CLINICAL PROFILE AND OUTCOME OF GLOMERULAR DISEASES IN CHILDREN ADMITTED IN A SEMIURBAN MEDICAL COLLEGE HOSPITAL

Dissertation submitted to

THE TAMIL NADU DR. M.G.R.MEDICAL UNIVERSITY

In partial fulfillment of the regulations
for the award of degree of

M.D. DEGREE (PEDIATRICS) BRANCH VII

CHENGALPATTU MEDICAL COLLEGE
CHENGALPATTU

APRIL 2015

CERTIFICATE

This is to certify that the dissertation titled, "**CLINICAL PROFILE AND OUTCOME Of GLOMERULAR DISEASES IN CHILDREN ADMITTED IN A SEMIURBAN MEDICAL COLLEGE HOSPITAL"** submitted by **Dr.D. SREENANDINI** 2012-2015 session to the Faculty of Pediatrics, The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirements for the award of M.D. Degree (Pediatrics) is a bonafide research work carried out by her under our direct supervision and guidance.

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DECLARATION

I, **Dr. D. SREENANDINI** solemnly declare that the dissertation titled **"CLINICAL PROFILE AND OUTCOME OF GLOMERULAR DISEASES IN CHILDREN ADMITTED IN A SEMIURBAN MEDICAL COLLEGE HOSPITAL"** has been prepared by me.

This is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulations for the M.D. Degree Examination in Pediatrics.

Place: Chengalpattu **Dr .D. SREE NANDINI**
Date :

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I sincerely thank all the children and their parents who have submitted themselves for this study.

Dr .D. SREE NANDINI

INSTITUTIONAL ETHICS COMMITTEE

CHENGALPATTU MEDICAL COLLEGE , CHENGALPATTU

APPROVAL OF ETHICAL COMMITTEE

To

Dr.D.Sree Nandini
Post Graduate
Dept of Pediatrics

Dear Dr.

The Institutional Ethical Committee of Chengalpattu Medical College reviewed and discussed your application to conduct the clinical / dissertation work entitled

CLINICAL PROFILE AND OUTCOME OF ALL CHILDREN WITH GLOMERULAR DISEASES IN A URBAN MEDICAL COLLEGE HOSPITAL

On 13.11.2013

The following documents reviewed

a. Trial protocol, dated _____version no
b. Patient information sheet and informed consent form in English and / or vernacular language.
c. Investigators Brochure, dated _____version
d. Principal Investigators current CV
e. Investigators undertaking

The following members of the Ethics committee were present at the meeting held on

