30-34	Urban	Slum	8669478027	Hinduism	7	Three ge	Skilled wo	Clerical / Shop	High school cert	High school cer	II-Upper Mi	16
5	30-34	Rural	Non Slum	8551054806	Buddhism	5	Nuclear	Semi skill	Clerical / Shop	High school cert	High school cer	III-Lower Mi	18
6	25-29	Urban	Slum	7757872958	Muslim	8	Three ge	Unskilled	Clerical / Shop	Primary school c	High school cer	IV-Upper Lo	14
7	25-29	Urban	Slum	9011145816	Muslim	8	Three ge	Unskilled	Clerical / Shop	Illiterate	Primary school	III-Lower Mi	5
8	35-39	Rural	Slum	8624994040	Muslim	10	Three ge	Unskilled	Clerical / Shop	Illiterate	Illiterate	IV-Upper Lo	17
9	35-39	Urban	Slum	8830318571	Muslim	8	Three ge	Unskilled	Clerical / Shop	Illiterate	Illiterate	III-Lower Mi	21
10	30-34	Rural	Non Slum	9404068438	Hinduism	5	Nuclear	Semi skill	Semi Professi	High school cert	High school cer	II-Upper Mi	16
11	30-34	Urban	Non Slum	9970085525	Hinduism	4	Nuclear	Semi skill	Clerical / Shop	High school cert	High school cer	II-Upper Mi	15
12	25-29	Urban	Non Slum	9075383839	Buddhism	5	Nuclear	Unskilled	Clerical / Shop	High school cert	Graduate	II-Upper Mi	12
13	20-24	Urban	Non Slum	7888281161	Hinduism	3	Nuclear	Unskilled	Clerical / Shop	High school cert	High school cer	II-Upper Mi	4
14	25-29	Urban	Non Slum	7888386645	Buddhism	8	Joint	Unskilled	Clerical / Shop	Middle school c	High school cer	II-Upper Mi	10
15	25-29	Urban	Slum	9175395939	Muslim	10	Joint	Unskilled	Clerical / Shop	Illiterate	Illiterate	IV-Upper Lo	15
16	35-39	Urban	Non Slum	8788350820	Hinduism	5	Nuclear	Semi Prof	Semi Professi	High school cert	Intermediate o	I-Upper	24
17	20-24	Rural	Non Slum	9975017637	Muslim	10	Joint	Unskilled	Clerical / Shop	Middle school c	High school cer	V-Lower	4
18	45-49	Urban	Slum	9158631919	Buddhism	5	Nuclear	Unskilled	Skilled worker	Middle school c	High school cer	IV-Upper Lo	18
19	20-24	Urban	Non Slum	9203558885	Hinduism	3	Nuclear	Unskilled	Semi Professi	High school cert	Intermediate o	I-Upper	4
20	15-19	Rural	Non Slum	7429595841	Muslim	12	Joint	Unskilled	Clerical / Shop	Middle school c	High school cer	IV-Upper Lo	3
21	25-29	Rural	Non Slum	7276834062	Hinduism	4	Nuclear	Unskilled	Semi Professi	Graduate	Graduate	II-Upper Mi	10
22	20-24	Rural	Non Slum	9881835344	Hinduism	3	Nuclear	Unskilled	Skilled worker	Graduate	Graduate	II-Upper Mi	6
23	20-24	Rural	Non Slum	7057008538	Muslim	12	Joint	Unskilled	Clerical / Shop	Middle school c	High school cer	V-Lower	5
24	25-29	Urban	Slum	7057008238	Muslim	9	Joint	Unskilled	Clerical / Shop	Middle school c	High school cer	IV-Upper Lo	16
25	20-24	Urban	Non Slum	8208846323	Buddhism	7	Joint	Semi Prof	Semi Professi	Graduate	Graduate	I-Upper	4
26	25-29	Rural	Non Slum	8206663279	Hinduism	4	Nuclear	Clerical / S	Clerical / Shop	High school cert	Graduate	II-Upper Mi	12
27	20-24	Urban	Slum	8806957985	Buddhism	5	Three ge	Semi skill	Semi skilled	High school cert	Intermediate o	III-Lower Mi	4
28	30-34	Urban	Slum	8806954367	Muslim	6	Nuclear	Unskilled	Unskilled	Illiterate	High school cer	V-Lower	20
29	20-24	Urban	Non Slum	9545100380	Buddhism	2	Nuclear	Professio	Professional	Graduate	Graduate	I-Upper	2
30	25-29	Rural	Slum	8390834143	Buddhism	6	Three ge	Semi skill	Semi skilled	Middle school c	High school cer	IV-Upper Lo	10
31	20-24	Urban	Non Slum	9766253086	Buddhism	3	Nuclear	Semi skill	Skilled worker	High school cert	Graduate	I-Upper	4
32	25-29	Urban	Non Slum	9730380091	Muslim	7	Joint	Unskilled	Clerical / Shop	Illiterate	High school cer	IV-Upper Lo	16
