CORRELATION OF CUMULATIVE DOSE AND DURATION OF STEROID THERAPY WITH OCULAR MANIFESTATIONS IN CHILDREN WITH NEPHROTIC SYNDROME - A ONE-YEAR CROSS SECTIONAL STUDY

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ABBREVIATIONS

NS	Nephrotic Syndrome
INS	Idiopathic Nephrotic Syndrome
FSGS	Focal Segmental Glomerulosclerosis
SDNS	Steroid Sensitive Nephrotic Syndrome
SRNS	Steroid Resistant Nephrotic Syndrome
CNS	Congenital Nephrotic Syndrome
ESRD	End Stage Renal Disease
ISKDC	International Study of Kidney Disease in Children
GFB	Glomerular Filtration Barrier
AKF	Acute Kidney Failure
MMF	Mycophenolate mofetil
TB	Tuberculosis
ANA	Anti-Nuclear Antibody
HIV	Human Immunodeficiency Virus
DVT	Deep Vein Thrombosis
VLDL	Very Low Density Lipoprotein

LDL	Low Density Lipoprotein
GAG	Glycosaminoglycans
HPA	Hypothalamic-Pituitary-Adrenal
BCVA	Best Corrected Visual Acuity
IOP	Intra Ocular Pressure
PSC	Posterior Subcapsular Cataract
PCIOL	Posterior Chamber Intra Ocular Lense
NAD	No Abnormality Detected
DNMO	Details Not Made Out
OCT	Optical Coherence Tomography

ABSTRACT

Introduction: Nephrotic syndrome (NS) is the most common kidney disease in children aged 2 to 18 years, which presents with massive proteinuria (40mg/m2/hour), hypoalbuminemia (< 2.5 gm/dl), hypercholesterolemia and edema. Corticosteroids and sodium restriction are the mainstay therapy for nephrotic syndrome. The disease has a chronic, relapsing course requiring repeated, prolonged course of steroid therapy. Long term use of corticosteroids is associated with ocular complications like increased risk of cataract formation and development of glaucoma.

Objective of the Study:

- To study correlation of cumulative dose and duration of steroid therapy with ocular manifestations in children with nephrotic syndrome.
- To study the steroid independent ophthalmic findings in children with NS

Methodology: This is a cross sectional study conducted at Departments of ophthalmology and Pediatrics Nephrology, KLE'S Dr Prabhakar Kore Hospital and Medical Research Centre, Belagavi during the period of August 2022 to July 2023. Total 61 children between 2-18 years of age diagnosed of nephrotic syndrome on corticosteroid therapy were included in the study.

Detailed history was taken with the year when disease started, the course of therapy, any history of hypertension, any other medications or other systemic illness, diminution of vision, headache. General physical examination was done. Thorough ophthalmic examination was done with best corrected visual acuity, slit lamp examination, intra ocular pressure measurement, fundus examination. Total cumulative dose of steroid therapy per meter square was calculated manually. Data was statistically analysed.

Results: A total of 61 patients were enrolled in the study, between age group of 2 to 18 years. The majority patients (45.9%) were from 6-10 years of age group. The mean age was 8 years. 39 (63.93%) were males and 22 (36.07%) were females. 83.61% were patients with steroid dependent nephrotic syndrome (SDNS) and 16.39% patients were with steroid resistant nephrotic syndrome (SRNS). Most of the patients had good vision. 22% patients had myopia. 6.56% patients had PSC. No patients had increased IOP or abnormal fundus findings. There is no significant correlation between total cumulative dose with steroid dependent ocular manifestation but there is significant correlation between duration of steroid therapy with steroid dependent ocular manifestation.

Conclusion: Posterior subcapsular cataract is the most common steroid dependent ocular manifestation in nephrotic syndrome children. Duration of steroid therapy is significantly related with cataract in nephrotic syndrome. All patients with nephrotic syndrome taking steroid therapy should have regular ophthalmological examination for early detection of these complications.

Keywords: Nephrotic Syndrome, Steroid therapy, Cataract

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INTRODUCTION

Nephrotic syndrome (NS) is the commonest kidney disease in children aged 2 to 18 years with incidence of approximately 2-3 cases per 1,00,000 population. It presents with massive proteinuria (40mg/m2/hour), hypoalbuminemia (< 2.5 gm/dl), hypercholesterolemia and edema.(1) Several plasma proteins necessary for other metabolic functions are excreted in the urine in nephrotic syndrome leading to several complications. Patients with nephrotic syndrome are also at risk for fatal infections and thromboembolic episodes due to significant loss of plasma proteins like albumin, coagulation factors, immunoglobulins.

Corticosteroids and sodium restriction are the mainstay therapy for nephrotic syndrome. The disease has a chronic, relapsing course requiring repeated, prolonged course of steroids. Prednisolone acetate is the most commonly used corticosteroid therapy. Duration and dose of steroid therapy depends on disease entity like steroid dependent nephrotic syndrome (SDNS) and steroid resistance nephrotic syndrome (SRNS). Most nephrotic syndrome patients relapse within the first six months of starting steroid therapy. Patients with frequently relapsing steroid dependent nephrotic syndrome are initially treated with long-term, alternate-day oral prednisolone. After slow tapering to a maintenance dose of 0.25-0.5 mg/kg on alternate days, these doses are given for extended periods of 9–12 months, but many still relapse, especially during intercurrent infections. Patients who require prednisolone at doses greater than 1 mg/kg on alternate days to maintain remission are likely to experience side effects and should be treated with steroid sparing agents. Long term use of corticosteroids either given orally, intravenously or topically is associated with ocular complications like increased risk of cataract formation and development of glaucoma.

Posterior subcapsular cataract is the most common steroid induced ocular manifestation. Steroids in high doses have multiple effects on trabecular meshwork increasing risk of glaucoma. Other ocular manifestations like eyelid skin atrophy, recurrent hordeolum, keratitis are associated with long term corticosteroid usage.(2) Nephrotic syndrome can also cause some ocular complications like lid edema, diminution of vision, hypertensive retinopathy and macular changes.

Nephrotic syndrome children undergoing corticosteroid therapy should undergo thorough ophthalmological examination including BCVA, slit-lamp examination, intraocular pressure measurement and dilated fundus examination for early detection of steroid dependent and steroid independent ocular manifestations.

The visual impairment due to cataract and glaucoma seen in these children due to prolonged use of corticosteroids will have negative impact on their emotional and social wellbeing and also causes socioeconomic burden on family. It is possible to avoid cataract-induced amblyopia, and permanent blindness from optic nerve damage in steroid-induced glaucoma by identifying and treating these adverse effects early. Therefore, it is needed that all the nephrotic syndrome children who are on prolonged treatment with corticosteroids should undergo timely examination by ophthalmologist to rule out any ocular complications.

There are many studies on ocular manifestations due to corticosteroid therapy in children with NS but currently there are very few studies on the correlation of cumulative dose and duration of steroid therapy with ocular manifestations in children with NS.

Therefore, studying the relationship between the total dose and duration of corticosteroid therapy with various ocular manifestations in children with nephrotic syndrome is very crucial.

AIMS AND OBJECTIVES

- To study correlation of cumulative dose and duration of steroid therapy with ocular manifestations in children with nephrotic syndrome.
- To study the steroid independent ophthalmic findings in children with NS.

REVIEW OF LITERATURE

Nephrotic syndrome

Definitions:

Nephrotic syndrome, also referred as nephrosis, is a disorder in which damaged glomeruli allow blood protein to seep into the urine. The hallmark symptoms include hypoalbuminemia (<2.5 g/L), extensive edema, hyperlipidemia, and proteinuria in the nephrotic range (≥40 mg/m2 /hour or urine protein/creatinine ratio > 2 mg/mg or 3 + protein on urine dipstick).(1)

1) STEROID SENSITIVE NEPHROTIC SYNDROME(SSNS): In 85–90% of patients, treatment with prednisolone completely resolves proteinuria; this condition is known as SSNS.(3,4)

2) STEROID RESISTANT NEPHROTIC SYNDROME(SRNS): Absence of total remission after six weeks of treatment with daily prednisolone dosage of 2 mg/kg (or 60 mg/m2).(4)

3) STEROID DEPENDENCE: Two relapses in a row when using an alternate-day steroid, or within 14 days of stopping it.

4)RELAPSE: After being in remission earlier, urine protein ≥3+ for three consecutive early morning specimens.

5)FREQUENT RELAPSES: 2 or more Relapses occurring within the first six months following the end of first therapy, three or more in any six-month period, or four or more in a single year.(4)

Epidemiology: Nephrotic syndrome, with an annual incidence of 2–7 per 100,000 children and a prevalence of 12–16 per 100,000, is the most prevalent kidney disease in children globally.(5) Children who are dark coloured or Hispanic appear to be at higher prevalance for FSGS and children from Southwest Asia, India, and Japan are more likely to develop INS.(6) Males tend to be affected more than females in nephrotic syndrome children at a ratio of 2:1.(7)

Aetiology: NS is currently classified into both primary and secondary forms. The majority of children with Nephrotic syndrome have a form of primary or idiopathic nephrotic syndrome, which is further subdivided into focal glomerulosclerosis, minimal-change kidney disease, membranous nephropathy.(8) Minimal change nephropathy is the most usual glomerular lesion. The majority of cases of idiopathic nephrotic syndrome appear between the age of two to six years and are steroid-sensitive in most cases [95%]. The cause of the idiopathic nephrotic syndrome is unknown, although evidence indicates the primary T cell disorder results in glomerular podocyte dysfunction. Secondary causes can consist of systemic conditions like amyloidosis, lupus erythematosus, diabetes mellitus. Congenital or hereditary focal glomerulosclerosis can develop because of mutations in genes in podocyte proteins like podocin and nephrin.(9)

Pathophysiology: The kidney has filtration system, known as the glomerular filtration barrier (GFB). Three layers make up the GFB: glomerular basement membrane, fenestrated endothelium, and epithelial layer made up of podocytes and their foot processes. These foot processes create filtration slits connected by the slit diaphragm. This barrier is selectively permeable, allows tiny solutes and water to pass through urinary space while restricting larger molecules based on size and charge. Under

electron microscopy, the podocyte foot processes in nephrotic syndrome can be shown to be effaced. This disruption of the GFB leads to the proteinuria-characteristic of nephrotic syndrome.(10)

NS can result from various mutations in genes that cause defects in different parts of the GFB. This can manifest as isolated nephrotic syndrome , such as steroid resistant nephrotic syndrome or focal segmental glomerulosclerosis (FSGS), or as part of more complex syndromes like nail-patella syndrome or Denys-Drash syndrome. Most cases of congenital nephrotic syndrome (CNS) appear in the first three months of life. It is brought on by mutations in the nephrin gene, which codes for a critical slit diaphragm protein. Additionally, CNS may be secondary to illnesses like syphilis, CMV and toxoplasmosis as well as maternal lupus and neonatal autoantibodies to neutral endopeptidase.(11)

The immune system and podocytes play key roles in the pathophysiology of idiopathic nephrotic syndrome. Two main theories have been proposed: [1] Dysfunction of immune system that leads to circulating factors production, such as soluble urokinase plasminogen activator receptor, which modify podocyte structure and function and lead to proteinuria; and [2] T-cell dysfunction resulting in release of cytokines, which leads to increased glomerular permeability.(12)

It is divided into two categories: Steroids-Sensitive NS and Steroid-Resistant NS depending on steroid response. SSNS patients typically respond to steroids, but relapses are common. In contrast, SRNS, which is linked to focal segmental glomerulosclerosis (FSGS), will develop to end stage renal disease (ESRD).(1,13)

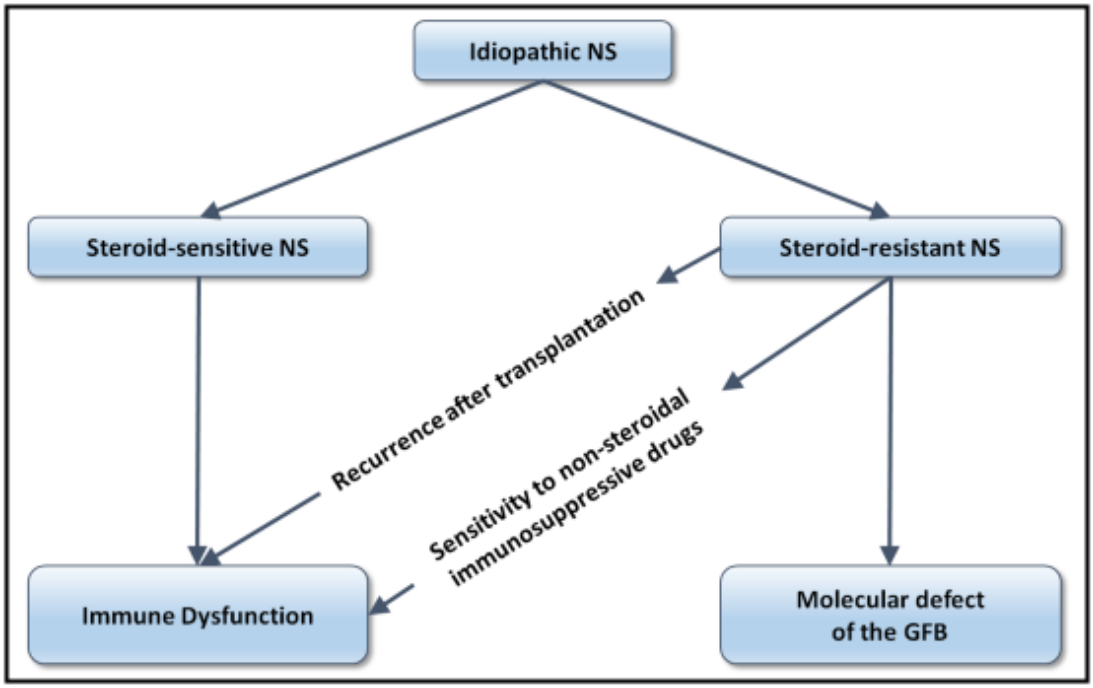


Figure 1: Pathophysiology of NS

Clinical features: Edema, usually periorbital, labial, scrotal, and in the lower limbs, is the hallmark presenting symptom of nephrotic syndrome (NS). Anasarca may develop in extreme situations, which can result in ascites and pericardial or pleural effusions. Dyspnea, cold extremities, and pain in the abdomen are possible complications. Due to T-cell malfunction and urinary loss of immunoglobulins, children with NS are more susceptible to catastrophic bacterial infections such as pneumonia, sepsis, and peritonitis. In NS, intravascular volume depletion and oliguria might occur. Acute kidney damage (AKI), a serious consequence, can occasionally arise from this.

NS is also recognized as a hypercoagulable state, increasing the risk of thrombotic events such as pulmonary embolism, cerebral sinus venous thrombosis, deep vein thrombosis (DVT), renal vein thrombosis. Increased prothrombotic factor levels, abnormal platelet aggregation, urine loss of anticoagulant factors, and intravascular volume reduction are all linked to multifactorial hypercoagulability.(12)

Hyperlipidemia is a usual consequence of NS, resulting from multiple mechanisms: increased hepatic synthesis of lipoproteins, triglycerides, cholesterol; hypoalbuminemia (since albumin transports cholesterol in circulatory system); diminished activity of lipoprotein lipase, which typically aids in the conversion of VLDL to LDL.(14)

Diagnostic investigations: When evaluating NS initially, essential investigations are : (i) Urine microscopy and urinalysis; (ii) Quantification of the protein-to-creatinine ratio on a 24-hour collection or spot urine sample (iii) CBC, serum electrolytes, albumin, RFT and cholesterol levels. Serum complement levels, antinuclear antibody, anti-double stranded DNA if ANA is positive, antineutrophil cytoplasmic antibodies, immunoglobulins, and anti-streptolysin O titres may be used as further tests if a nephritic component is suspected. Based on clinical indications, infectious causes like syphilis, HIV, hepatitis B, hepatitis C , TB, schistosomiasis should be taken into consideration.

Genetic testing is recommended in specific scenarios: (i) Congenital nephrotic syndrome (ii) Steroid resistant nephrotic syndrome (SRNS) (iii) NS present in family history. Renal biopsy should be considered if certain risk factors exist, although it is usually not necessary at the time of initial diagnosis.