Date 13.11.2013 Time 12.00 Noon Place Chengalpattu Medical College

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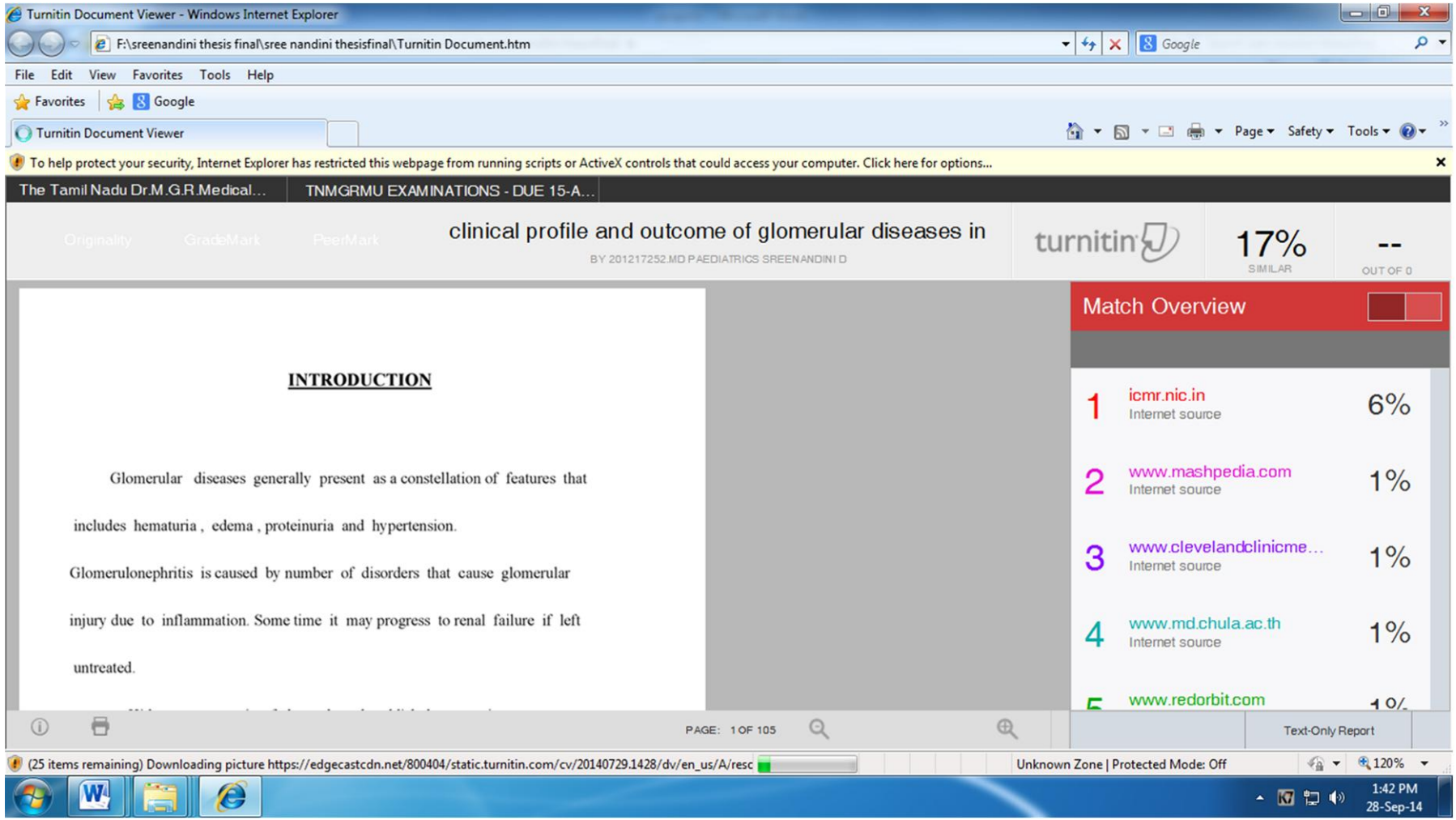
We approve the clinical trial to be conducted in its presented form

The Institutional Ethics Committee expects to be informed about the progress of the study and any SAE occurring in the course of the study, any changes in protocol and patient information / informed consent and asks to provide copy of final report.

Yours sincerely

13/11/13

Member secretary, Ethics Committee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INTRODUCTION
Glomerular diseases generally present as a constellation of features that includes hematuria , edema , proteinuria and hypertension.
Glomerulonephritis is caused by number of disorders that cause glomerular injury due to inflammation. Some time it may progress to renal failure if left untreated.
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CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF FIGURES

ABBREVIATIONS

APIGN	-	Acute post infectious glomerular nephritis
GFR	-	Glomerular filtration rate
ASO	-	Anti strepto lysin
GBM	-	Glomerular basement membrane
AS	-	Alport syndrome
ESRD	-	End stage renal disease
CKD	-	Chronic kidney disease
HSP	-	Henoch scholein purpura
RFT	-	Renal function test
CRP	-	C-Reactive protein
ESR	-	Erythrocyte sedimentation rate
URI	-	Upper respiratory tract infection
UTI	-	Urinary tract infection
RBC	-	Red blood cells
ANA	-	Anti nuclear antibody
LDH	-	Lactate dehydrogenase
SLE	-	Systemic lupus erythematosis
LM	-	Light microscopy

EM	-	Electron microscopy
GN	-	Glomerular Nephritis
NS	-	Nephrotic syndrome
ISKDC	-	Nternational study kidney disease in children
HIV	-	Human immunodeficiency virus
AIDS	-	Aquired immuno deficiency syndrome
NSAID	-	Non steroidal anti inflammatory drug
FSGS	-	Focal segmental glomerulosclerosis
SSNS	-	Steroid sensitive nephrotic syndrome
SRNS	-	Steroid resistant nephrotic syndrome
MCD	-	Minimal change disease
HLA	-	Human leukocyte antigen
MPGN	-	Membrano proliferative glomerular nephritis
MCNS	-	Minimal change nephrotic syndrome
SDNS	-	Steroid dependant nephrotic syndrome
MMF	-	Mycophenolate mofetil
IVIG	-	Intra venous immunoglobulin
PCR	-	Protein creatinine ratio
LFT	-	Liver function test
HTN	-	Hyper tension

RPGN	-	Rapidly progressive glomerular nephritis
ELISA	-	Enzyme linked immunosorbent assay
RIA	-	Radio immuno assay
HUS	-	Hemolytic uremic syndrome

INTRODUCTION

Glomerular diseases generally present as a constellation of features that includes hematuria, edema , proteinuria and hypertension. Glomerulonephritis is caused by number of disorders that cause glomerular injury due to inflammation. Some time it may progress to renal failure if left untreated.