33	35-39	Urban	Non Slum	7775981267	Buddhism	5	Nuclear	Unskilled	Skilled worker	High school cert	Graduate	II-Upper Mi	18
34	25-29	Urban	Non Slum	8698362730	Hinduism	5	Three ge	Skilled wo	Skilled worker	Graduate	Graduate	I-Upper	4
35	25-29	Rural	Non Slum	9822428166	Muslim	6	Nuclear	Unskilled	Clerical / Shop	Middle school c	High school cer	V-Lower	14
36	30-34	Rural	Non Slum	9970275536	Muslim	9	Joint	Unskilled	Clerical / Shop	Illiterate	Illiterate	IV-Upper Lo	18
37	25-29	Urban	Slum	9529085106	Hinduism	4	Nuclear	Clerical / S	Clerical / Shop	High school cert	Graduate	I-Upper	9
38	15-19	Urban	Non Slum	9579854561	Hinduism	2	Nuclear	Skilled wo	Clerical / Shop	Intermediate or	Graduate	I-Upper	2
39	25-29	Urban	Non Slum	9657522218	Muslim	4	Nuclear	Semi Prof	Semi Professi	Graduate	Graduate	I-Upper	6
40	30-34	Urban	Non Slum	9112259466	Hinduism	5	Three ge	Unskilled	Clerical / Shop	Graduate	Graduate	I-Upper	14
41	40-44	Urban	Non Slum	9112259466	Buddhism	8	Three ge	Unskilled	Clerical / Shop	Illiterate	Middle school (	V-Lower	28
42	20-24	Urban	Non Slum	8421854442	Buddhism	3	Nuclear	Clerical / S	Clerical / Shop	High school cert	Graduate	II-Upper Mi	5
43	30-34	Urban	Non Slum	9823031345	Hinduism	4	Nuclear	Semi Prof	Professional	Graduate	Graduate	I-Upper	8
44	30-34	Urban	Non Slum	9890282362	Muslim	4	Nuclear	Semi Prof	Professional	Graduate	Post graduate	I-Upper	10
45	35-39	Urban	Slum	9822550794	Hinduism	7	Three ge	Unskilled	Clerical / Shop	High school cert	Intermediate o	II-Upper Mi	15
46	20-24	Rural	Slum	9855440794	Buddhism	5	Three ge	Unskilled	Clerical / Shop	High school cert	High school cer	II-Upper Mi	2
47	25-29	Urban	Slum	8975078127	Buddhism	3	Nuclear	Skilled wo	Skilled worker	Graduate	Graduate	II-Upper Mi	4
48	20-24	Rural	Non Slum	9326729124	Muslim	8	Joint	Unskilled	Clerical / Shop	High school cert	High school cer	III-Lower Mi	4
49	15-19	Urban	Non Slum	8530506294	Hinduism	2	Nuclear	Skilled wo	Semi Professi	High school cert	Graduate	I-Upper	1
50	30-34	Urban	Non Slum	8421131467	Muslim	10	Joint	Unskilled	Clerical / Shop	Illiterate	High school cer	V-Lower	18

no.	t marriage	er of live children	y preference	ous method of contracep	of injectable contracept	t (kg)	t (cm)	HT (m)		mic illnesses	ation		ur cycle regular	s your menstrual flow	ou pregnant	g of first dose of injectab
1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
2	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
3	More than 18	1	Wanted child	Switched from traditio	Tertiary care cent	55	153	1.53	23.50	None	No	31-12-2020	Yes	Dysmenor	No	Interval
4	More than 18	+3	No more child	Switched from a non-	Tertiary care cent	68	162	1.62	25.91	None	No	01-01-2021	Yes	Hypomen	No	Interval
5	Less than 18	+3	No more child	Switched from a non-	Tertiary care cent	64	157	1.57	25.96	None	No	31-12-2020	Yes	Normal	No	Interval
6	Less than 18	+3	Don't know	New user	Tertiary care cent	57	158	1.58	22.83	None	No	01-01-2021	No	Hypomen	No	Interval
7	More than 18	1	Wanted child	Switched from traditio	Tertiary care cent	54	157	1.57	21.91	None	No	01-01-2021	Yes	Normal	No	Interval
8	More than 18	+3	No more child	New user	Tertiary care cent	68	159	1.59	26.90	None	No	31-12-2020	Yes	Normal	No	Interval
9	Less than 18	+3	No more child	Switched from a non-	Tertiary care cent	70	158	1.58	28.04	None	No	01-01-2021	Yes	Normal	No	Interval
10	Less than 18	+3	No more child	Switched from a non-	Tertiary care cent	58	156	1.56	23.83	None	No	02-01-2021	Yes	Normal	No	Interval