Management: Oral steroids are the primary treatment for nephrotic syndrome. Corticosteroids function via a number of methods, but the main one is that they control the production of cytokine genes through the glucocorticoid receptor. Genes for anti-inflammatory cytokines are induced by this regulation, whereas pro-inflammatory cytokine genes are suppressed. Additionally, corticosteroids have been shown in recent research to stabilize the podocyte cytoskeleton and inhibit T-cell activity.(15)

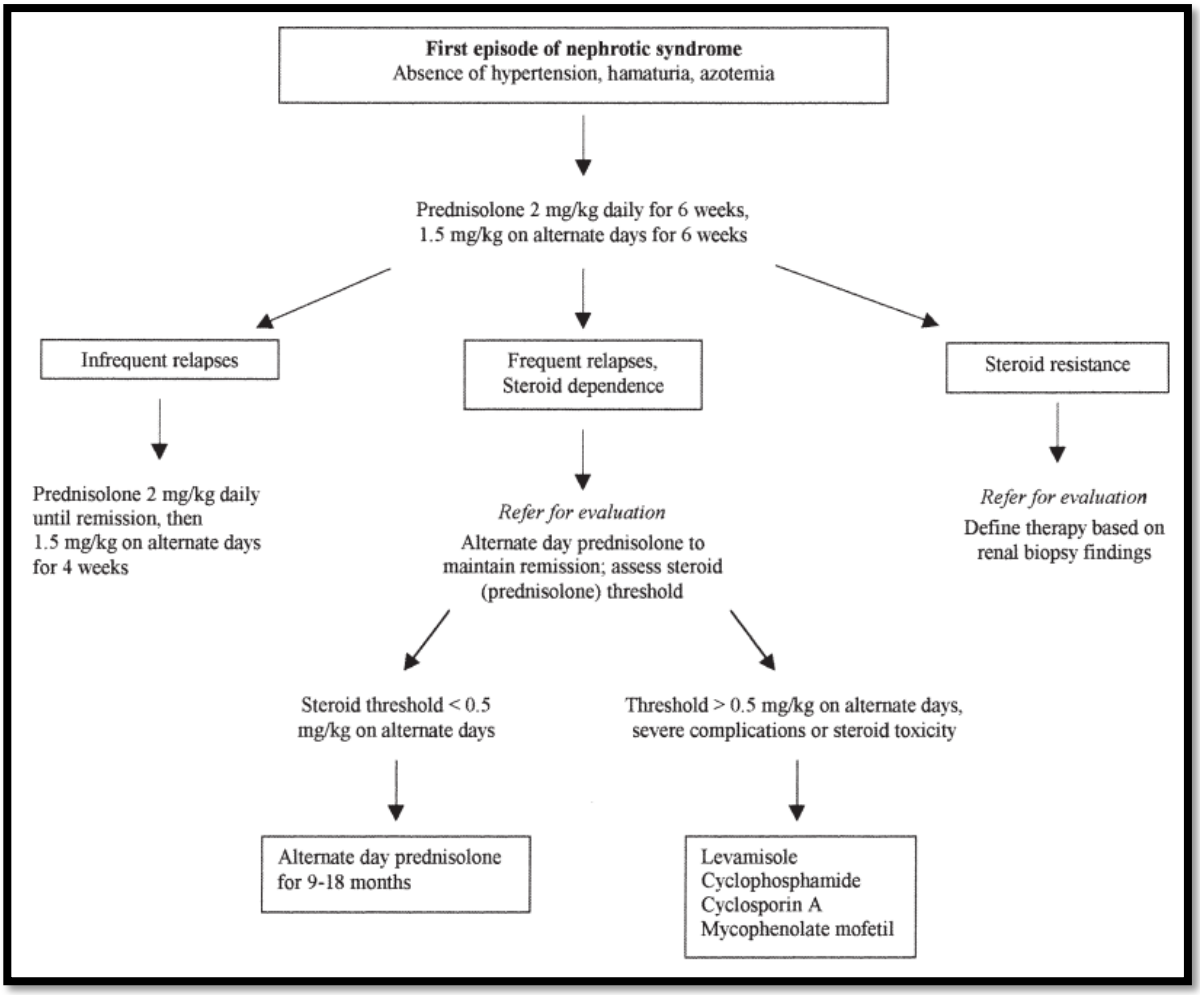


Figure 2: Management of childhood nephrotic syndrome

The first course of corticosteroid therapy for NS is defined by the current kidney Disease Improving Global Outcomes (KDIGO) guidelines as giving 60 mg/m²/day of oral prednisolone, up to a maximum of 60 mg/day, once daily for four to six weeks. After that, patients receive 40 mg/m²/day on alternate days for two to five months, with a gradual tapering of the dose to ensure that the entire course of therapy lasts at least 12 weeks.(16)

Prolonged corticosteroid medication, however, can have a number of negative effects on children, such as stunted growth, significant weight gain, cataract, mental health issues like melancholy, anxiety, and aggressive behavior. Because they require

numerous treatment rounds over the course of their lifetime, children with NS who relapse frequently or who are dependent on steroids are especially vulnerable to these side effects.(17)

Corticosteroids and systemic side effects

Corticosteroids have immunosuppressive and anti-inflammatory actions. They can be administered alone or in combination with other medications and prescribed for varying durations based on the specific condition and patient response. Short-term corticosteroid can cause sleep disturbances, mood and behavioral changes. (18)

Prolonged corticosteroid therapy causes:

- Osteoporosis
- Hypothalamic-pituitary-adrenal (HPA) axis suppression: Which increases the risk of infections, including viral, bacterial,fungal.(19)
- Gastrointestinal: Peptic ulcer disease and gastritis
- Cushingoid features: Patient will present with weight gain, buffalo hump, moon facies, truncal obesity(20)
- Diabetes and hyperglycemia
- Hypertention
- Myopathy
- Dermatologic adverse effects: Skin atrophy, reduction in thickness of skin, purpura and striae.(21)

Corticosteroids induced ocular manifestations

Long term use of corticosteroids lead to ocular adverse effects like steroid-induced glaucoma, cataract formation, central serous retinopathy, delayed wound healing, and increased susceptibility to infection.(22,23)

Posterior subcapsular cataract: In 1960 black noticed first about relation between use of steroid and cataract. He also obsereved higher steroid doses correlated with a greater prevalence of posterior subcapsular cataract (PSC) (24). Steroid induced cataract is mostly bilateral.(25)

Characteristics of PSC: Just inside the posterior capsule, in the polar area of the posterior cortex, is where PSC is situated. It extended erratically forward into the cortex, occasionally seeming to enter the capsule and frequently obliterating the posterior zone of disjunction. Its borders are typically sharp but sometimes surrounded by a light grey haze. The slender structure appeared granular and conglomerate, with occasional linear marks, composed of tiny whitish yellow crystalline opacities separated by equally minute vacuoles.(26)

Mechanism of steroid induced cataract formation:

I. Inhibition of the Na+-K+ ATPase Pump Mechanism by Corticosteroids

The "pump-leak" mechanism of the lens could possibly be connected to PSC. The acellular posterior capsule promotes passive diffusion, whereas the anterior epithelium acts as an active transport mechanism. Corticosteroids influence the movement of water and raise the cation permeability of lenses.(27)

Clinically, lens hydration appears as generalized swelling or localized fluid accumulation, altering refractive index and reducing light transmission.

II. Corticosteroid Binding to Lens Proteins and the Resultant Lysine-Ketosteroid Adduct Formation

Covalent glucocorticoid-lens protein adduct formation has been related to corticosteroid-induced lens opacities. The corticosteroid's C-20 carbonyl and a protein amino group produce a Schiff base in this nonenzymatic reaction, which is then followed by a Heyns rearrangement involving the C-21 hydroxyl group and a stable product. Cataract formation is partially caused by nonenzymatic alteration of lens proteins by low-molecular-weight substrates like as glucose and cyanate. Due to this alteration, lens crystallins' natural conformation is altered, which causes disulfide cross-linking and the creation of aggregates with high molecular weight that scatter light.(28)

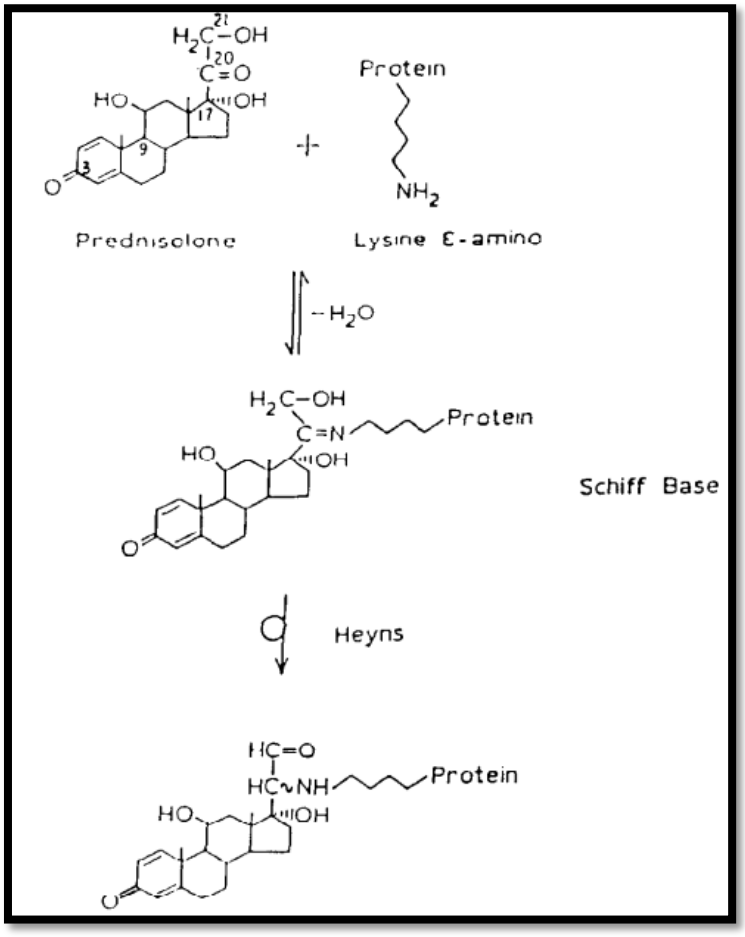


Figure 3 : Molecular diagram of mechanism of steroid induced cataract

III. Crystallin Aggregation Due to Secondary Oxidation of -SH Protein Groups

Prednisolone reacts nonenzymatically with lysine residues in lens crystallin inducing conformational changes that expose sulfhydryl groups or increase their susceptibility to oxidation. Over time, this leads to disulfide cross-linking, forming light-refracting complexes. Both in vitro and in vivo, prednisolone-lens protein adducts are present as high molecular weight sulfhydryl complexes, according to gel filtration analysis of proteins from corticosteroid-induced cataracts.(29)

IV. Aberrant cell behaviour

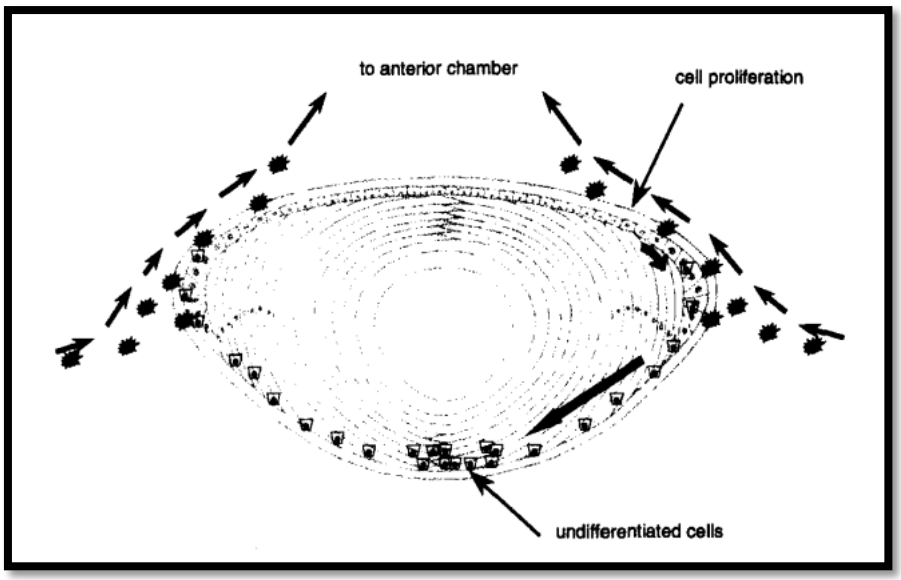


Figure 4: Diagram of Aberrant cell behaviour

Steroid cataracts often exhibit a peculiar characteristic: Collection of undifferentiated epithelial cells under the capsule, which is usually found at the lens's posterior pole. These cells are often limited to the lens mass's anterior surface. This finding suggests that aberrant cell behavior may play a role in the formation of cataracts. (30)

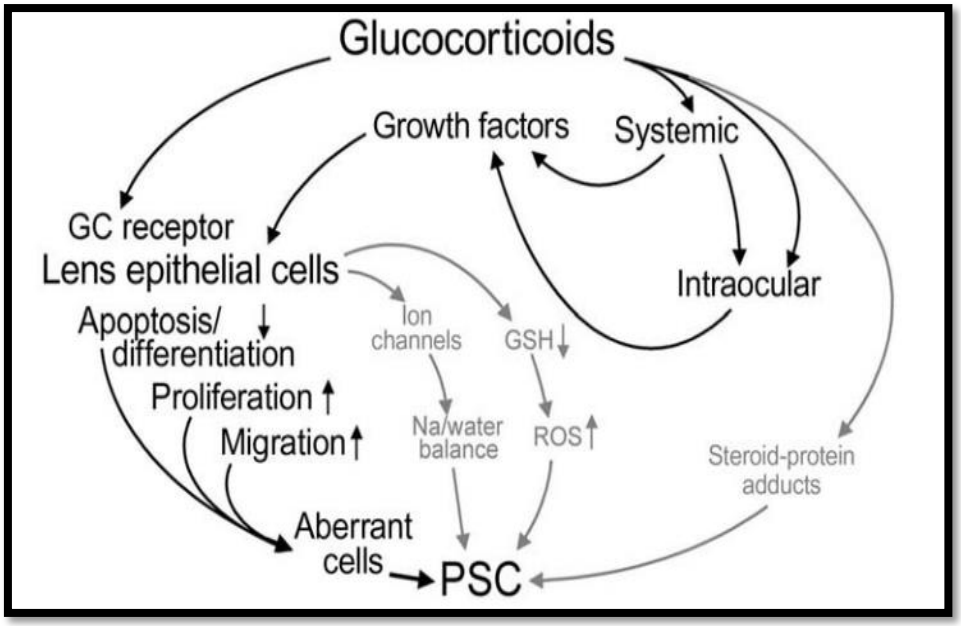


Figure 5: Summary of mechanism of steroid induced cataract

Steroid induced glaucoma:

The earliest report of steroid-induced ocular hypertension dates back to 1950, when it was discovered that prolonged systemic steroid use raised intraocular pressure (IOP). Any type of prolonged steroid therapy can raise IOP, which may result in disc atrophy and steroid-induced glaucoma.(31)

Steroid-induced glaucoma is a type of open-angle glaucoma. Although the exact mechanism behind the elevation of intraocular pressure (IOP) following steroid use is not entirely understood, it is primarily attributed to a decreased aqueous outflow. Several theories have been proposed to explain the steroid-induced increase in IOP.(32)

Mechanism for increased IOP after prolonged steroid therapy:

- Steroids cause polymerized glycosaminoglycans (GAGs) to accumulate in the trabecular meshwork and stabilize lysosomal membranes. The hydration of these polymerized GAGs causes "biologic edema" and raises the outflow

resistance. Furthermore, glucocorticoids promote the expression of extracellular matrix proteins in trabecular meshwork cells, including GAGs, fibronectin, laminin, and elastin, which increases resistance.(33)

- Ultrastructural studies of glaucoma due to steroids show an accumulation of basement membrane-like material that stains for collagen type IV. Additionally, corticosteroids prevent endothelial cells lining the trabecular meshwork from being phagocytic, which causes aqueous debris to accumulate.(34)
- Glucocorticoids have been shown to alter the morphology of trabecular meshwork cells by increasing nuclear size and DNA content.(35)
- Glucocorticoids decrease the synthesis of prostaglandin, regulator of aqueous outflow. Additionally, genetic factors influence the response of trabecular meshwork cells to glucocorticoid treatment, with certain genes associated with either protective or damaging effects on these cells.(36)

In many cases, it is possible to avoid steroids and opt for nonsteroidal anti-inflammatory alternatives. When steroid use is unavoidable, it is crucial to monitor IOP regardless of the duration and dose of steroid treatment. The ocular hypertensive response to steroids is typically reversible if addressed promptly, preventing vision-threatening complications. This monitoring is particularly important in children to safeguard their visual health.