Kidneys are a pair of bean shaped reddish brown urinary excretory organ located by each side of vertebral column T12 – L3 of about 11cm X 6cm X 2.5cm , weighing 120 – 175g each. Each kidney has cortex and medulla. Renal cortex consists of glomerulus, proximal and distal tubules. Renalmedulla consists of the descending and ascending limb of loop of Henle and the collecting ducts.

Each kidney has a million of Nephrons – the functional unit of kidney, consists of 2 parts. 1) Renal Corpuscle -which has glomerulus and Bowman's capsule 2) Renal Tubules Kidney cannot regenerate a new nephron[1].

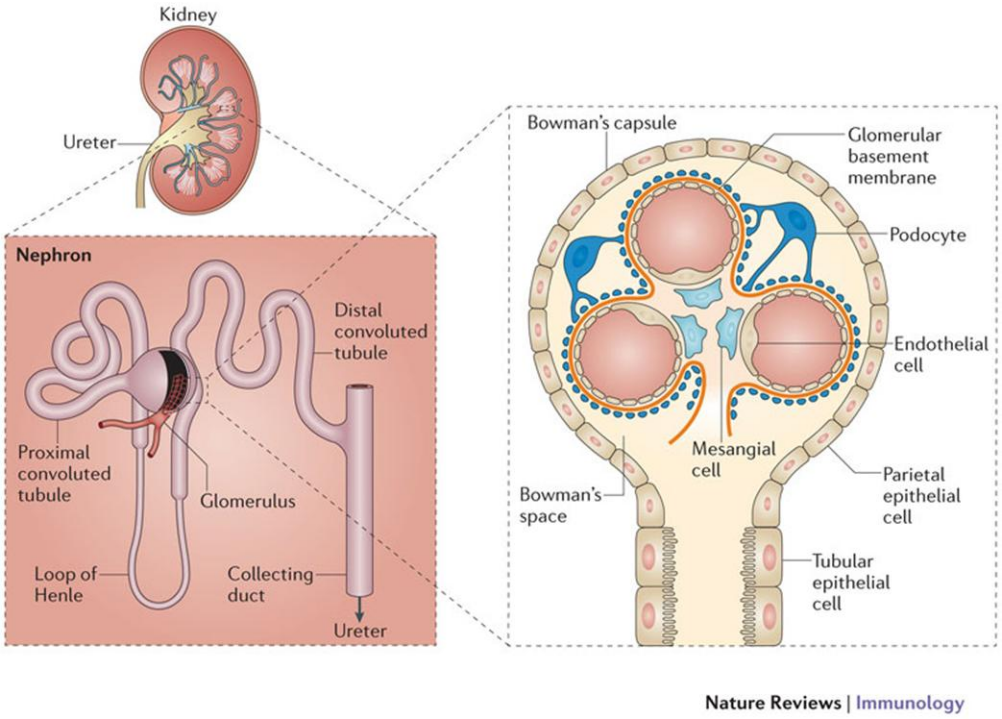
Glomerulus - a greek word means filter. Glomerulus is made up of tuft of capillaries and mesangium. The capillary arises from the afferent arteriole, the last division of renal artery and they join to form efferent arteriole.

There are four glomerular cell types – Endothelial cells, podocytes or visceral epithelial cells, parietal epithelial cells and basement membrane Basement membrane is made up of type IV collagen, Laminin , heparin sulfate and proteoglycan. Podocytes in bowman's capsule wrap the capillaries of glomerulus[2].

Bowman capsule filter blood, holding the larger molecular proteins and passing through small molecules such as water, waste products and sugar through slit diaphragm , which is made up of Nephrin,CD2AP , calyxin and P-cadherin proteins. Glomerular diseases is generally caused by genetic , immune mediated, hemodynamic , metabolic and coagulation disorders.

Genetic causes are due to the mutation in the exons of DNA encoding proteins of glomerulus, resulting in congenital glomerular diseases. Immune mediated diseases is due to deposition of circulatory antigen and antibody immune complex. This mechanism is the most common cause for glomerular injury in children.

Figure 1. Nephron



AIM OF THE STUDY

- To study the clinical profile and glomerular diseases in children admitted.
- To study the outcome of glomerular diseases in children admitted.
- To study the treatment response of glomerular diseases in children admitted.