11	More than 18	2	No more child	Switched from a non-	Tertiary care cent	60	158	1.58	24.03	None	No	02-01-2021	Yes	Normal	No	Interval
12	More than 18	+3	No more child	Switched from a non-	Tertiary care cent	64	158	1.58	25.64	None	No	02-01-2021	Yes	Normal	No	Interval
13	More than 18	1	Wanted child	New user	Tertiary care cent	58	162	1.62	22.10	None	No	02-01-2021	Yes	Normal	No	Interval
14	More than 18	2	No more child	Switched from a non-	Tertiary care cent	63	157	1.57	25.56	None	No	02-01-2021	Yes	Normal	No	Interval
15	Less than 18	+3	Don't know	Switched from a non-	Tertiary care cent	57	158	1.58	22.83	None	No	03-01-2021	Yes	Dysmenor	No	Post_ab
16	Less than 18	+3	No more child	Switched from a non-	Tertiary care cent	74	160	1.6	28.91	None	No	05-01-2021	Yes	Hypomen	No	Interval
17	More than 18	1	Don't know	New user	Tertiary care cent	54	147	1.47	24.99	None	No	05-01-2021	Yes	Menorrha	No	Interval
18	More than 18	+3	No more child	Switched from a non-	Tertiary care cent	68	154	1.54	28.67	None	No	05-01-2021	No	Normal	No	Interval
19	More than 18	1	Wanted child	Switched from traditio	Tertiary care cent	58	162	1.62	22.10	None	No	06-01-2021	Yes	Normal	No	Post_ab
20	Less than 18	1	Wanted child	Switched from traditio	Tertiary care cent	47	156	1.56	19.31	None	No	06-01-2021	Yes	Normal	No	Interval
21	More than 18	2	No more child	Switched from a non-	Tertiary care cent	58	158	1.58	23.23	None	No	07-01-2021	Yes	Normal	No	Interval
22	More than 18	1	Wanted child	Switched from a non-	Tertiary care cent	65	162	1.62	24.77	None	No	09-01-2021	No	Menorrha	No	Interval
23	More than 18	1	Wanted child	New user	Tertiary care cent	54	162	1.62	20.58	None	No	09-01-2021	Yes	Normal	No	Interval
24	Less than 18	+3	Don't know	Switched from traditio	Tertiary care cent	64	158	1.58	25.64	None	No	10-01-2021	Yes	Normal	No	Interval
25	More than 18	1	Wanted child	Switched from a non-	Tertiary care cent	58	155	1.55	24.14	None	No	01-12-2020	Yes	Normal	No	Postpar
26	More than 18	2	No more child	Switched from a non-	Tertiary care cent	68	158	1.58	27.24	None	No	10-01-2021	Yes	Dysmenor	No	Interval
27	More than 18	1	Wanted child	Switched from a non-	Tertiary care cent	62	158	1.58	24.84	None	No	15-01-2021	Yes	Menorrha	No	Interval
28	Less than 18	+3	Don't know	New user	Tertiary care cent	75	158	1.58	30.04	None	No	14-01-2021	No	Hypomen	No	Interval
29	More than 18	0	Wanted child	New user	Tertiary care cent	52	156	1.56	21.37	None	No	15-01-2021	Yes	Normal	No	Interval
30	More than 18	+3	Don't know	New user	Tertiary care cent	65	158	1.58	26.04	None	No	16-01-2021	Yes	Normal	No	Interval
31	More than 18	1	Wanted child	Switched from a non-	Tertiary care cent	62	158	1.58	24.84	None	No	26-11-2020	Yes	Normal	No	Post_ab
32	More than 18	+3	Don't know	Switched from traditio	Tertiary care cent	66	158	1.58	26.44	None	No	17-01-2021	Yes	Normal	No	Interval
33	More than 18	+3	No more child	Switched from a non-	Tertiary care cent	64	160	1.6	25.00	None	No	15-01-2021	Yes	Normal	No	Interval
34	More than 18	1	Wanted child	New user	Tertiary care cent	58	160	1.6	22.66	None	No	19-01-2021	Yes	Normal	No	Interval
35	Less than 18	+3	No more child	Switched from traditio	Tertiary care cent	74	155	1.55	30.80	None	No	18-01-2021	No	Hypomen	No	Interval
36	Less than 18	+3	No more child	Switched from traditio	Tertiary care cent	68	158	1.58	27.24	None	No	19-01-2021	Yes	Normal	No	Interval