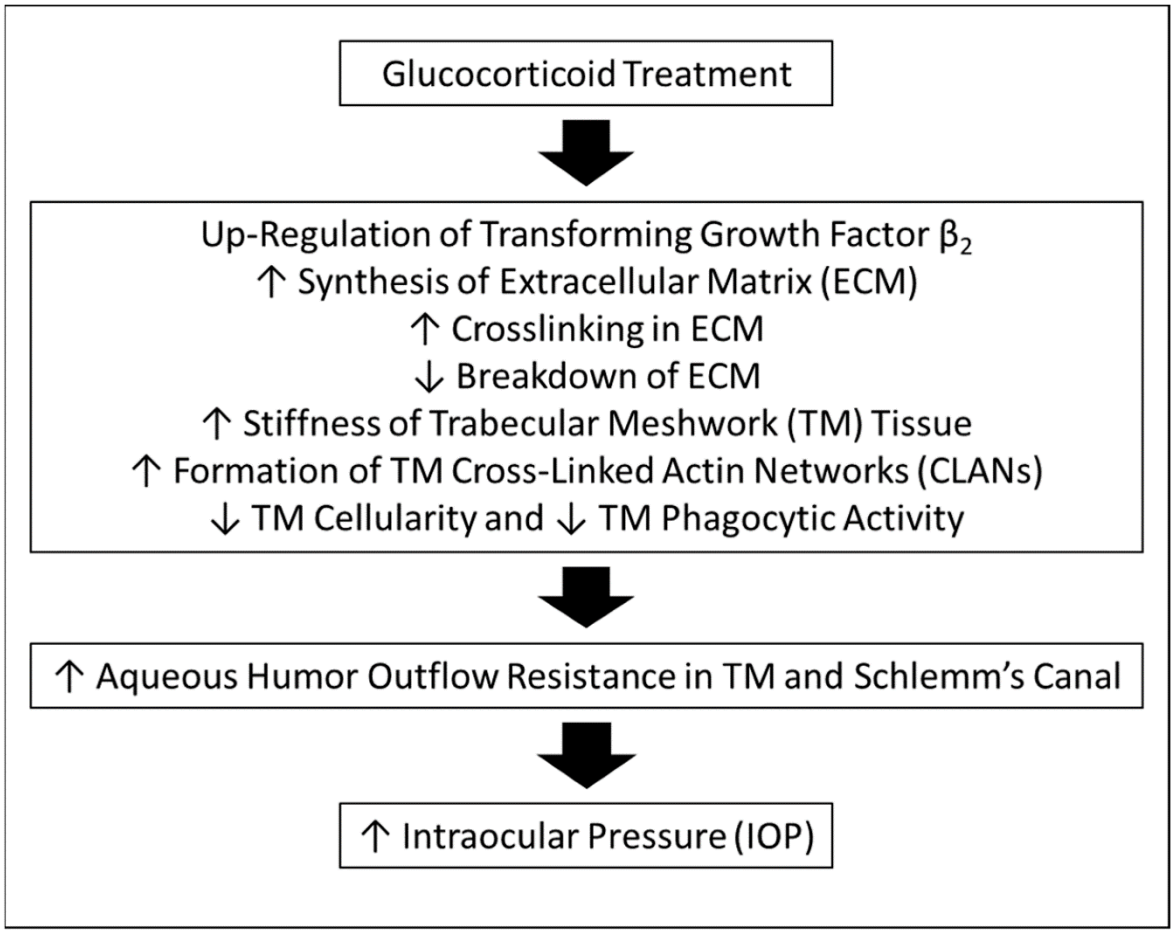


Figure 6 : Mechanism of steroid induced glaucoma

MATERIALS AND METHODS

The current study was conducted at Departments of Ophthalmology and Pediatrics Nephrology, KLE'S Dr Prabhakar Kore Hospital and Medical Research Centre, Belagavi during the period of August 2022 to July 2023.

Method of data collection:

Study population:

Children between 2 to18 years of age diagnosed with nephrotic-syndrome on corticosteroid therapy attending Department of Ophthalmology and Department of Pediatrics Nephrology at KLE'S Dr. Prabhakar Kore Hospital and Medical Research Center, Belagavi.

Study Design: A hospital based prospective one year cross sectional study

Study Duration: One year, from August 2022 to July 2023.

Sampling technique: Convenient sampling

Sample Size: 61

Formula used for sample size calculation was

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

sample size required is n, percentage occurrence of a state or condition (proportion or prevalence) is p, percentage maximum error required is d , Z is the value corresponding to level of confidence required.

Prevalence of ocular complication was observed as 80% for the children with nephrotic syndrome. With percentage of maximum error as 10% at 95% confidence level sample size is given by,

$$n = \frac{80 \times (100-80) \times (1.96)^2}{10^2}$$

$$n = 61.46 \approx 61$$

Minimum sample size required is 61, with 95% confidence level and with 10% error.

Selection criteria:

Inclusion Criteria:

- Children between 2 to 18 years of age who were diagnosed with nephrotic syndrome (NS) and taking corticosteroid therapy.
- Patients receiving corticosteroids either as monotherapy or combined therapy.
- Children and parents/guardian who gave consent for the study.

Exclusion Criteria:

- Syndromic forms of NS
- Patients who were non-cooperative for ophthalmologic evaluation
- Presence of any other systemic disease with NS.
- Previous history of ocular trauma

Data collection procedure: All children with nephrotic syndrome between the age of two to eighteen years who were receiving corticosteroid medication and who satisfied the inclusion criteria and provided permission to take part in study were assessed.

A thorough medical history was obtained from the children and their parents, covering demographic information, the year the condition first manifested, the course

of therapy, any history of hypertension, and any extra medications used. Details of ocular symptoms like defective vision, headache, eyelid swelling and use of spectacles were taken.

General physical examination was done. Height and weight of a child was measured. BMI was calculated with weight divided by height in meter square. Systemic examination was done thoroughly.

Snellen's chart in older children and teller acuity chart in younger children was used to evaluate distant visual acuity. Best corrected visual acuity and visual acuity with spectacles was recorded. Near visual acuity was also evaluated with snellen's near vision chart. Objective wet retinoscopy readings of both the eyes was taken and subjective correction was given to the children having refractive error Ocular alignment was checked by Hirschberg corneal reflex test and cover uncover test. Extraocular movement was examined in all cardinal directions of gaze. Anterior segment evaluation was done by slit lamp examination. After dilating the pupil with mydriatics, a second slit lamp examination was performed to look for posterior subcapsular cataract. Fundus examination was done by direct and indirect ophthalmoscopy. Intraocular pressure of both the eyes was measured by non-contact tonometer or I care tonometer.

Duration of disease was recorded from past history. NS with up to three relapses within a year following the termination of therapy or one recurrence within six months was considered infrequently relapsing nephrotic syndrome and NS with at least two relapses in the first half-year following therapy termination or at least four relapses in the last twelve months following therapy termination was considered frequently relapsing nephrotic syndrome. After diagnosis with NS, for the first episode prednisolone acetate was given orally 2 mg/kg/day(60mg/m2/day) in one or

two divided doses for 6 weeks, then for the next six weeks on alternate days it was tapered with 1.5 mg/kg/day (40 mg/m2/day) as single morning dose and finally stopped after 9-10 months of treatment. Prolonged treatment with prednisolone upto a dose of 0.5–0.7 mg/kg on alternate days for a duration of 6–12 months was given in patients who experienced relapses often. Additionally, steroid sparing agents like Tacrolimus (0.1-0.2 mg/kg/day), Levamisole (2-2.5 mg/kg on alternate day), Cyclosporine (4-5 mg/kg/day), Mycophenolate mofetil (600-1200 mg/m2/day) were given for patients who continued relapsing.

Duration of steroid therapy given during the disease and total cumulative dose was calculated manually from past history. Cumulative dose per square meter was calculated by dividing total cumulative dose with body surface area (BSA).

Data processing and statistical analysis:

R version 4.3.1 statistical tools and Microsoft Excel were used for data analysis. Categorical variables were represented by frequency tables. Continuous variables were presented in the form of Mean ± SD / Median (Min, Max). The chi square test was used to examine if categorical variables were related. Shapiro Wilk test was used to check the normality of continuous variables. The parametric test was employed if the data had a normal distribution. Otherwise, non-parametric test was used. Two sample t test was used to compare the mean of variables over ocular manifestation. Mann Whitney U test was used to compare the distribution of variables over ocular manifestation. P-value of 0.05 or less denoted statistical significance.

RESULTS

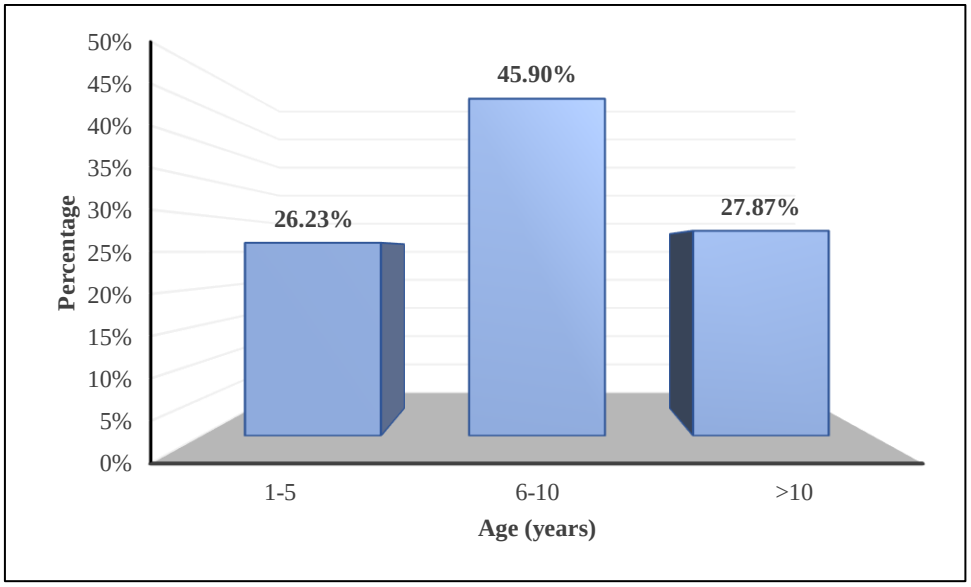
The present study included a total 61 subjects whose age ranged from 2 - 18 years with mean age of 8.27 ± 3.58 years.

The distribution of subjects by age is seen in the following table.

Table 1 : Subjects distribution based on age.

Age (years)	Number of subjects (%)
2-5	16 (26.23%)
6-10	28 (45.9%)
>10	17 (27.87%)
Mean ± SD	8.27 ± 3.58
Median (Min, Max)	8 (2.5, 17)

The majority of subjects (45.9%) were in the 6-10 years age group, followed by those aged over 10 years (27.87%) and those aged 2-5 years (26.23%).



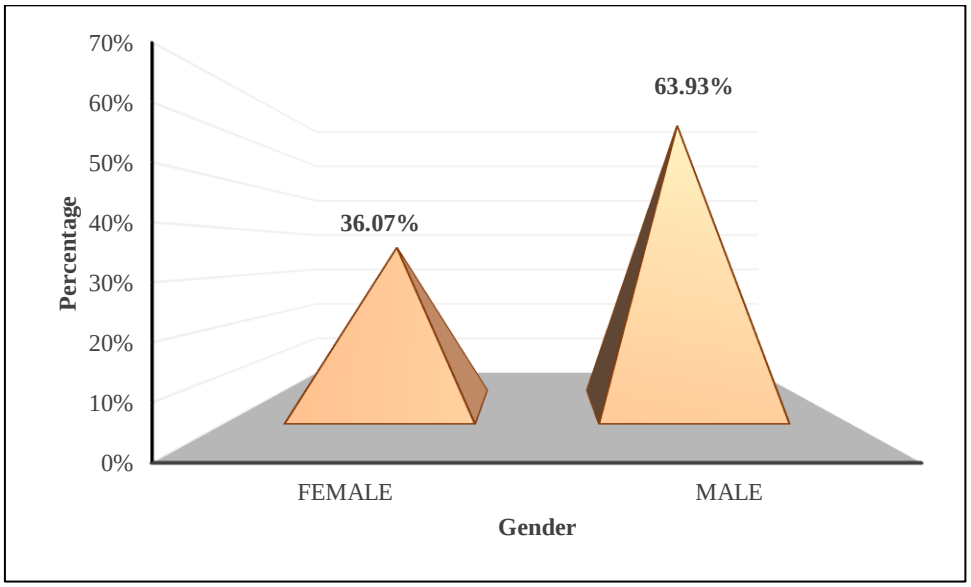
Graph 1 : Subjects distribution based on age.

The gender distribution of the subjects is shown in the following table.

Table 2 : Subjects distribution based on gender

Gender	Number of subjects (%)
Female	22 (36.07%)
Male	39 (63.93%)

39 (63.93%) of the 61 participants were boys, while 22 (36.07%) were girls.



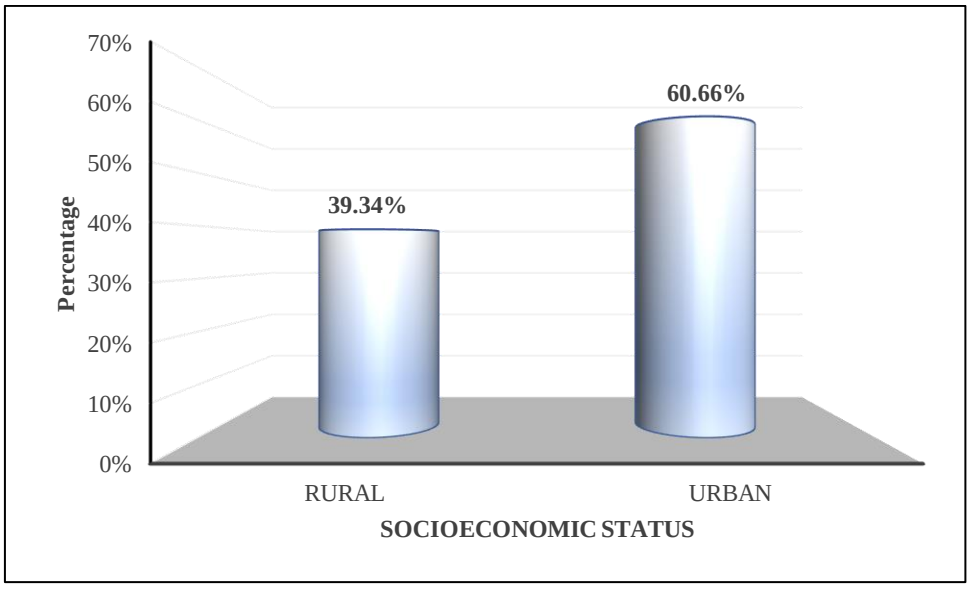
Graph 2 : Subjects distribution based on gender

Subjects distribution based on socioeconomic status is shown in following table.

Table 3: Subjects distribution based socioeconomic status.

Socioeconomic status	Number of subjects (%)
Rural	24 (39.34%)
Urban	37 (60.66%)

With regard to Socioeconomic status, 37 (60.66%) were from urban area while 24 (39.34%) were from rural area.



Graph 3 : Subjects distribution based on socioeconomic status.

Distribution of subjects according to height, mean weight, mean BMI and BSA is given in the table below.

Table 4: Distribution of subjects according to height, mean weight, mean BMI and BSA.