REVIEW OF LITERATURE

An inflammation of the glomeruli, bundles of tiny vessels inside the kidney results in glomerular pathology . Glomerular injury may be caused by various insults including hemodynamic, infection, immunity, hereditary, toxicity and metabolic diseases. The waste products and excess water from the blood could not be filtered by damaged glomerulus. Hence the kidney becomes enlarged, fatty and congested .

This results in hematuria, edema,oliguria, hypertension, anemia, ascites, proteinuria and hypoalbuminemia. Early diagnosis and management results in good prognosis.

HISTORICAL ASPECTS

Aristotle (384-322 BC) described excess liquid from blood is separated by kidney and modifies the liquid, which is excreted via ureter , bladder and Urethra[3].

Galen (130-200 AD) described the urine formation.

- 1666 – Marcello Malphigi [4,5] - described micro anatomy of kidney, formation of urine through filter in between blood and renal tubules.
- 1816-1892 – William Bowman – Glomerular capillary network,

- Giovani Bathista Morgagini[6] father of Pathological anatomy.
- 1789-1858 – Richart Bright[7] – Macrosopic appearance of the diseased kidney.
- 1837 Gabriel Valentine- Renal histology of massive proteinuria
- 1809-1855 – Friedrich Henle – Loop of Henle.
- 1885-1966 - Sir Arthur Allis – Clinicopathology of glomerular diseases[4].
- 1905-Fried rich Muller- Inflammatory glomerular nephritis
- 1913-Munk- lipoid nephrosis
- 1944 - Nils Alwell - Renal needle biopsy
- 1955 - Mellors - Immune fluorescence / microscopy on renal tissue
- 1955- Schering & Cepjohn- prednisone and prednisolone was introduced.
- 1970 - 2010 - New numerous renal pathologists defined the etiology ,pathogenesis ,clinic pathology of glomerular disease.

Epidemiology

Glomerular diseases are the one of the common causes of end stage renal diseases world wide probably due to prevalence of infectious diseases in developing countries[8].

Glomerulonephritis accounts 10-15% of glomerular diseases in USA.

In GN, Males are more prone than females[9] particularly affecting children and young adolescents of 5-15 years of age[10]

IgA nephropathy is most common GN world wide.

The incidence of post infectious GN has been reduced in most of western countries, but remains more common in countries like Africa, The Caribbean, Pakisthan, Malaysia, India and South America[10].

The reduction in incidence is due to better health care system and economic conditions improvement.

Minimal change disease is most common cause for nephrotic syndrome in children of 1-8 year accounts for 90% but also can occur in older children and adults[11], Boys are more prone than girls.

Classification of Primary Glomerular Disease Based on Clinical Syndrome

Nephrotic Syndrome

- Minimal change disease
- Membranous glomerular nephropathy
- Focal segmental glomeruli sclerosis
- Membranous proliferative glomerulonephritis
- C1q nephropathy
- Fibrillary glomerulonephritis

Acute Glomerulonephritis

- Membranous proliferative glomerulonephritis
- IgA nephropathy,
- Post infective GN

Rapidly Progressive Glomerulonephritis

- Antiglomerular basement membrane disease
- Immune complex crescentic glomerulonephritis
- Pauci-immune crescentic glomerulonephritis
- IgA nephropathy
- Membrano proliferative glomerulonephritis