37	More than 18	2	No more child	Switched from a non-	Tertiary care cent	62	156	1.56	25.48	None	No	17-01-2021	Yes	Normal	No	Interval
38	More than 18	0	Wanted child	Switched from a non-	Tertiary care cent	54	152	1.52	23.37	None	No	23-01-2021	Yes	Normal	No	Interval
39	More than 18	1	Wanted child	Switched from a non-	Tertiary care cent	64	153	1.53	27.34	None	No	24-01-2021	Yes	Hypomen	No	Interval
40	More than 18	2	No more child	Switched from a non-	Tertiary care cent	68	154	1.54	28.67	None	No	24-01-2021	Yes	Normal	No	Interval
41	Less than 18	+3	No more child	Switched from traditio	Tertiary care cent	74	158	1.58	29.64	Hyper	YES	17-01-2021	No	Hypomen	No	Interval
42	More than 18	1	Wanted child	Switched from a non-	Tertiary care cent	58	154	1.54	24.46	None	No	24-01-2021	Yes	Normal	No	Interval
43	More than 18	2	No more child	Switched from a non-	Tertiary care cent	66	158	1.58	26.44	None	No	28-01-2021	Yes	Hypomen	No	Interval
44	More than 18	2	No more child	Switched from a non-	Tertiary care cent	74	160	1.6	28.91	None	No	28-01-2021	Yes	Normal	No	Interval
45	More than 18	2	No more child	Switched from a non-	Tertiary care cent	65	156	1.56	26.71	None	No	28-01-2021	Yes	Normal	No	Interval
46	More than 18	0	Wanted child	Switched from a non-	Tertiary care cent	60	148	1.48	27.39	None	No	26-01-2021	Yes	Normal	No	Interval
47	More than 18	1	Wanted child	Switched from a non-	Tertiary care cent	62	164	1.64	23.05	None	No	08-12-2020	Yes	Normal	No	Post_ab
48	More than 18	1	Wanted child	Switched from traditio	Tertiary care cent	54	155	1.55	22.48	None	No	28-01-2021	Yes	Normal	No	Interval
49	More than 18	0	Wanted child	Switched from a non-	Tertiary care cent	54	154	1.54	22.77	None	No	27-01-2021	Yes	Normal	No	Interval
50	Less than 18	+3	Don't know	Switched from traditio	Tertiary care cent	77	157	1.57	31.24	None	No	28-01-2021	Yes	Hypomen	No	Interval

no.	ECTFUL CARE [Treated	ECTFUL CARE [Question	ECTFUL CARE [Respond	ECTFUL CARE [Felt aud	ECTFUL CARE [Felt info	ECTFUL CARE [Felt visu	OD SELECTION [Was as	OD SELECTION [Was as	OD SELECTION [Was as	OD SELECTION [Was as	OD SELECTION [Was to	OD SELECTION [Receive	OD SELECTION [Receive	CTIVE USE OF METHOD	CTIVE USE OF METHOD	CTIVE USE OF METHOD	CTIVE USE OF METHOD	CTIVE USE OF METHOD
1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
2	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
3	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes
4	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes
5	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
6	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
7	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No
8	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
9	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	No
10	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	No
11	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No
12	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No	No
13	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
14	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No
15	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes
16	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
17	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	Yes
18	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
19	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
20	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes
21	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No