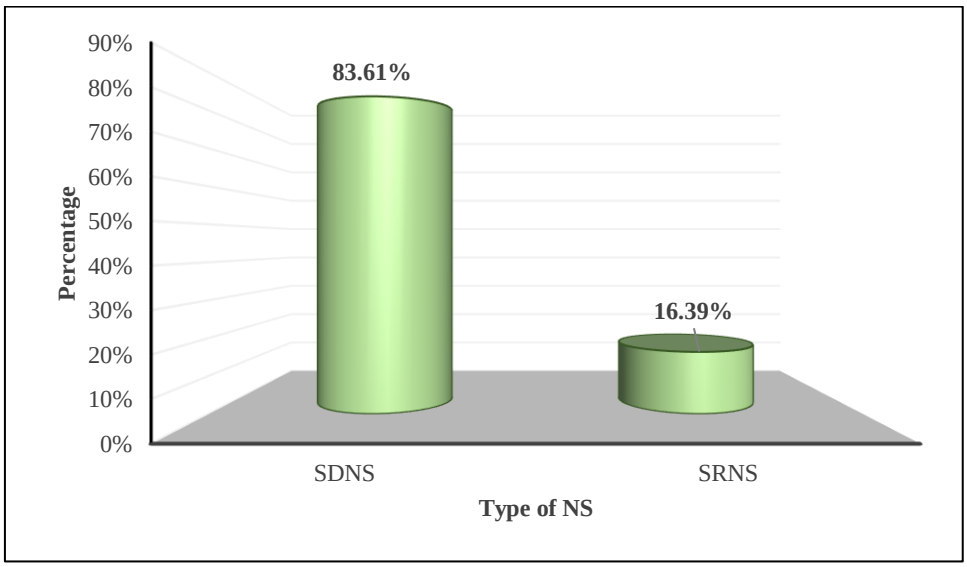
Variables	Mean ± SD	Median (Min, Max)
Height(cm)	117.26 ± 17.33	116 (75, 155)
Weight(kg)	25.38 ± 11.11	23.60 (10, 58)
BMI	17.68 ± 4.30	16.60 (10.90, 34.40)
Mean height (cm)	111.93 ± 16.57	112 (75, 155)
Mean weight (kg)	21.33 ± 8.00	21 (8.80, 48)
BSA (kg/m2)	0.82 ± 0.23	0.84 (0.39, 1.61)
Mean BMI	16.66 ± 2.97	16.20 (12.30, 27.10)

The table for distribution of subjects based on type of nephrotic syndrome is given below.

Table 5: Subjects distribution based on type of nephrotic syndrome.

Type of NS	Number of subjects (%)
SDNS	51 (83.61%)
SRNS	10 (16.39%)

The majority, 51 (83.61%) subjects had SDNS, while a smaller portion, 10 (16.39%) subjects had SRNS.



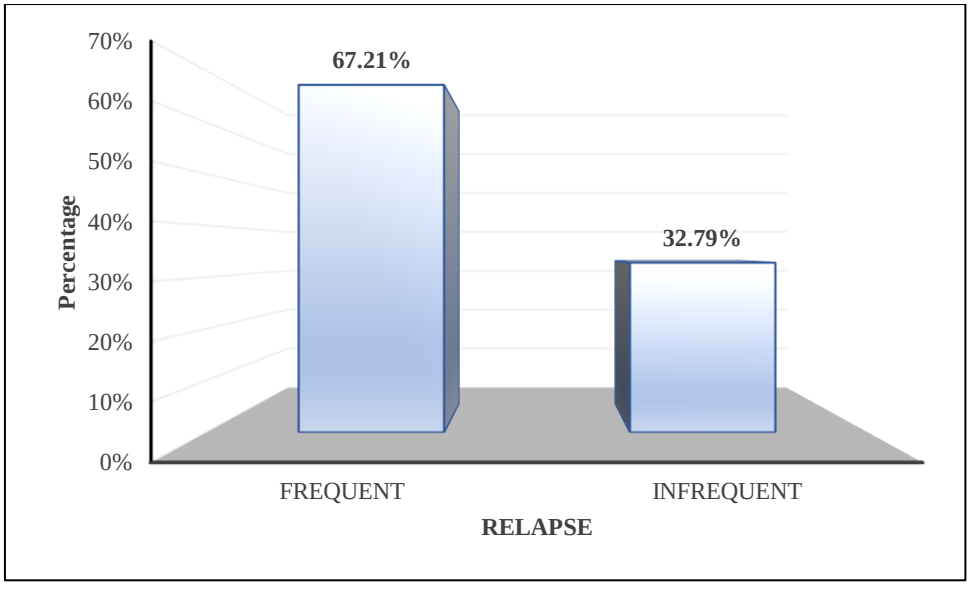
Graph 4: Subjects distribution based on type of NS.

The following table gives the distribution of subjects according to episodes of relapses.

Table 6: Subjects distribution based on episodes of relapses

Relapses	Number of subjects (%)
Frequent	41 (67.21%)
Infrequent	20 (32.79%)

Out of 61 subjects, a majority 41 (67.21%) subjects experienced frequent relapses, while 20 (32.79%) subjects had infrequent relapses.



Graph 5 : Subjects distribution based on relapses.

Table for distribution of subjects based on hypertension history is given below.

Table 7: Subjects distributions based on history of hypertension.

Hypertension	**Number of subjects (%)**
Present	56 (91.8%)
Absent	5 (8.2%)

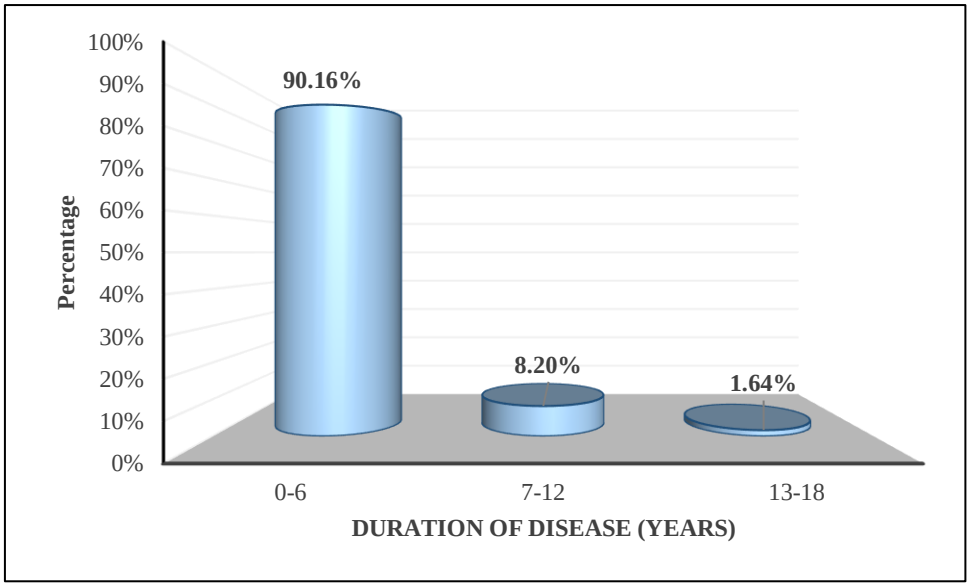
HTN was present in 56 (91.8%) subjects.

Table for distribution of subjects according to duration of disease is given below

Table 8: Distribution of subjects according to duration of disease.

Duration of disease (years)	**Number of subjects (%)**
0-6	55 (90.16%)
7-12	5 (8.2%)
13-18	1 (1.64%)

The vast majority 55 (90.16%) subjects had the disease for 0-6 years. A smaller group, 5 (8.2%) subjects had the disease for 7-12 years, and only 1 (1.64%) subject had the disease for 13-18 years.



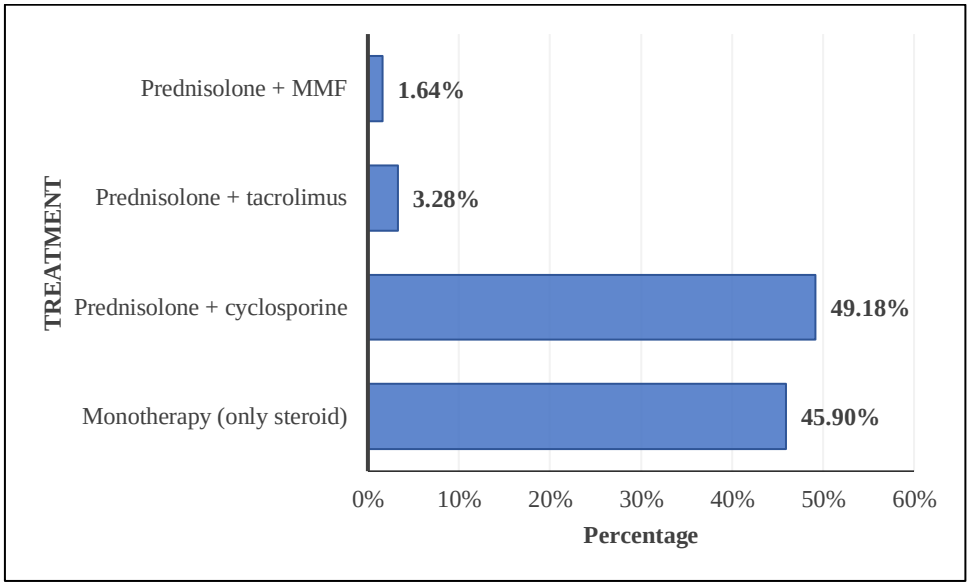
Graph 6 : Subjects distribution based on duration of disease.

The following table gives the distribution of subjects according to type of treatment given in NS.

Table 9: Subjects distributions based on type of treatment given in NS.

Treatment	Number of subjects (%)
Monotherapy (only steroid)	28 (45.9%)
Prednisolone + cyclosporine	30 (49.18%)
Prednisolone + tacrolimus	2 (3.28%)
Prednisolone + MMF	1 (1.64%)

Among the 61 subjects, 28 (45.9%) received monotherapy, which consisted solely of prednisolone acetate. A larger portion, accounting for 30 (49.18%) subjects, were treated with a combination of prednisolone acetate and cyclosporine. Only a small minority, comprising of 2 (3.28%) subjects, received prednisolone acetate in combination with tacrolimus, while a single subject (1.64%) was treated with prednisolone acetate alongside mycophenolate mofetil. A significant proportion of 33 (54.1%) subjects, were administered combined therapy, involving corticosteroids along with steroid-sparing immunosuppressants.



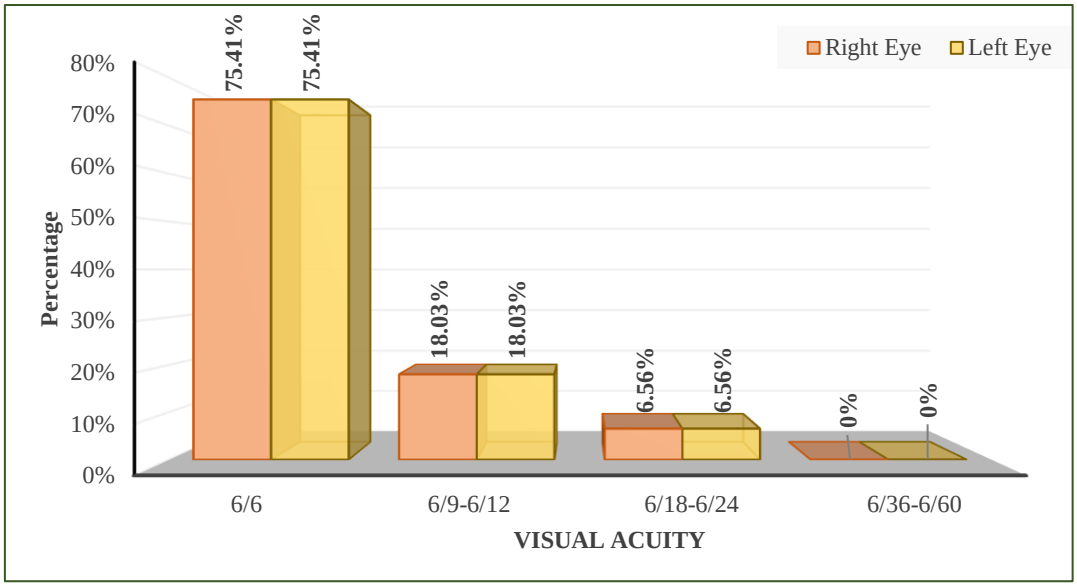
Graph 7 : Subjects distribution based on treatment given.

Table for subjects distributions based on visual acuity in both eyes is given below.

Table 10: Subjects distributions based on visual acuity in both eyes.

Visual acuity	Right Eye	Left Eye
6/6	46 (75.41%)	46 (75.41%)
6/9-6/12	11 (18.03%)	11 (18.03%)
6/18-6/24	4 (6.56%)	4 (6.56%)
6/36-6/60	0 (0%)	0 (0%)

The majority of subjects had excellent visual acuity, with 46 (75.41%) subjects achieving a visual acuity of 6/6 in both eyes. Additionally, 11 (18.03%) subjects had slightly lower but still good visual acuity ranging from 6/9 to 6/12 in both eyes. A smaller group of 4 (6.56%) subjects had visual acuity falling within the range of 6/18 to 6/24 in both eyes. Importantly, no subjects exhibited poorer visual acuity falling in the 6/36 to 6/60 range or worse in either eye.



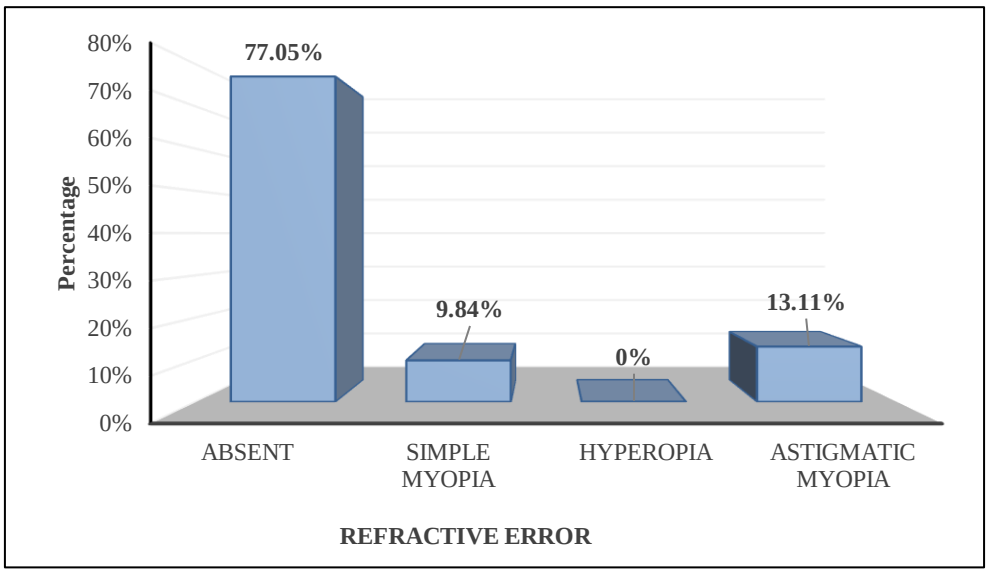
Graph 8: Subjects distribution based on visual acuity with respect to eye.

The following table gives the distribution of subjects according to refractive error.

Table 11: Subjects distributions based on refractive error.

Refractive error	Number of subjects (%)
Absent	47 (77.05%)
Simple myopia	6 (9.84%)
Hyperopia	0 (0%)
Astigmatic myopia	8 (13.11%)

Among the 61 subjects, 47 (77.05%) did not demonstrate any refractive errors, 8 (13.11%) had astigmatic myopia and 6 (9.84%) had simple myopia. Totally out of 61 subjects , 14 (22.95%) had refractive error.



Graph 9 : Subjects distribution based on refractive error.

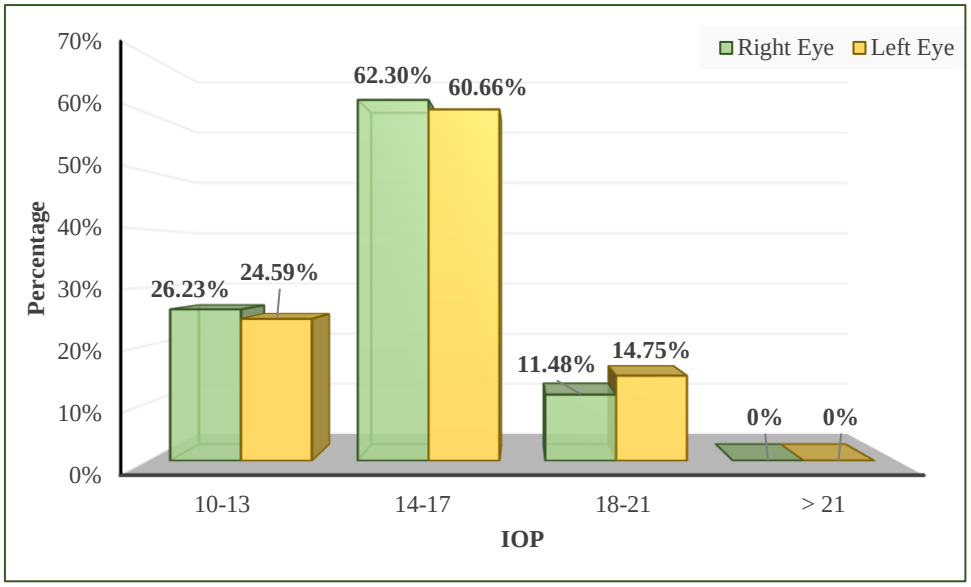
The following table gives the distribution of subjects according to IOP.

Table 12: Subjects distribution based on IOP.

IOP (mmHg)	Right Eye	Left Eye
10-13	16 (26.23%)	15 (24.59%)
14-17	38 (62.3%)	37 (60.66%)
18-21	7 (11.48%)	9 (14.75%)
>21	0 (0%)	0 (0%)
Mean ± SD	15.03 ± 2.13	15.28 ± 2.41
Median (Min, Max)	15.20 (10.90, 19.60)	15.20 (9.30, 20.10)

Out of 61 subjects, 16 (26.23%) in the right eye and 15 (24.59%) in the left eye had IOP values between 10 to 13 mmHg. A large proportion of subjects, 38 (62.3%) in the right eye and 37 (60.66%) in the left eye had IOP within 14 to 17 mmHg range. A smaller subset of subjects had IOP measurements ranging from 18 to 21 mmHg, with 7 (11.48%) subjects in the right eye and 9(14.75%) subjects in the left eye. Notably, no subjects exhibited IOP values greater than 21 mmHg in either eye.

The mean IOP values were found to be 15.03 ± 2.13 mmHg for the right eye and 15.28 ± 2.41 mmHg for the left eye, with median values of 15.20 mmHg for both eyes. The range of IOP measurements varied from 10.90 to 19.60 mmHg for the right eye and from 9.30 to 20.10 mmHg for the left eye.



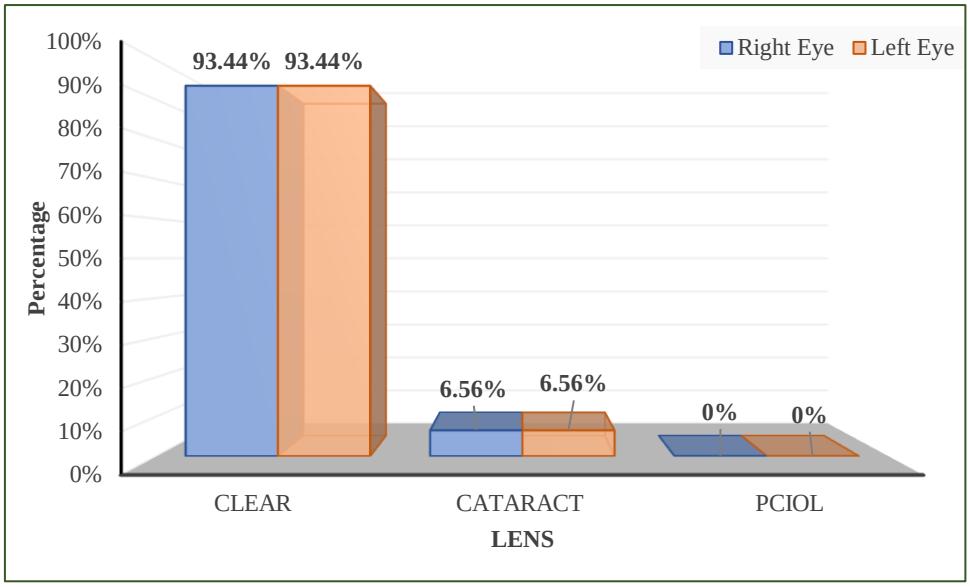
Graph 10 : Subjects distribution based on IOP with respect to eye.

The table given below shows the distribution of subjects according to lens.

Table 13: Subjects distributions based on lens.

Lens	Right Eye	Left Eye
Clear	57 (93.44%)	57 (93.44%)
Cataract	4 (6.56%)	4 (6.56%)
PCIOL	0 (0%)	0 (0%)

The majority of subjects, 57 (93.44%) in both the right eye and the left eye had clear lens on anterior segment examination. However, a small proportion of subjects, 4 (6.56%) showed posterior subcapsular cataract in both the eyes. All the 4 subjects were in P1 and P2 grade of posterior subcapsular cataract according to LOCS III grading scale, All 4 subjects who were diagnosed with posterior subcapsular cataract were kept under repeated evaluation to look for any progression of cataract.



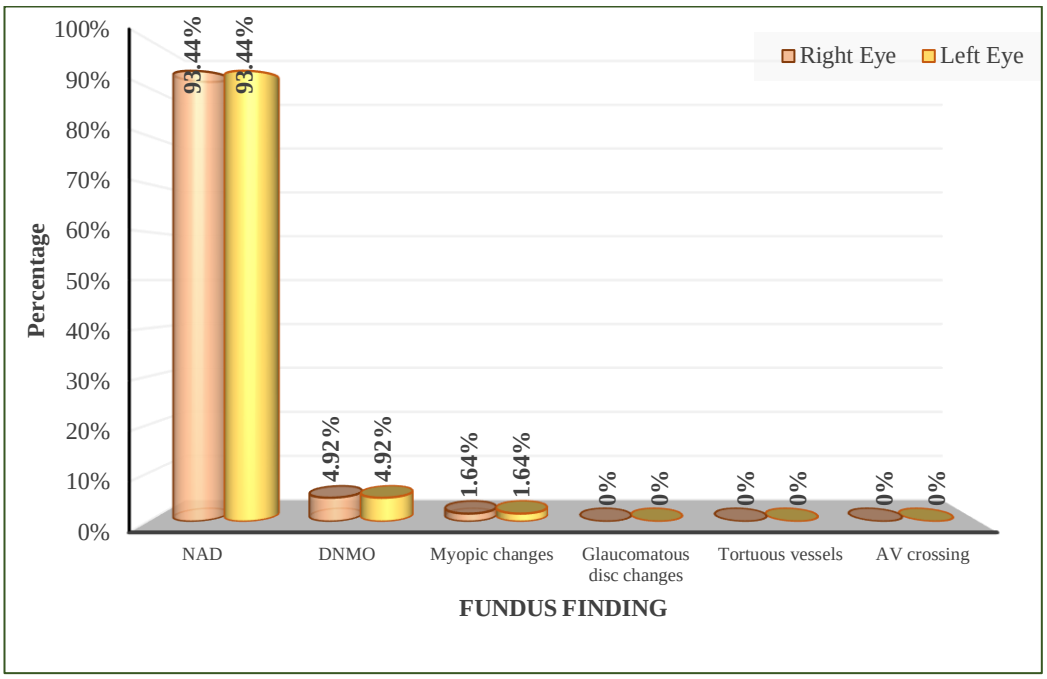
Graph 11 : Subjects distribution based on lens with respect to eye.

Table given below shows the distribution of subjects according to fundus findings.

Table 14: Subjects distributions based on fundus findings.

Fundus finding	Right Eye	Left Eye
NAD	57 (93.44%)	57 (93.44%)
DNMO	3 (4.92%)	3 (4.92%)
Myopic changes	1 (1.64%)	1 (1.64%)
Glaucomatous disc changes	0 (0%)	0 (0%)
Tortuous vessels	0 (0%)	0 (0%)
AV crossing	0 (0%)	0 (0%)

The majority of subjects 57 (94.44%) had no abnormal fundus findings in both eyes. In small percentage of subjects, 3 (4.92%) details of fundus could not be made out due to hazy media caused by cataract in both eyes. Additionally, a single subject (1.64%) had myopic fundus changes in both eyes. No subjects were reported to have glaucomatous disc changes or hypertensive retinopathy changes like tortuous vessels, or arteriovenous crossings in either eye.



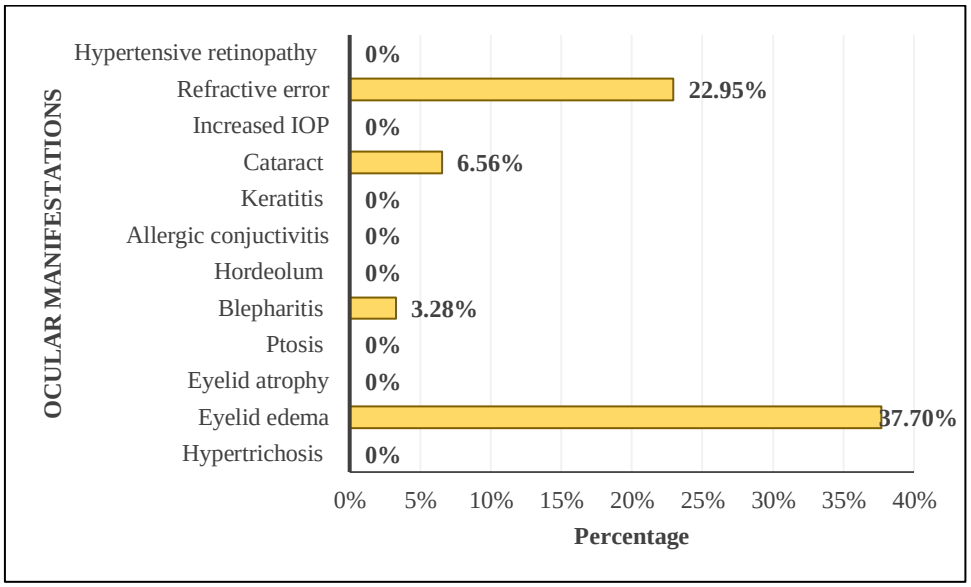
Graph 12 : Subjects distributions based on fundus findings with respect to eye.

The following table gives the distribution of subjects according to type of ocular manifestations among children with nephrotic syndrome.

Table 15: Type of ocular manifestations among children with nephrotic syndrome.

Ocular manifestations	Number of subjects (%)
Hypertrichosis	0 (0%)
Eyelid edema	23 (37.7%)
Eyelid atrophy	0 (0%)
Ptosis	0 (0%)
Blepharitis	2 (3.28%)
Hordeolum	0 (0%)
Allergic conjuctivitis	0 (0%)
Keratitis	0 (0%)
Cataract	4 (6.56%)
Increased IOP	0 (0%)
Refractive error	14 (22.95%)
Hypertensive retinopathy	0 (0%)

Eyelid edema was reported in 23 (37.7%) subjects, blepharitis reported in 2 (3.28%), cataract was reported in 4 (6.56%) subjects and refractive errors were reported in 14 (22.95%) subjects.



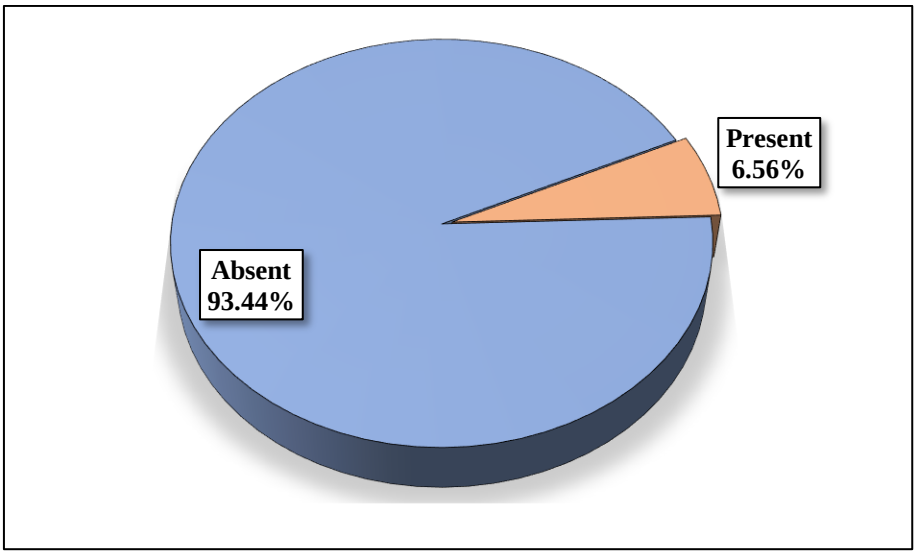
Graph 13 : Subjects distributions based on ocular manifestations in NS

Table given below reflects the distribution of subjects according to steroid dependent and independent ocular manifestations.

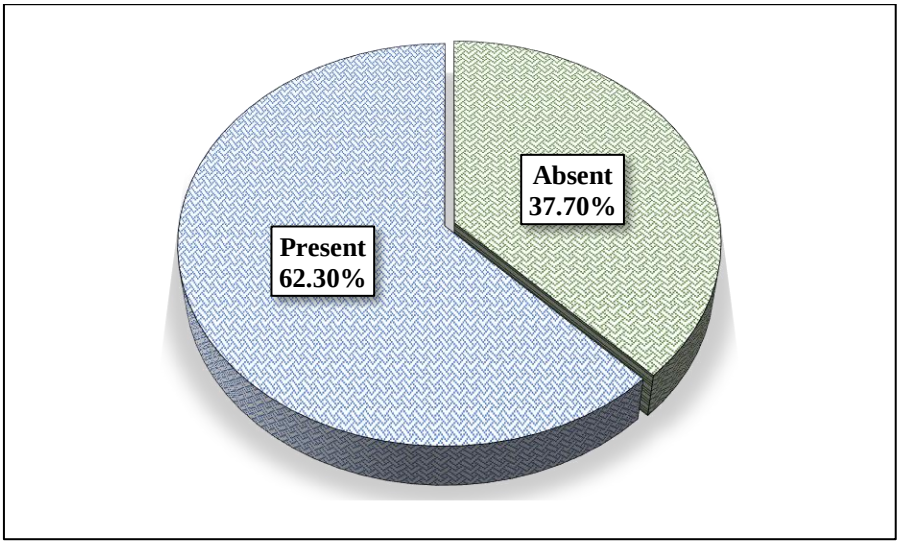
Table 16: Subjects distribution based on ocular manifestations.

Variables	Sub Category	Number of subjects (%)
Steroid dependent ocular manifestation	Absent	57 (93.44%)
	Present	4 (6.56%)
Steroid independent ocular manifestation	Absent	23 (37.7%)
	Present	38 (62.3%)

Out of 61 subjects, steroid dependent ocular manifestations were present in 4 (6.56%) subjects and steroid independent ocular manifestations were present in 38 (62.3%) subjects.



Graph 14 : Distribution of subjects according to Steroid dependent ocular manifestation.



Graph 15 : Distribution of subjects according to steroid independent ocular manifestations.

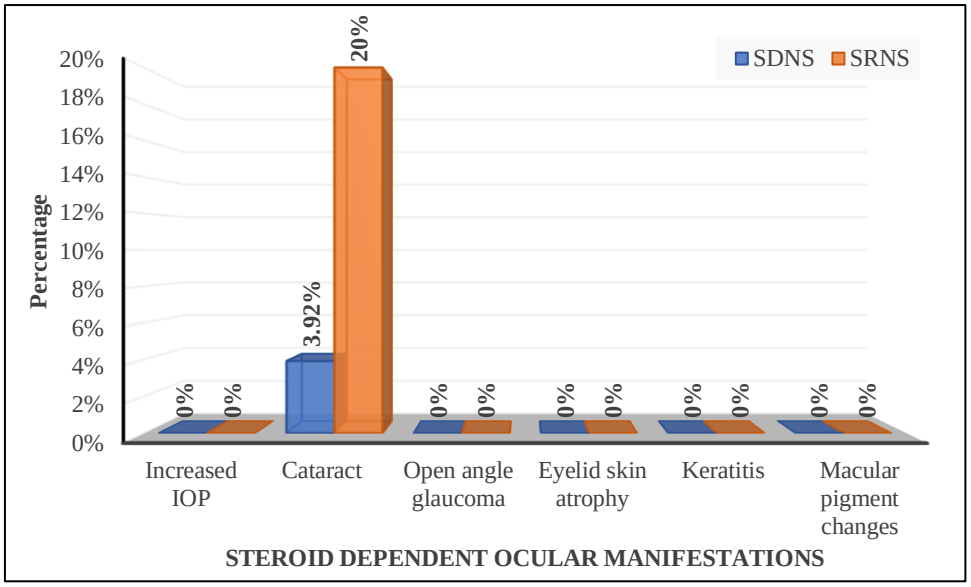
Note: Type of refractive error, Squint, Hypertensive retinopathy and Lid edema are steroid independent ocular manifestations. Glaucomatous disc changes and Cataract are steroid dependent ocular manifestations.

The following table gives the distribution of steroid dependent ocular manifestation according to type of NS.

Table 17: Steroid dependent ocular manifestations according to type of NS.