22	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
23	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
24	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
25	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No
26	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
27	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
28	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes
29	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes
30	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
31	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
32	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
33	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
34	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
35	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
36	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No
37	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
38	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No
39	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
40	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
41	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No
42	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No
43	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
44	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
45	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
46	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes
47	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
48	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
49	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
50	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

no.	INUITY OF CONTRACEP	INUITY OF CONTRACEP	INUITY OF CONTRACEP	trual cycle	weight	ving second dose of inje	ns for continuation	effects
1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
2	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
3	Yes	Yes	Yes	Not disturbed	58	No		
4	Yes	Yes	Yes	Not disturbed	67	No		
5	Yes	Yes	Yes	Not disturbed	67	No		
6	Yes	Yes	Yes	Disturbed	57	No		
7	Yes	Yes	Yes	Not disturbed	58	No		
8	Yes	Yes	Yes	Not disturbed	72	No		
9	Yes	Yes	Yes	Not disturbed	69	No		
10	Yes	Yes	Yes	Not disturbed	64	No		
11	Yes	Yes	No	Not disturbed	62	No		
12	Yes	Yes	Yes	Not disturbed	63	No		
13	Yes	Yes	Yes	Not disturbed	60	No		
14	Yes	Yes	Yes	Not disturbed	64	No		
15	Yes	Yes	Yes	Not disturbed	64	No		
16	Yes	Yes	Yes	Not disturbed	75	No		
17	Yes	Yes	Yes	Not disturbed	56	No		
18	Yes	Yes	No	Not disturbed	70	No		
19	Yes	Yes	Yes	Not disturbed	59	No		
20	Yes	Yes	Yes	Not disturbed	49	No		
21	Yes	Yes	Yes	Not disturbed	59	Yes	Low cost,	Irregular ble
22	Yes	Yes	Yes	Disturbed	66	No		
23	Yes	Yes	Yes	Not disturbed	56	Yes	Feel safe,	None
24	Yes	Yes	Yes	Not disturbed	67	No		
25	Yes	Yes	Yes	Disturbed	60	No		
26	Yes	Yes	Yes	Not disturbed	65	No		
27	Yes	Yes	Yes	Disturbed	63	No		
28	Yes	Yes	Yes	Not disturbed	72	No		
29	Yes	Yes	Yes	Not disturbed	56	Yes	Low cost,	Irregular ble
30	Yes	Yes	Yes	Disturbed	64	No		
31	Yes	Yes	Yes	Disturbed	60	Yes	Low cost,	Breast pain
32	Yes	Yes	Yes	Not disturbed	68	Yes	Feel safe,	Menstrual i
33	Yes	Yes	Yes	Not disturbed	65	No		
34	Yes	Yes	Yes	Disturbed	68	Yes	Low cost,	None
35	Yes	Yes	Yes	Disturbed	70	Yes	Low cost,	Irregular ble
36	Yes	Yes	No	Not disturbed	68	Yes	Low cost,	None
37	Yes	Yes	Yes	Not disturbed	65	No		
38	Yes	Yes	Yes	Not disturbed	54	Yes	Feel safe,	None
39	Yes	Yes	Yes	Not disturbed	64	Yes	Feel safe,	None
40	Yes	Yes	Yes	Disturbed	66	No		
41	Yes	Yes	Yes	Not disturbed	70	Yes	Low cost,	None
42	Yes	Yes	Yes	Not disturbed	56	No		
43	Yes	Yes	Yes	Not disturbed	67	Yes	Low cost,	None
44	Yes	Yes	Yes	Disturbed	68	Yes	Low cost,	Irregular ble
45	No	Yes	Yes	Not disturbed	66	No		
46	Yes	Yes	Yes	Disturbed	61	Yes	Low cost,	Irregular ble
47	Yes	Yes	Yes	Not disturbed	58	Yes	Low cost,	Headache /
48	Yes	Yes	Yes	Disturbed	56	Yes	Low cost,	None
49	Yes	Yes	Yes	Disturbed	55	Yes	Low cost,	Vaginal dry
50	Yes	Yes	Yes	Not disturbed	74	Yes	Low cost,	None

SL NO	TUDY ID	AGE	NDE	OCCUPATION	IMINUTION OF VISIO		DURATION	HTN	DM	BCVA		ANTERIOR SEGMENT		IOP(mm of Hg)		FUNDUS EXAMINATION		DIAGNOSIS	WC	TGL	HDL	BP	BSL
					RIGHT EYE	LEFT EYE				RIGHT EYE	LEFT EYE	RIGHT EYE	LEFT EYE	RIGHT EYE	LEFT EYE	OD	OS						
48	MS48	72	M	RETIRED	Y	N	2 years	3 years	7 years	6\24	6\24	pseudophakia+xanth	pseudophakia+xantho	18	17.6	Arteriolar attenuation+m	Arteriolar attenuation+m	BE pseudophakia+upper lid xan	104	346	40	142/78	188
49	MS49	45	F	MAID	Y	Y	6 months	3 month	6 years	6\6(P)	6\6(P)	Grade 1 NS	Grade 1 NS	11	16	WNL	WNL	BE Grade 1 NS	110	200	31	152/88	160
50	MS50	67	M	NONE	N	Y	1 year	10 years	10 years	6\24	CF 3m	Grade 2 NS	Grade 3 NS+PSC	21	20.8	WNL	WNL	RE Grade 2 NS+LE Grade 3 NS+I	104	187	28	176/94	150
51	MS51	41	M	JOB	Y	Y	3 months	6 month	1 year	6\6(P)	6\9(P)	Grade 1 NS	Grade 1 NS	18.4	25.6	WNL	CDR 0.4,optic disc cuppin	RE Grade 1 NS, LE Grade 1 NS+	105	280	29	180/88	179
52	MS52	56	M	FARMER	N	Y	1 year	6 month	1 year	6\18	6\60	Grade 2 NS +PSC	Grade 3 NS+PSC	19	16	WNL	WNL	RE- Grade 2 NS +PSC, LE- Grade	115	175	34	140/70	145
53	MS53	60	F	HOUSEWIFE	Y	N	1 year	2 years	4 years	CF 1m	6\18	Grade 1NS+dense PS	Grade 1NS+ PSC	15.4	17.7	Arteriolar attenuation +	Arteriolar attenuation +	RE NS2 thick PSC+Grade 1 HTN	107	188	28	170/90	180
54	MS54	60	F	HOUSEWIFE	Y	Y	6 months	2 years	3 years	6\12	6\12	pseudophakia	pseudophakia	16	14	Arteriolar attenuation +	Arteriolar attenuation +	BE pseudophakia+grade 1 HTN	103	189	33	144/94	230
55	MS55	70	M	RETIRED	Y	N	1 year	3 years	5 years	CF 2m	6\9	Grade 2 NS +PSC	pseudophakia	12.5	10.7	WNL	WNL	RE- Grade 2 NS +PSC	105	234	34	150/94	187
56	MS56	61	M	FARMER	N	Y	1 year	3 years	6 years	6\18	6\60	pseudophakia	Grade 4 NS	16	14.7	micro aneuryms	micro aneuryms	RE pseudophakia+mild NPDR,LE	108	314	29	176/86	311
57	MS57	58	M	SHOP	Y	Y	3 years	3 years	10 years	CF 2m	PL -	Grade 2 NS	NVI,Hyphema,pseudo	33.9	7.4	CDR 0.6, optic disc cuppi	no glow	RE grade 2 NS+advanced PDR+I	107	250	33	150/90	332
58	MS58	64	F	HOUSEWIFE	Y	N	1 year	3 month	4 years	CF 1\2 m	6\6(P)	Grade 3 NS+PSC	pseudophakia	18.7	14.9	CDR 0.7, large disc, healt	CDR 0.7, large disc, healt	RE Grade 3 NS+PSC,LE- pseudo	110	213	35	160/88	234
59	MS59	62	F	HOUSEWIFE	Y	N	1 year	2 years	2 years	HMCF + PI	CF 3m	Grade 3 NS+PSC	Grade 3 NS+PSC	19	18	Arteriolar attenuation +	Arteriolar attenuation +	RE Grade 3 NS + dense psc+gra	99	253	28	144/88	348
60	MS60	60	F	HOUSEWIFE	Y	N	1 year	4 month	2 years	PL + PR ac	6\60	SMC	Grade 3 NS	34.2	11.5	No glow	drusens around macula	RE SMC+phacomorphic glaucor	94	180	40	162/96	210
61	MS61	61	F	HOUSEWIFE	Y	Y	1 year	4 years	3 years	6\60	6\36(P)	Grade 3 NS+PSC	Grade 2 NS	19.6	18.4	micro aneuryms+ Hard ex	micro aneuryms+ Hard ex	BE Grade 2-3 NS +moderate NP	98	166	42	140/78	143
62	MS62	69	F	HOUSEWIFE	N	Y	1 year	6 years	2 years	6\12	CF1m	pseudophakia	Grade 4 NS	15	15	Arteriolar attenuation +C	Arteriolar attenuation +	RE pseudophakia+grade 1 HTN	92	170	43	154/92	237