Steroid dependent ocular manifestations	SDNS Number (%)	SRNS Number (%)	Total Number (%)
Increased IOP	0 (0%)	0 (0%)	0 (0%)
Cataract	2 (3.92%)	2 (20%)	4 (6.56%)
Open angle glaucoma	0 (0%)	0 (0%)	0 (0%)
Eyelid skin atrophy	0 (0%)	0 (0%)	0 (0%)
Keratitis	0 (0%)	0 (0%)	0 (0%)
Macular pigment changes	0 (0%)	0 (0%)	0 (0%)

Cataracts were observed in 2 (3.92%) subjects with SDNS and 2 (20%) subjects with SRNS, totalling 4(6.56%). subjects



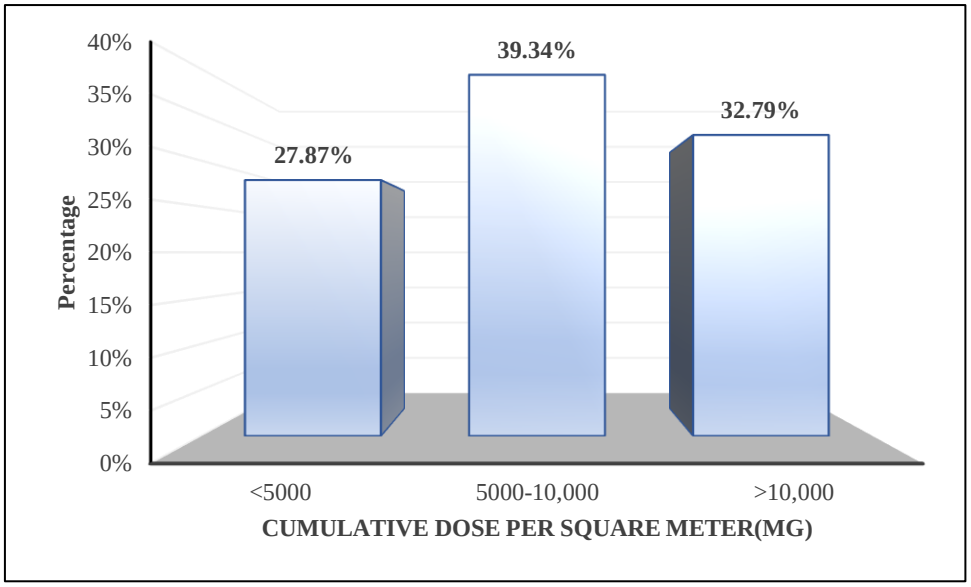
Graph 16 : Distribution of steroid dependent ocular manifestations according to type of NS.

The following table gives the distribution of subjects with cumulative dose of steroid per square meter.

Table 18: Subjects distribution based on cumulative dose of steroid per square meter

Cumulative dose per square meter(mg)	Number of subjects (%)
<5000	17 (27.87%)
5000-10,000	24 (39.34%)
>10,000	20 (32.79%)

Among the subjects, 17 (27.87%) received a cumulative dose of less than 5000 mg per square meter. A larger proportion, comprising 24 (39.34%) subjects were administered cumulative dose ranging between 5000 and 10,000 mg per square meter. A slightly smaller group, consisting of 20 (32.79%) subjects received cumulative doses exceeding 10,000 mg per square meter.



Graph 17 : Distribution of subjects according to cumulative dose per square meter.

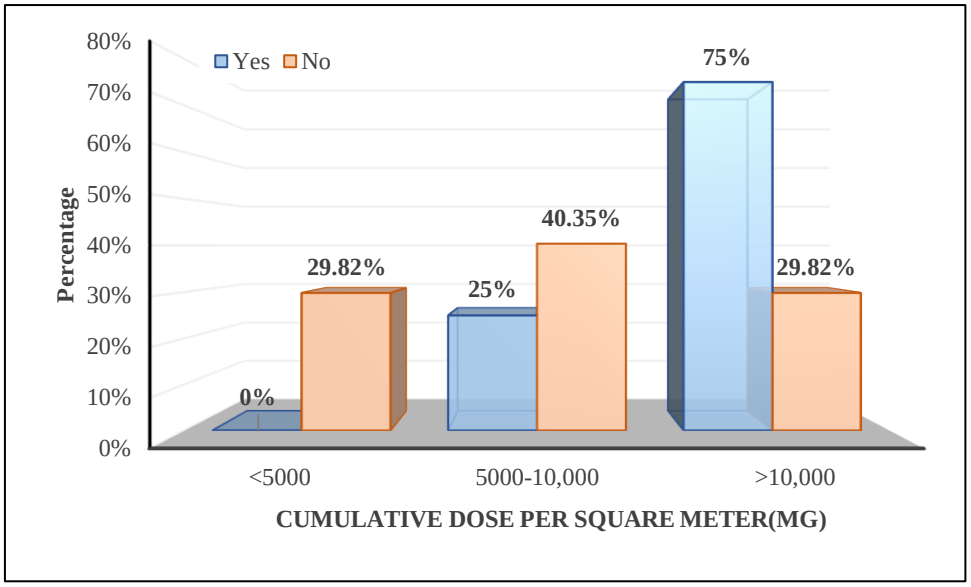
The following table gives the comparison of cumulative dose of steroid per square meter with steroid dependent ocular manifestations in children with NS.

Table 19: Comparison of cumulative dose of steroid per square meter with steroid dependent ocular manifestations in children with NS.

Cumulative dose per square meter(mg)	Steroid dependent ocular manifestations		p-value
	Yes	No	
<5000	0 (0%)	17 (29.82%)	0.1879[MC]
5000-10,000	1 (25%)	23 (40.35%)	
>10,000	3 (75%)	17 (29.82%)	

Abbreviation: MC – Chi square test with Monte Carlo simulation.

From Chi square test, it is noted that, there is no statistical significance in the distribution of cumulative dose of steroid per square meter with steroid dependent ocular manifestations in children with NS.



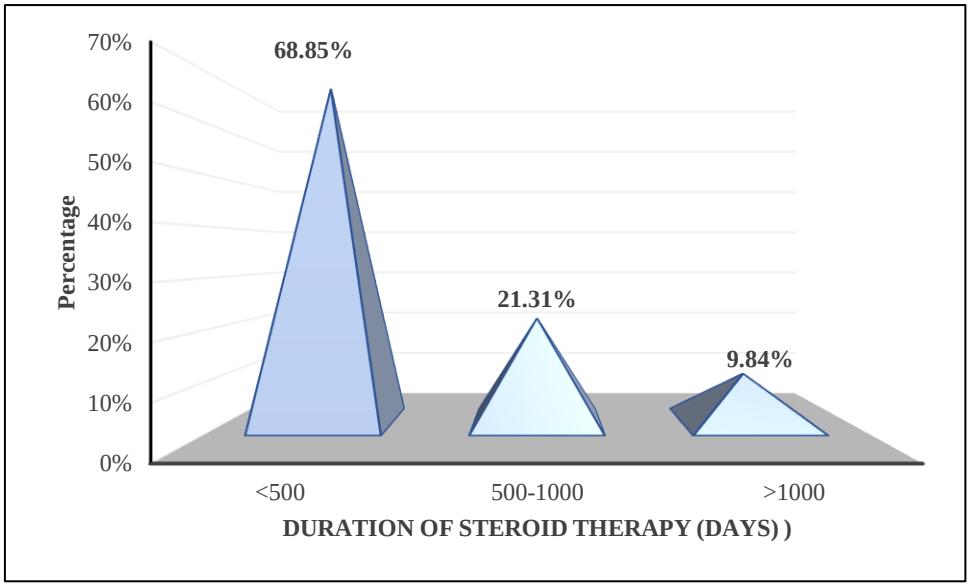
Graph 18 : Distribution of steroid dependent ocular manifestations according to cumulative dose per square meter.

The following table gives the distribution of subjects with duration of steroid therapy.

Table 20 : Subjects distribution based on duration of steroid therapy.

Duration of steroid therapy (days)	Number of subjects (%)
<500	42 (68.85%)
500-1000	13 (21.31%)
>1000	6 (9.84%)
Mean ± SD Median (Min, Max)	429.39 ± 351.61 309 (69, 1460)

A significant portion, comprising 68.85% of the subjects, received steroid therapy for less than 500 days, 21.31% of the subjects were administered steroids for duration falling between 500 and 1000 days and a smaller but notable group, constituting 9.84% of the subjects, endured steroid therapy for over 1000 days. The mean duration of steroid therapy was 429.39 days, with a standard deviation of 351.61 days. The median duration was 309 days, with treatment durations spanning from as short as 69 days to as long as 1460 days.



Graph 19 : Subject distribution based on Duration of steroid therapy.

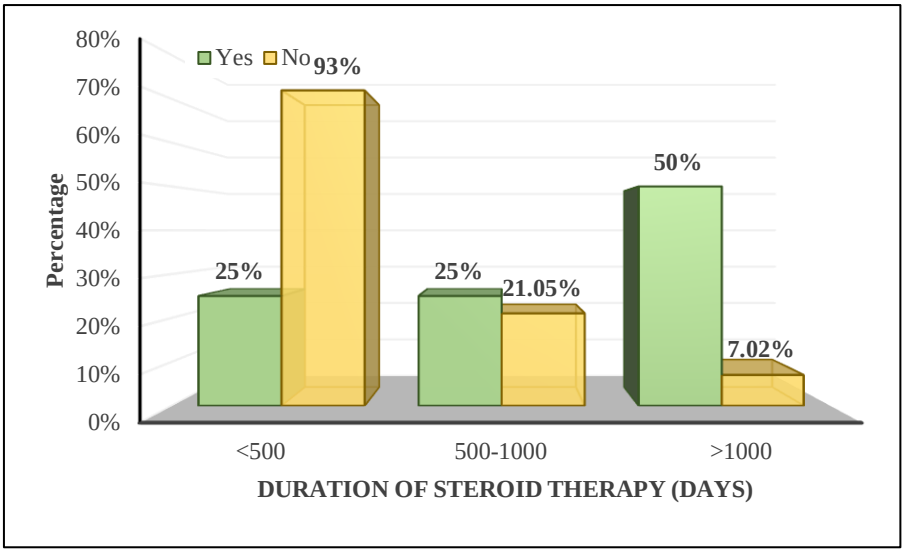
The following table gives the comparison of total duration of steroid therapy with Steroid dependent ocular manifestations in children with NS.

Table 21: Comparison of duration of steroid therapy with Steroid dependent ocular manifestations in children with NS.

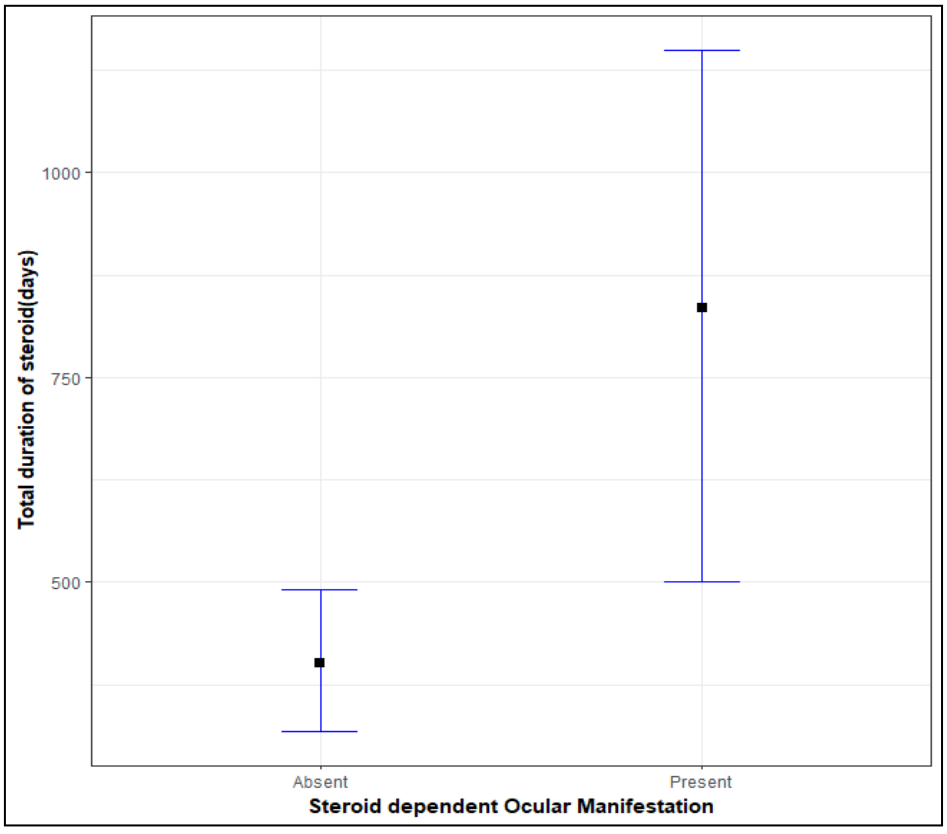
Duration of steroid therapy (days)	Steroid dependent ocular manifestations		p-value
	Yes	No	
<500	1 (25%)	41 (71.93%)	**0.0230^{MC}***
500-1000	1 (25%)	12 (21.05%)	
>1000	2 (50%)	4 (7.02%)	

*Abbreviation: MC – Chi square test with Monte Carlo simulation, * indicates statistical significance.*

From Chi square test, it is observed that, there is significant difference in the distribution of duration of steroid therapy with Steroid dependent ocular manifestations in children with NS.



Graph 20 : Distribution of steroid dependent ocular manifestations with Duration of steroid therapy



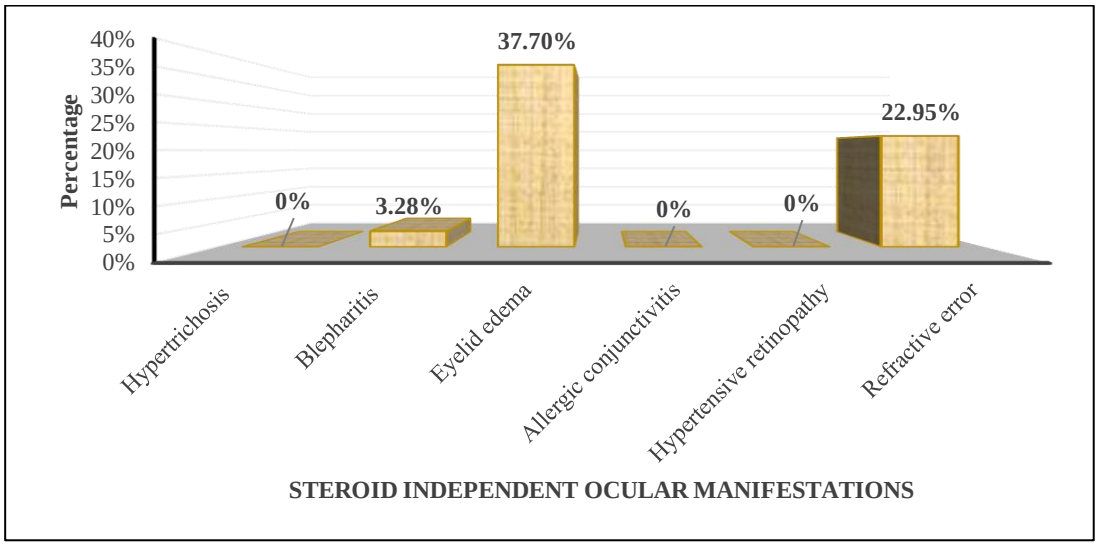
Graph 21 : Mean plot of total duration of steroid over steroid dependent ocular manifestation

The following table gives the distribution of subjects according to steroid independent ocular manifestations.

Table 22 : Subjects distribution based on steroid independent ocular manifestations.

Steroid independent ocular manifestations	Number of subjects (%)
Hypertrichosis	0 (0%)
Blepharitis	2 (3.28%)
Eyelid edema	23 (37.7%)
Allergic conjunctivitis	0 (0%)
Hypertensive retinopathy	0 (0%)
Refractive error	14 (22.95%)

None of the subjects exhibited hypertrichosis or allergic conjunctivitis. However, 2 (3.28%) subjects had blepharitis, while a larger proportion, 23 (37.7%) subjects had eyelid edema. Similarly, hypertensive retinopathy was not observed in any subjects. Refractive error was present in 14 (22.95%) subjects.



Graph 22 : Subject distribution based on steroid independent ocular manifestations.

DISCUSSION

The present study, " Correlation of cumulative dose and duration of steroid therapy with ocular manifestations in children with nephrotic syndrome ” was conducted in a tertiary care teaching hospital in Karnataka from August 2022 to July 2023.