63	MS63	51	M	JOB	Y	N	6 months	3 years	2 years	CF2m	6\19	Grade 3 NS+PSC	pseudophakia	14.2	12	drusens in the backgroun	drusens in the backgroun	RE Grade 3 NS+ARMD,LE pseud	108	321	27	180/96	258
64	MS64	60	F	HOUSEWIFE	N	Y	6 months	6 month	2 years	6\9	CF1m	pseudophakia	Grade 3 NS+PSC	10	10.4	WNL	Faint glow, details not ma	RERE pseudophakia,LE grade 3	104	346	30	140/94	202
65	MS65	68	M	FARMER	Y	Y	3 months	4 years	8 years	CF1m	CF3m	Grade 3 NS+PSC+CC	Grade 2 NS +PSC +CC	10	13	micro aneuryms+ Hard ex	micro aneuryms+ Hard ex	RE grade 3 NS+PSC+CC+modera	111	234	34	178/88	280
66	MS66	62	M	FARMER	Y	Y	1 year	3 years	6 years	CF1 m	6\60	Grade 2 NS +PSC	Grade 2 NS +PSC	13	11	NVD,blurred disc margins	WNL	RE Grade 2 RAPD+Grade 2 NS+I	114	366	25	142/86	310
67	MS67	52	F	HOUSEWIFE	Y	Y	1 year	6 years	2 years	CF 2m	CF1m	Grade 3 NS	Grade 4 NS	16.7	14	micro aneuryms	Faint glow, details not ma	RE grade 3 NS+MILD NPDR,LE-	102	160	35	150/80	137
68	MS68	69	F	HOUSEWIFE	N	Y	1 year	3 years	2 years	6\12	CF1m	pseudophakia	Grade 3 NS	15	15	WNL	WNL	RE pseudophakia,LE grade 3 NS	89	155	42	140/82	133
69	MS69	57	F	HOUSEWIFE	Y	Y	2 years	2 years	4 years	CF1m	CF1/2m	Grade 4 NS	Grade 3 NS	17.4	15.3	drusens in the backgroun	CNVM	RE Grade 4 NS+dry ARMD,LE gr	96	187	40	160/88	181
70	MS70	65	M	FARMER	N	Y	3 years	2 years	2 years	6\36	6\60	Grade 2 NS +PSC	Grade 2 NS	16.4	16.3	WNL	CNVM	RE Grade 2 NS+PSC, LE Grade 2	111	390	28	180/82	288
71	MS71	61	M	FARMER	Y	N	2 years	3 years	2 years	6\36	6\24(P)	Grade 3 NS	Grade 2 NS	14.6	14.6	WNL	WNL	RE Grade 3 NS,LE Grade 2 NS	104	200	32	150/80	147
72	MS72	72	M	FARMER	N	Y	2 years	2 years	2 years	6\9	6\60	pseudophakia	Grade 3 NS+PSC	17	17.7	WNL	WNL	RE pseudophakia,LE grade 3 NS	103	196	33	172/90	156
73	MS73	73	F	HOUSEWIFE	Y	Y	1 year	2 years	2 years	CF 1m	PL + PR ac	Grade 4 NS+xanthon	SMC	14	15	Faint glow, details not ma	No glow, details not mad	RE- grade 4 NS+xanthoma, LE-S	107	234	24	154/90	180
74	MS74	65	M	CLERK	Y	Y	1 year	2 years	3 years	6\36	6\60	Grade 2 NS +PSC	Grade 3 NS	20.8	20	WNL	drusens in the backgroun	RE- grade 2 NS+PSC,LE- grade 3	113	280	30	180/10(	179
75	MS75	68	M	FARMER	Y	Y	1 year	2 years	2 years	6\24	6\36	Grade 3 NS+PSC	Grade 2 NS +PSC	18	16	WNL	WNL	RE-Grade 3 NS+PSC,LE-Grade 2	104	240	34	162/96	150
76	MS76	60	F	FARMER	Y	Y	2 years	2 years	3 years	6\24(P)	HMCF PL+	Grade 3 NS	SMC	17.3	20.6	WNL	No glow, details not mad	RE- grade 3 NS,LE-SMC	96	234	40	170/90	167
77	MS77	54	F	WORKER	Y	Y	1 year	3 years	3 years	6\18	6\18	Grade 2 NS +PSC	Grade 2 NS +PSC	17.3	20.6	micro aneuryms	micro aneuryms,Dot blot	RE grade 2 NS+mild NPDR,LE-gr	100	346	41	162/88	259
78	MS78	59	F	HOUSEWIFE	Y	Y	3 years	3 years	4 years	6\36	CF2m	Grade 2 NS	Grade 2 NS +PSC +CC	16	18	WNL	CNVM,sub retinal fibrosis	RE grade 2 NS,LE grade NS+PSC	99	235	43	148/90	179
79	MS79	52	F	HOUSEWIFE	Y	Y	4 years	2 years	3 years	6\60	6\36	Grade 3 NS+PXF	Grade 2 NS+CC+PXF	26	19.8	CDR 0.6, optic disc cuppi	CDR 0.4, optic disc cuppi	RE- grade 3 NS,LE-Grade 2 NS+(	105	291	36	172/90	187
80	MS80	49	M	FARMER	Y	Y	2 years	2 years	6 years	HMCF PL+	6\36	Grade 1 NS	Grade 1 NS+PSC	16.9	18	Tractional bands over the	Hard exudates+dot blot h	RE grade 1 NS+Tractional RD+h	104	180	35	150/80	187
81	MS81	54	M	FARMER	Y	Y	6 months	3 years	6 years	6\12	6\60	Grade 2 NS +PSC	Grade 3 NS+PSC+CC	16	13,8	WNL	WNL	RE- Grade 2 NS+PSC,LE- grade 3	108	193	28	178/88	200
82	MS82	42	F	HOUSEWIFE	Y	N	2 months	1 month	1 year	6\9	6\6	Grade 1 NS	PSC	29.4	19	PPA+Lrage disc,temporal	PPA+Lrage disc,temporal	RE grade 1 NS+PSC,LE-PSC Wth	96	238	44	162/80	241
83	MS83	54	F	HOUSEWIFE	Y	Y	6 months	2 years	2 years	6\60	6\9	Grade 2 NS	Grade 1 NS	15	13	CDR 0.8, optic disc cuppi	WNL	RE-grade 2 NS+POAG, LE-grade	98	269	40	170/86	234
84	MS84	43	F	FARMER	Y	Y	1 year	1 year	1 year	6\9(P)	6\12	Grade 1 NS	Grade 2 NS	16.4	14	drusens in the backgroun	drusens in the backgroun	RE-Grade 1 NS+Dry ARMD,LE-G	94	234	38	154/92	348
85	MS85	50	F	HOUSEWIFE	Y	Y	1 year	2 years	6\36	6\60	Grade 2 NS +PSC +PX	Grade 3 NS +PXF	22	26	CDR 0.4, optic disc cuppi	CDR 0.7, optic disc cuppi	RE-Grade 2 NS+PSC, LE-Grade 3	102	350	39	162/94	287
86	MS86	56	M	SHOP	Y	Y	2 years	6 years	2 years	6\9(P)	6\12	Grade 1 NS	Grade 1 NS	16	18	drusens in the backgroun	drusens in the backgroun	BE-Grade 1 NS+Dry ARMD	114	271	32	170/92	244
87	MS87	46	F	HOUSEWIFE	Y	Y	3 years	3 years	4 years	6\6(P)	6\6	WNL	WNL	12	21	WNL	WNL	WNL	92	246	40	158/82	160
88	MS88	41	F	TEACHER	Y	Y	4 Months	2months	2 years	6\6	6\6	WNL	WNL	15.8	15.9	WNL	WNL	WNL	93	189	40	140/90	142
89	MS89	58	M	FARMER	Y	Y	6 months	4 years	2 years	6\60	6\36	Grade 2 NS +PSC	Grade 2 NS	28	24	CDR 0.7, optic disc cuppi	WNL	RE- Grade 2 NS+PSC+POAG,LE-(	106	320	33	174/80	348
90	MS90	46	M	SHOP	Y	Y	6 months	3 month	2 years	6\6	6\6	WNL	WNL	16	16.8	WNL	WNL	WNL	103	187	35	140/78	155
91	MS91	54	M	JOB	N	Y	1 year	3 years	3 years	6\36	CF2m	Grade 2 NS+xanthon	Grade 2 NS+PSC+Xan	19	17	Arteriolar attenuation +	flame shaped haemorrha	RE- Grade 2 NS+Xanthoma+gra	109	380	30	188/96	275
92	MS92	64	M	RETIRED	Y	N	1 year	4 years	6 years	6\60	6\12	Grade 2 NS	Grade 2 NS	20.6	14	NVD,blurred disc margins	Arteriolar attenuation +	RE-grade 2 NS+non ischemic CR	107	231	34	156/90	201
93	MS93	62	F	RETIRED	N	Y	6 months	3 years	4 years	6\24	6\60	Grade 2 NS +PSC	Grade 3 NS+PSC+CC	17	17	Arteriolar attenuation+m	Arteriolar attenuation+m	RE-grade 2 NS+PSC,LE-grade 3	94	308	40	172/86	217
94	MS94	56	F	HOUSEWIFE	N	Y	1 year	3 month	2 years	6\18	CFCF	Grade 1 NS	SMC	16	13	WNL	No glow, details not mad	RE- grade 1 NS,LE-SMC	99	244	39	174/92	280
95	MS95	54	M	FARMER	N	Y	1 year	2 month	2 years	6\18	CF2m	Grade 2 NS +PSC	Grade 2 NS +PSC	14.9	15.6	drusens in the backgroun	drusens in the backgroun	BE-grade 2 NS+PSC+Dry ARMD	95	299	39	140/90	249
96	MS96	70	F	HOUSEWIFE	Y	N	6 months	6 month	2 years	6\18	6\9	Grade 2 NS +PSC	pseudophakia	14	16.3	WNL	WNL	RE-grade 2 NS+PSC,LE-Pseudop	96	310	40	138/90	269
97	MS97	58	M	FARMER	N	Y	6 months	2 years	3 years	6\12	PL + PR ac	Grade 2 NS	SMC	13	15	WNL	No glow, Details not mad	RE- grade 2 NS,LE-SMC	92	151	40	142/86	115
98	MS98	54	M	TEACHER	N	Y	6 months	3 years	2 years	6\9(P)	PL + PR ac	Grade 1 NS	SMC	12	9	WNL	No glow, Details not mad	RE- grade 1 NS,LE-SMC	104	157	43	140/90	156
99	MS99	78	M	RETIRED	Y	Y	1 year	2 years	1 year	CFCF	CFCF	Grade 3 NS+PSC	Grade 3 NS	10	6	Arteriolar attenuation+m	Arteriolar attenuation+m	BE Grade 3 NS+grade 1 HTN re	98	160	44	140/80	147
100	MS100	70	F	RETIRED	Y	N	1 year	3 years	2 years	CF1M	6\18	Grade 3 NS+PSC	Grade 2 NS +PSC	19	16.8	WNL	WNL	RE-Grade 3 NS+PSC,LE-Grade 2	107	244	40	156/90	275
101	MS101	73	M	RETIRED	N	Y	6 months	4 years	3 years	6\9(P)	HMCF PL+	pseudophakia	Grade 3 NS+PSC	14.9	17	WNL	WNL	RE pseudophakia,LE grade 3 NS	93	189	41	172/86	142
102	MS102	62	M	FARMER	Y	N	6 months	3 years	2 years	6\36(P)	6\36	Grade 2 NS +PSC	Grade 2 NS	18.3	13	WNL	WNL	RE-Grade 2 NS +PSC, LE-Grade	99	231	48	158/82	160