A total of 61 patients were enrolled in the study, between age group of 2 to 18 years. The majority 45.9% children were from 6-10 years of age group. The mean age was 8.27 ± 3.58 years. Nakubulwa et al observed in their study that most cases were from 7-12 years of age group with mean age of 7 years, which is similar to our study.(2) Another study done by Elsharkawy et al also showed mean age of 8 year.(37)

In present study, 39 (63.93%) were males and 22 (36.07%) were females. Toruan Y et al study showed male predominance of 60.9% .(38) In the study done by Gaur et al it was observed that majority of the patients were male(73.2%) which is similar to our study.(39) But Nakubulwa et al observed female predominance in their study.(2)

In our study, 83.61% were patients with steroid dependent nephrotic syndrome (SDNS) and 16.39% patients were with steroid resistant nephrotic syndrome (SRNS). According to Gaur et al 54.9% patients diagnosed with SDNS and 31.7% with SRNS.(39) In contradictory to Toruan Y et al study, which had majority 63% SRNS and 3%SDNS patients.(38) Similarly Gheissari A et al also showed SRNS patients more than SDNS.(40)

In present study, 67.21% patients experienced frequent relapses, while 32.79% patients had infrequent relapses. Nakubulwa et al noticed 1% patient had frequent and 99% patients had infrequent relapses.(2) Kulsoom et al observed 46.1% patients had frequent relapses and 53% patients had infrequent relapses.(41)

In our study, most of the patients had good vision of 6/6 and best corrected vision in patients having cataract was between 6/12-6/24. One patient had high myopia and was having best corrected vision of 6/24. No patient had poor visual acuity more than 6/24. Jezeela K et al observed 50% of the children had 6/6 vision and 44.3% had a visual acuity in the range of 6/9 to 6/12, 4.3% had vision between 6/18-6/24(42)

In our study 22% patients had myopia, among them 9.84% patients had simple myopia and 13.11% patients had astigmatic myopia. Nakubulwa et al showed 56% patients had refractive error and 29% patients had astigmatic myopia.(2) According to Jezeela K et al 20% had myopia with astigmatism and 12.9% were having simple myopia.(42) Most commonly observed refractive error was astigmatic myopia in our study which was similar to other studies.

In our study, majority of the patients (94.44%) had clear lens. 4 patients (6.56%) were having cataract, which was most common finding of steroid dependent ocular manifestations. Kulsoom et al showed 14.9% patients had PSC.(41) Ghessari A et al observed 9.3% PSC in nephrotic syndrome children.(40) Joan SK et al found 10.3% patients had cataract.(43) According to Jezeela et al 82.9% had clear lens and 15.7% had posterior subcapsular cataract in both eyes.(42) Similar to our study, posterior subcapsular cataract was the commonest steroid dependent ocular manifestation according to Ryan, Gheissari and Hayasaka.(40,44,45) A study done by

Brocklebank showed 14% patient developed PSC due to prolonged steroid therapy in nephrotic syndrome children.(46)

In our study, all patients had intraocular pressure (IOP) within normal limit between 10-21 mmHg. Majority of patients had IOP between 14-17 mmHg. No patient had increased IOP >21 mmHg in our study. Jezeela K et al showed 84% of the patients were having IOP in range of 10-14 mmHg which is similar to our study and no patient had increased IOP.(47) which is similar to our study. According to Chaudhury at el 9.8% patients had raised IOP.(48) Gheissari A et al recorded that 5.3% patients were having raised IOP and 1.3% patients had open angle glaucoma.(40)

In our study fundus examination was normal in majority of the cases. Only one patient had myopic fundus changes. Glaucomatous disc changes, hypertensive changes or any macular changes were not found in any patient. Gheissari A et al observed 4% patients had macular pigment changes.(40) In Joan SK et al study 3.2% patient were found with hypertensive retinopathy.(43) A study done by Mun-Wei L et al in Malaysia showed no macular fundus findings in children with nephrotic syndrome.(49)

In our study, in nephrotic syndrome children we reported ocular manifestations like eyelid edema, blepharitis, cataract, myopia. Among these 6.56% patients had steroid dependent ocular manifestation which was subcapsular posterior cataract and 62.3% patients had steroid independent ocular manifestations which were eyelid edema (37.7%), blepharitis(3.2%), myopia(22.95%). In our study cases like hypertrichosis, ptosis, eyelid atrophy, hordeolum, keratitis, allergic conjunctivitis were not found. Hayasaka et al reported other steroid dependent ocular manifestations like elevated IOP, superficial punctate keratitis, conjunctivitis and hordeolum.(45)

Nakubulwa et al also noted ocular findings like hypertrichosis, conjunctivitis, hordeolum, corneal scar in their study.(2) 6.3% ptosis patients were reported in a study done by Elsharkawty.(37)

In present study, 27.87% patient received cumulative dose of less than 5000 mg per square meter from which no one had steroid dependent ocular findings. 39.34% patients received dose ranging between 5000-10,000 mg per square meter, from which one patient had PSC. 32.79% subjects received cumulative doses more than 10,000 mg per square meter from which 3 patient had PSC from which 3 patients had PSC. Total cumulative steroid dose was higher in those with steroid dependent ocular manifestation compared to those without steroid dependent ocular manifestation But there is no statistical significant correlation between cumulative dose of steroid per square meter with Steroid dependent ocular manifestations in children with NS as p-value is 0.18.

Duration of disease was less than 7 years for 90.16% of the patients,7-12 years for 8.2% of patient and more than 12 years for 1.64% patients. There was statistical significant correlation between duration of disease with steroid dependent ocular manifestation in children with NS as p-value is 0.025.

In present study, 68.85% patients have received steroid therapy for less than 500 days. 21.31% patients received corticosteroid treatment between 500 to 1000 days. 9.84% of the subjects, endured steroid therapy for over 1000 days. Patients with steroid dependent ocular findings were increasing with increasing number of days of steroid therapy. The p-value of 0.023 indicates a significant association between duration of steroid therapy and steroid-dependent ocular symptoms in children with NS.

Toruan Y et al found significant correlation between cumulative dose and duration of corticosteroid therapy with steroid dependent ocular manifestation like PSC.(38)

Vijay Agrawal et al study done in Rajasthan remarked significant relation between cumulative dose of steroid with steroid induced cataract.(50)

Kulsoom and Joan found significant association of cumulative dose of steroid with steroid induced cataract in children with nephrotic syndrome (41,43) but they didn't mention about association with duration of steroid therapy.

A study done by chaudhury et al conducted in Bangladesh showed there was no significant association between the duration of steroid therapy and cataract formation, but a significant association between the steroid doses and development of cataract (48) which was contradictory to our study.

Gaur S et al study conducted in Bangalore reported no significant correlation between cumulative dose and duration of corticosteroid therapy with steroid dependent ocular manifestations.(39)

Limitations:

OCT macula to evaluate macular thickness was not done in this study.

CONCLUSION

This study was done to evaluate correlation between cumulative dose and duration of corticosteroid therapy in nephrotic syndrome children with ocular manifestation. We noticed posterior subcapsular cataract was the commonest ocular manifestation due to prolonged steroid therapy in nephrotic syndrome. In this study no patients had raised IOP. This study showed that there was no statistically significant correlation between cumulative dose of steroid therapy with steroid dependent ocular manifestation. There was statistically significant correlation between duration of disease and duration of steroid therapy with steroid dependent ocular manifestation. We concluded that all patients with nephrotic syndrome taking steroid therapy should have regular ophthalmological examination for early detection of these ocular manifestations.

SUMMARY

This study was conducted at Departments of Ophthalmology and Pediatrics Nephrology, KLE'S Dr Prabhakar Kore Hospital and Medical Research Centre, Belagavi during the period of August 2022 to July 2023. Total 61 nephrotic syndrome children between 2-18 years of age group taking corticosteroid therapy were evaluated.

- Majority 45.9% patients were from 6-10 years of age group.
- There were 63.93% males and 36.07% females with M:F ratio of 1.7 : 1.
- 83.61% patients were diagnosed with steroid dependent nephrotic syndrome (SDNS) and 16.39% patients with steroid resistant nephrotic syndrome (SRNS).
- Posterior subcapsular cataract was the most common steroid dependent ocular manifestation observed in nephrotic syndrome children.
- 6.56% patients had posterior subcapsular cataract.
- No patients had increased intra ocular pressure.
- Myopia was the most common steroid independent ocular manifestation observed in nephrotic syndrome.
- 22% patients had myopia.
- There was no statistically significant correlation between cumulative dose of steroid therapy and steroid dependent ocular manifestation.
- There was statistically significant correlation between duration of disease and duration of steroid therapy with steroid dependent ocular manifestation.
- All patients with nephrotic syndrome taking steroid therapy should have regular ophthalmological examination for early detection of these ocular manifestations.

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ANNEXURE –I - INFORMED CONSENT

TITLE OF THE STUDY: CORRELATION OF CUMULATIVE DOSE AND DURATION OF STEROID THERAPY WITH OCULAR MANIFESTATIONS IN CHILDREN WITH NEPHROTIC SYNDROME: A ONE-YEAR CROSS SECTIONAL STUDY

Objective: To determine correlation of cumulative dose and duration of steroid therapy with ocular manifestations in children with nephrotic syndrome.

Introduction: Your child is being invited to participate in this study to determine correlation of cumulative dose and duration of steroid therapy in nephrotic syndrome.

Explanation of procedure: If, you agree for your child to be part of the research study, you will be asked the relevant history and your child/ward 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 your child will participate in this study or continue participation once enrolled. In case you decide to withdraw your child's participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study: your child will not 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 your child. 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 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 for my child to participate in the study "**CORRELATION OF CUMULATIVE DOSE AND DURATION OF STEROID THERAPY WITH OCULAR MANIFESTATIONS IN CHILDREN WITH NEPHROTIC SYNDROME: A ONE-YEAR CROSS SECTIONAL STUDY**" My signature below indicates that I have decided for my child 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.

Signature or left thumb impression of the authorized representative/ parent:

Name of the authorized representative/ parent:

Relation to the subject:

Signature or left thumb impression of the witness:

Name of the witness:

Signature of the investigator

Name of the investigator:

Date:

Place:

ANNEXURE – II - PROFORMA

GENERAL INFORMATION

PATIENT ID NUMBER:

NAME:

_____

AGE: _____ GENDER: F/M CONTACT NUMBER: _____

ADDRESS: _____

_____

_____

Has informed consent been given? YES/NO

Informant – self , parents

CHIEF COMPLAINTS: -

Onset of disease:

Treatment details:

Year of starting steroids:

History of hypertension:

Additional drugs:

HISTORY OF PRESENTING ILLNESS

Diminution of vision:

Duration: RE: _____ days/months/years

LE: _____ days/months/years

Diplopia: Present/Absent

Coloured halos: Present/Absent

Headache : Present /absent

Swelling of the eyelids : Present / absent

Allergic diseases of eye : Present / absent

Spectacle use: Present/absent

Last refraction done: _____ days/months/years back

PAST HISTORY

Ocular surgery: Yes/No

Type of Surgery: _____

Ocular trauma: Yes/No

GENERAL PHYSICAL EXAMINATION

General appearance: Well-built/Moderately built/Poorly built/Emaciated

Pallor:Present/Absent If present: Mild/Moderate/Severe

Height: _____cm Weight: _____kg BMI_____

Pulse: _____ beats/minute BP: _____ mmHg

Temperature: _____ ^{o}F Respiratory Rate: _____/minute

SYSTEMIC EXAMINATION:

CVS: Normal/Abnormal

Specify: _____

RS: Normal/Abnormal

Specify: _____

CNS: Normal/Abnormal

Specify: _____

Per abdomen: Normal/Abnormal

Specify: _____

Head posture: Erect/Tilted

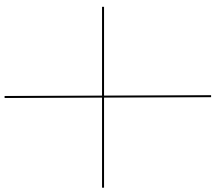
Visual axis: Parallel/Deviated

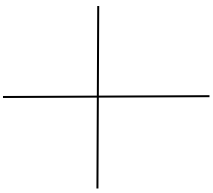
Hirschberg corneal reflection test –

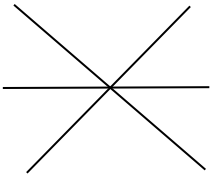
Cover uncover test –

Facial symmetry: Symmetrical/Asymmetrical

Extra-ocular movements: Normal/Restricted/Partially restricted

RE: 

LE: 

Binocular: 

VISUAL ACUITY:

	OD	OS
DISTANT		
NEAR		
PINHOLE		
AIDED		

RETINOSCOPY:

SUBJECTIVE CORRECTION:

	RE	SPH	CYL	AXIS	SPH	CYL	AXIS	LE
DIST.VN								

ANTERIOR SEGMENT EXAMINATION:

	OD	OS
LIDS		
CONJUNCTIVA		
CORNEA		
ANTERIOR CHAMBER		
IRIS		
PUPIL		
LENS		

FUNDUS FINDINGS:

	OD	OS
GLOW		
MEDIA		
DISC		
C:D RATIO		
BLOOD VESSELS		
BACKGROUND		
MACULA		

IOP- RE- mmhg

LE- mmhg

Provisional diagnosis:-

RE-

LE-

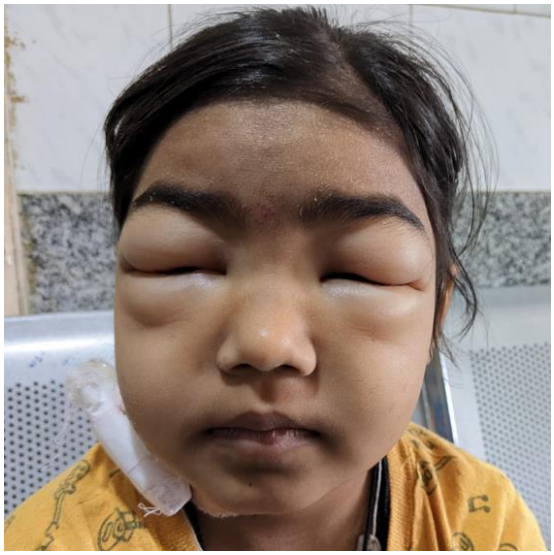
NAME OF INVESTIGATOR:

SIGNATURE:_____

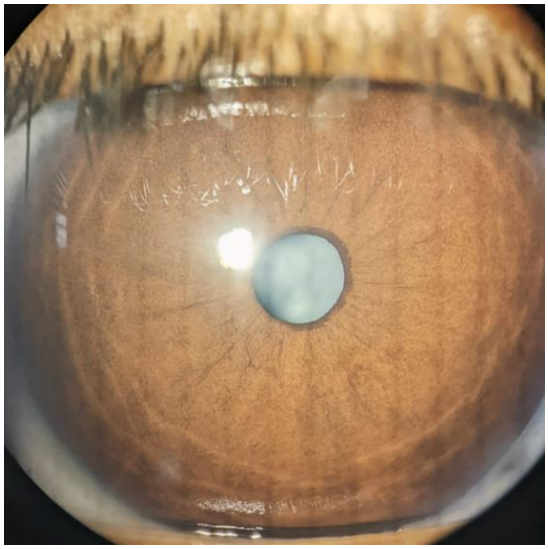
NAME OF GUIDE:

SIGNATURE:_____

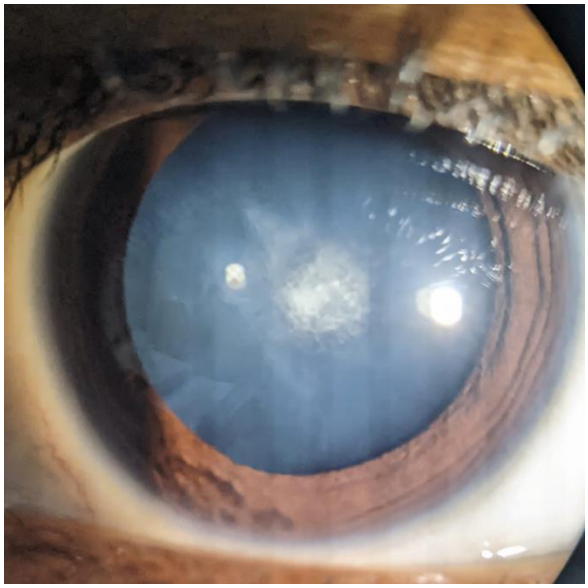
ANNEXURE III : PHOTOGRAPHS

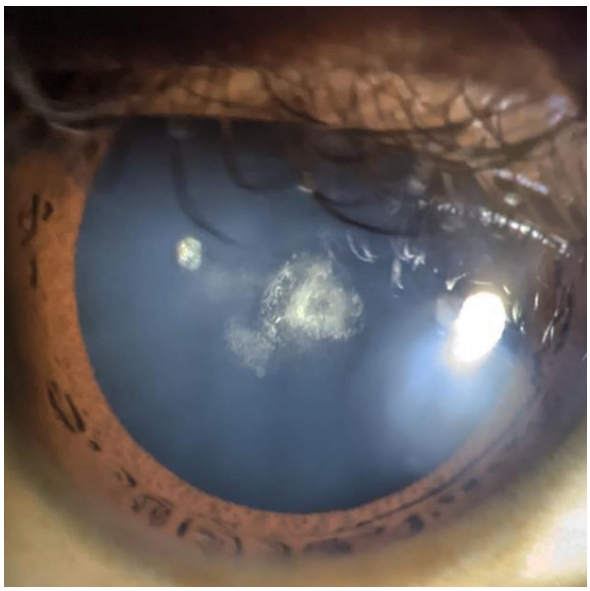


Periorbital edema in Nephrotic syndrome

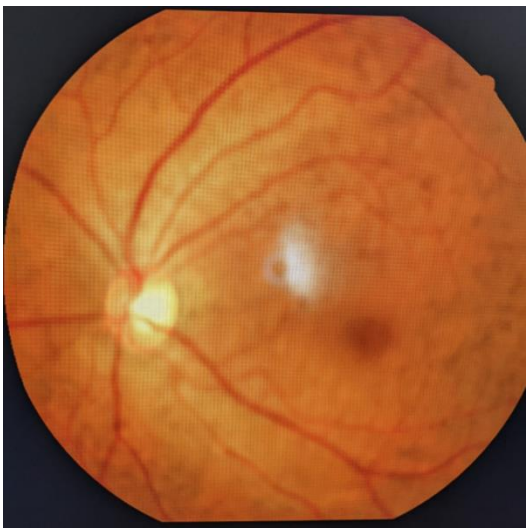


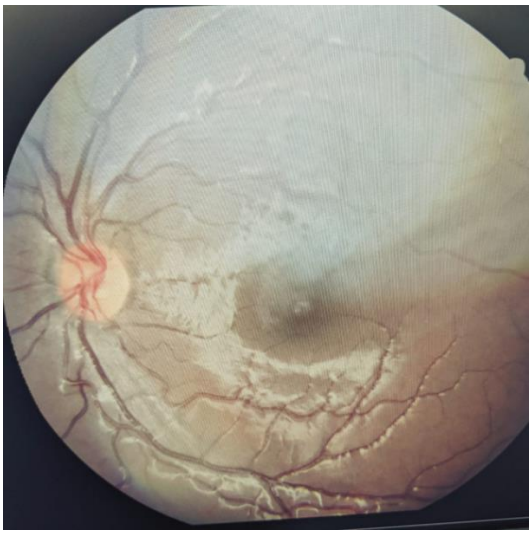
Posterior subcapsular cataract





Posterior subcapsular cataract under slit lamp examination





Normal fundus pictures in nephrotic syndrome children

ANNEXURE IV: KEY TO MASTER CHART

Age- Y-years M-months

Male-M

Female-F

Body Mass Index-BMI

Body surface area-BSA

Steroid Resistance Nephrotic Syndrome-SRNS

Steroid Dependant Nephrotic Syndrome-SDNS

Relapse - F-Frequent, IF-Infrequent

Diminution Of Vision-DOV

Visual Acuity-Va

Right Eye-RE

Left Eye-LE

Intra Ocular Pressure-IOP

Posterior Subcapsular Cataract-PSC

ANNEXURE V :MASTERCHART

SR no.	Age	Gender	Socioeconomic status	BSA(kg/m2)	Mean BMI	Type of NS	Relapse	HTN	Duration of desease	Total duration of steroid(days)	Total cumulative steroid	Cumulative dose per square meter(mg)	Va		Sub. Correction	RE Anterior segment			LE anterior segment			RE Fundus				LE Fundus				IOP(mmHg)		Diagnosis		Type of refractive error	Cat aract
													RE	LE		LIDS	LENS		LIDS	LENS		Media	Disc c/d	b/g	Macula	Media	Disc c/	b/g	macula	RE	LE	RE	LE		
1	9y	M	Urban	0.87	20.6	SRNS	F	P	4Y	443	21,545	24,764	6/12	6/12	-2.00X180	edema	Clear		edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	19.6	20.1	Myopia	Myopia		A
2	6y	F	Rural	0.69	16.02	SDNS	IF	A	2Y	150	1550	2,246	6/9	6/9	-0.50X180	edema	Clear		edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	14.2	17.2	Myopia	Myopia	myopia	A
3	11y	M	Rural	0.98	15.3	SDNS	F	P	1Y	127	5200	5,306	6/6	6/6	A	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	13.8	11.8	N	N	NA	A
4	6y	M	Urban	0.59	16.5	SDNS	IF	A	5Y	309	4007	6,792	6/6	6/6	A	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	14.8	17.7	N	N	NA	A
5	7y	M	Urban	0.85	17.4	SDNS	F	P	3 Y	111	2910	3,424	6/6	6/6	A	blepharitis	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	16.5	18.2	N	N	NA	A
6	12Y	F	Urban	0.96	24.7	SDNS	IF	P	9M	124	1840	1,917	6/9	6/9	-0.50X180	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	14.1	17.9	Myopia	Myopia	Myopia	A
7	11Y	M	Rural	0.72	16.02	SDNS	F	P	9Y	1169	15557	21,607	6/12	6/12	NA	N	Greyish		N	Greyish		Hazy	DNMO	DNMO	Hazy	DNMO	DNMO	DNMO	DNMO	15.5	16.2	PSC	PSC	NA	P
8	8Y	M	Rural	0.67	12.8	SRNS	F	P	3Y 3M	235	3985	5,948	6/24	6/24	-7.0/-2.0 X 20	N	Greyish		N	Greyish		Hazy	oval,PPA	Tes.	FR+	Hazy	Oval,PI	Tes.	FR+	19.4	17.7	PSC	PSC	High myo	P
9	17y	F	Urban	0.91	17.3	SDNS	F	P	11Y	565	16810	18,473	6/9	6/9	-0.50X50	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	14.2	12.1	Myopia	Myopia	Myopia	A
10	3y	M	Rural	0.55	13.8	SDNS	IF	P	1Y	138	1585	2,882	6/6	6/6	A	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	14.2	13.2	N	N	NA	A
11	13Y	M	Rural	1.34	18.6	SDNS	F	P	6M	94	3270	2,440	6/6	6/6	A	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	15.5	15.3	N	N	NA	A
12	9Y	M	Urban	0.88	21.4	SDNS	IF	P	6Y	520	15900	18,068	6/6	6/6	A	edema	Clear		edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	14.4	16.5	Lid edema	Lid edema	NA	A
13	14Y	M	Urban	0.95	18.7	SDNS	F	P	6Y	1064	17570	18,495	6/6	6/6	A	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	16.7	15	N	N	NA	A
14	4Y	M	Urban	1.61	17.5	SDNS	IF	P	1Y	145	2230	1,385	6/6	6/6	A	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	15.6	14.2	N	N	NA	A
15	3Y	M	Urban	0.53	15.4	SDNS	F	P	5M	77	965	1,821	6/6	6/6	A	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	11.6	13.6	N	N	NA	A
16	5Y	M	Urban	0.72	16.3	SDNS	F	P	5M	70	1750	2,431	6/6	6/6	A	blepharitis	Clear		blepharitis	Clear		clear	N	N	FR+	Clear	N	N	FR+	15.6	18.9	N	N	NA	A
17	2.5y	M	Rural	0.42	17.7	SDNS	F	A	8M	215	3980	9,476	6/6	6/6	A	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	15.1	14.2	N	N	NA	A
18	5Y	M	Urban	0.64	14.4	SDNS	F	P	6M	69	1160	1,813	6/6	6/6	A	edema	Clear		edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	16.2	14.4	N	N	NA	A
19	10Y	M	Urban	1	18.3	SDNS	IF	P	5Y	880	11155	11,155	6/6	6/6	A	edema	Clear		edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	15.4	12.1	N	N	NA	A
20	12Y	M	Rural	0.9	15.6	SDNS	F	P	2Y	500	8253	9,170	6/6	6/6	A	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	14.2	12.5	N	N	NA	A
21	8y	F	Urban	0.65	13.6	SDNS	IF	P	4Y	508	6307	9,703	6/6	6/6	A	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	10.9	14.5	N	N	NA	A
22	8y	M	Urban	0.39	15.4	SDNS	F	P	4Y	237	2343	6,008	6/6	6/6	A	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	14.4	14.2	N	N	NA	A
23	5y	F	Rural	0.66	18.8	SDNS	F	P	5Y	204	2460	3,727	6/6	6/6	A	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	12.5	19.1	N	N	NA	A
24	5y	F	Urban	0.64	14.1	SDNS	F	P	5Y	276	4620	7,219	6/6	6/6	A	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	15.3	16.5	N	N	NA	A
25	6y	M	Urban	0.62	14.2	SDNS	F	P	6Y	810	11362	18,326	6/18	6/18	-0.25/-0.50 X 160	N	Greyish		N	Greyish		Hazy	DNMO	DNMO	DNMO	Hazy	DNMO	DNMO	DNMO	16.2	15.2	PSC	PSC	Myopia	P
26	9y	M	Rural	1	20.8	SRNS	F	P	5Y	623	6852	6,852	6/6	6/6	NA	N	Edema		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	14.2	13.1	N	N	NA	A
27	11Y	M	Urban	1.06	14.7	SDNS	F	P	1Y	165	5850	5,519	6/6	6/6	NA	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	15.3	12.2	N	N	NA	A
28	11y	M	Rural	0.89	14.7	SDNS	F	P	5Y	85	2820	3,169	6/6	6/6	NA	N	Edema		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	12.1	14.3	N	N	NA	A
29	16y	F	Urban	0.94	20.1	SDNS	F	P	15Y	1361	20282	21,577	6/6	6/6	NA	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	12.6	10.5	N	N	NA	A
30	11Y	M	Urban	0.98	14.05	SDNS	F	P	1Y	285	10650	10,867	6/24	6/24	-0.50/-1.00X80	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	18.5	19.5	Myopia	Myopia	Myopia	A
31	9Y	F	Urban	0.89	18.5	SDNS	F	P	4Y	417	5462	6,137	6/6	6/6	NA	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	14.7	17.3	N	N	NA	A
32	5Y	F	Rural	0.77	18.4	SDNS	IF	P	3Y	449	5600	7,273	6/6	6/6	NA	Edema	Clear		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	12.9	9.3	N	N	NA	A
33	11Y	F	Urban	0.98	16.2	SDNS	IF	P	6M	80	4500	4,592	6/6	6/6	NA	Edema	Clear		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	14.2	12.1	N	N	NA	A
34	3Y	F	Urban	0.58	17.6	SDNS	IF	P	8M	135	2850	4,914	6/6	6/6	NA	Edema	Clear		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	16.8	18.3	N	N	NA	A
35	5Y	F	Urban	0.52	19.6	SRNS	F	P	4Y	825	5787	11,129	6/6	6/6	NA	Edema	Clear		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	12.2	15.2	N	N	NA	A
36	10Y	M	Rural	0.89	14.5	SDNS	F	P	7Y	1229	16375	18,399	6/6	6/6	NA	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	15.7	16.2	N	N	NA	A
37	3Y	F	Urban	0.42	14.8	SRNS	IF	P	2Y	335	2871	6,836	6/6	6/6	NA	Edema	Clear		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	14.1	12.3	N	N	NA	A
38	5Y	M	Urban	0.64	17.7	SDNS	IF	P	2Y	410	5000	7,813	6/6	6/6	NA	Edema	Clear		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	11.8	12.2	N	N	NA	A
39	8Y	F	Urban	0.65	16.6	SRNS	IF	P	4Y	850	18750	28,846	6/6	6/6	NA	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	12.2	14.5	N	N	NA	A
40	8Y	F	Rural	0.87	16.8	SDNS	IF	P	4Y	662	10815	12,431	6/6	6/6	NA	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	17.3	18.4	N	N	NA	A
41	6Y	F	Rural	0.64	15	SDNS	IF	P	7M	217	6188	9,669	6/6	6/6	NA	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	18.4	18.2	N	N	NA	A
42	16Y	M	Rural	0.81	13.8	SRNS	F	P	8Y	1126	20300	25,062	6/18	6/18	-0.25/-0.50 X 60	Edema	Greyish		Edema	Greyish		Hazy	DNMO	DNMO	DNMO	Hazy	DNMO	DNMO	DNMO	18.3	17.1	PSC	PSC	Myopia	P
43	13Y	M	Urban	0.95	16.6	SDNS	F	P	7Y	770	15225	16,026	6/9	6/12	-0.50/-1.00X180	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	14.1	15.2	Myopia	Myopia	Myopia	A
44	6Y	M	Urban	0.84	14.5	SDNS	IF	A	2Y	220	4557	5,425	6/12	6/12	-0.25/-0.50 X 180	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	13.2	15.3	N	N	NA	A
45	7Y	F	Rural	0.92	17.5	SDNS	IF	P	3Y	380	53697	58,366	6/6	6/6	NA	Edema	Clear		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	13.1	14.2	N	N	NA	A
46	9Y	F	Urban	0.88	13.2	SDNS	IF	A	9Y	95	2850	3,239	6/6	6/6	NA	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	17.6	16.2	N	N	NA	A
47	10Y	F	Urban	0.79	15.9	SDNS	F	P	4Y	480	6060	7,671	6/9	6/9	-0.25 X 180	Edema	Clear		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	12.1	11.5	Myopia	Myopia	Myopia	A
48	8Y	F	Rural	0.92	14.8	SDNS	F	P	5Y	823	13360	14,522	6/6	6/6	NA	Edema	Clear		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	16.2	15.1	N	N	NA	A
49	8Y	M	Rural	0.81	18.1	SDNS	F	P	3Y	488	8995	11,105	6/9	6/9	-O.25 X 180	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	11.2	13.4	Myopia	Myopia	Myopia	A
50	4Y	M	Urban	0.55	13.2	SDNS	F	P	1Y	373	4235	7,700	6/6	6/6	NA	Edema	Clear		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	16.3	15.1	N	N	NA	A
51	4y	F	Rural	0.55	13.2	SDNS	IF	P	1Y 2M	207	3773	6,860	6/6	6/6	NA	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	15.2	17.1	N	N	NA	A
52	6Y	M	Rural	0.84	16.2	SRNS	IF	P	2Y	490	8885	10,577	6/6	6/6	NA	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	18.1	16.4	N	N	NA	A
53	6y	F	Urban	0.94	18.05	SDNS	F	P	2Y	330	6980	7,426	6/12	6/12	-0.25/-0.50 X 180	Edema	Clear		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	15.6	16.8	Myopia	Myopia	Myopia	A
54	8Y	M	Urban	0.93	18.05	SRNS	F	P	5Y	623	6852	7,368	6/6	6/6	NA	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	17	15.3	N	N	NA	A
55	4Y	M	Urban	0.6	14.9	SRNS	F	P	6M	107	2730	4,550	6/6	6/6	NA	Edema	Clear		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	13.1	14.5	N	N	NA	A
56	12Y	M	Urban	0.94	14.7	SDNS	F	P	1Y	172	6030	6,415	6/6	6/6	NA	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	16.3	14.1	N	N	NA	A
57	7Y	M	Urban	0.67	12.3	SDNS	IF	P	4Y	307	3043	4,542	6/6	6/6	NA	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	12.3	15.2	N	N	NA	A
58	10Y	M	Rural	0.95	14.3	SDNS	F	P	1Y	202	7230	7,611	6/6	6/6	NA	Edema	Clear		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	18.8	19.2	N	N	NA	A
59	12y	M	Rural	1.33	27.1	SDNS	F	P	1Y	187	6930	5,211	6/9	6/9	-0.25/-0.25 X 70	Edema	Clear		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	15.3	17.2	Myopia	Myopia	Myopia	A
60	15Y	M	Urban	1.35	25.2	SDNS	F	P	1Y 3M	185	6500	4,815	6/6	6/6	NA	N	Clear		N	Clear		clear	N	N	FR+	Clear	N	N	FR+	17.6	14.2	N	N	NA	A
61	9Y	M	Rural	0.8	14.3	SDNS	F	P	7Y	1460	16890	21,113	6/6	6/6	NA	Edema	Clear		Edema	Clear		clear	N	N	FR+	Clear	N	N	FR+	16.5	17.3	N	N	NA	A