Asymptomatic Hematuria and/or Proteinuria

- IgA nephropathy

❖ Membrano proliferative glomerulonephritis

Figure. 2 Glomerulus & Its Pathology

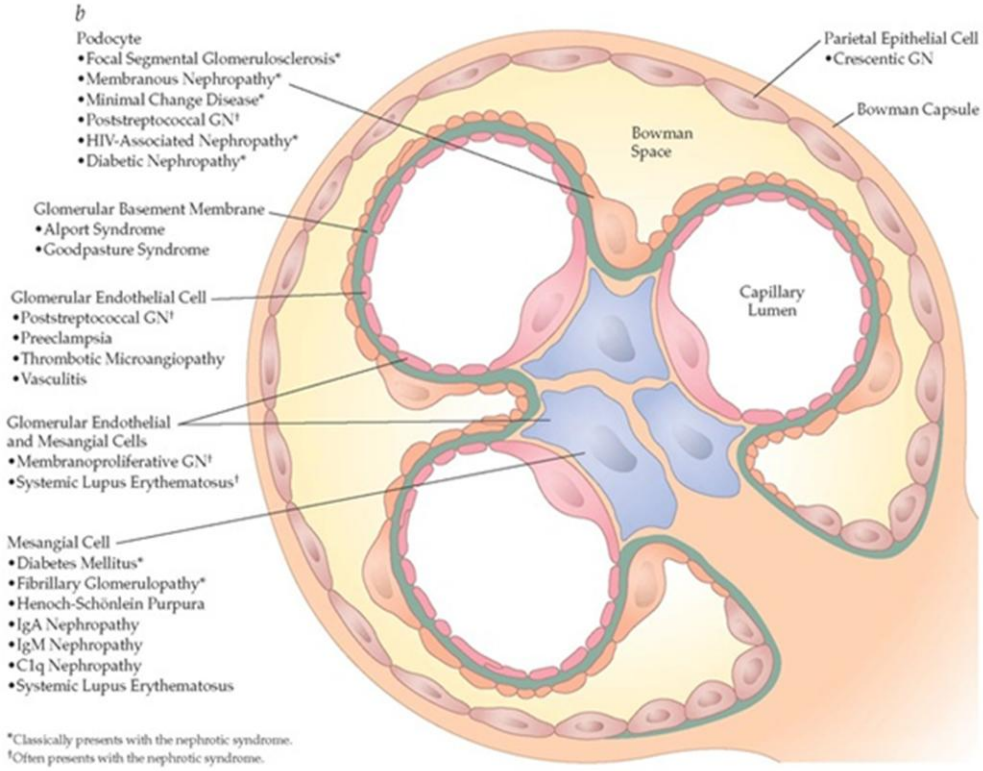


TABLE 1.

Common Clinical Syndromes of Primary Glomerular Diseases

Symptom	**Nephrotic Syndrome**	**Acute Glomerulonephritis**	**Rapidly Progressive Glomerulonephritis**	**Asymptomatic Hematuria and/or Proteinuria**
Proteinuria	>3.5 g/1.73 m 2 /per day	nephrotic range	nephrotic range	No or non-nephrotic range
Hematuria	Variable and usually monomorphic	RBC casts and dysmorphic RBCs	RBC casts and dysmorphic RBCs	dysmorphic with RBC casts)
Blood pressure	Normo- or hypertension	Hypertension	Hypertension	Normotension
GFR	Variable	Rapid decline)	Progressive decline	Decline uncommon

Figure 3. Pathogenesis Of Glomerular Disease

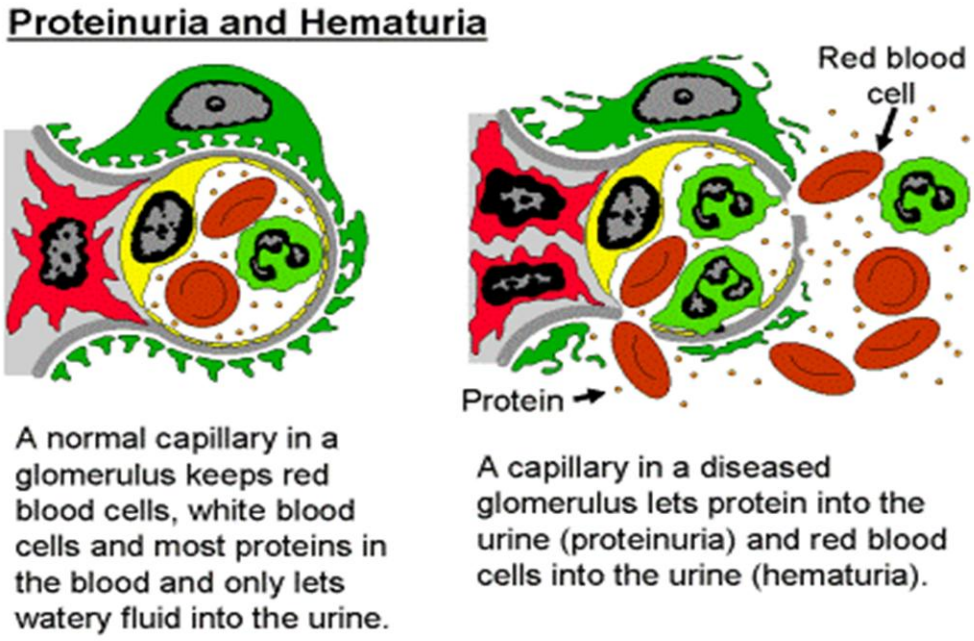
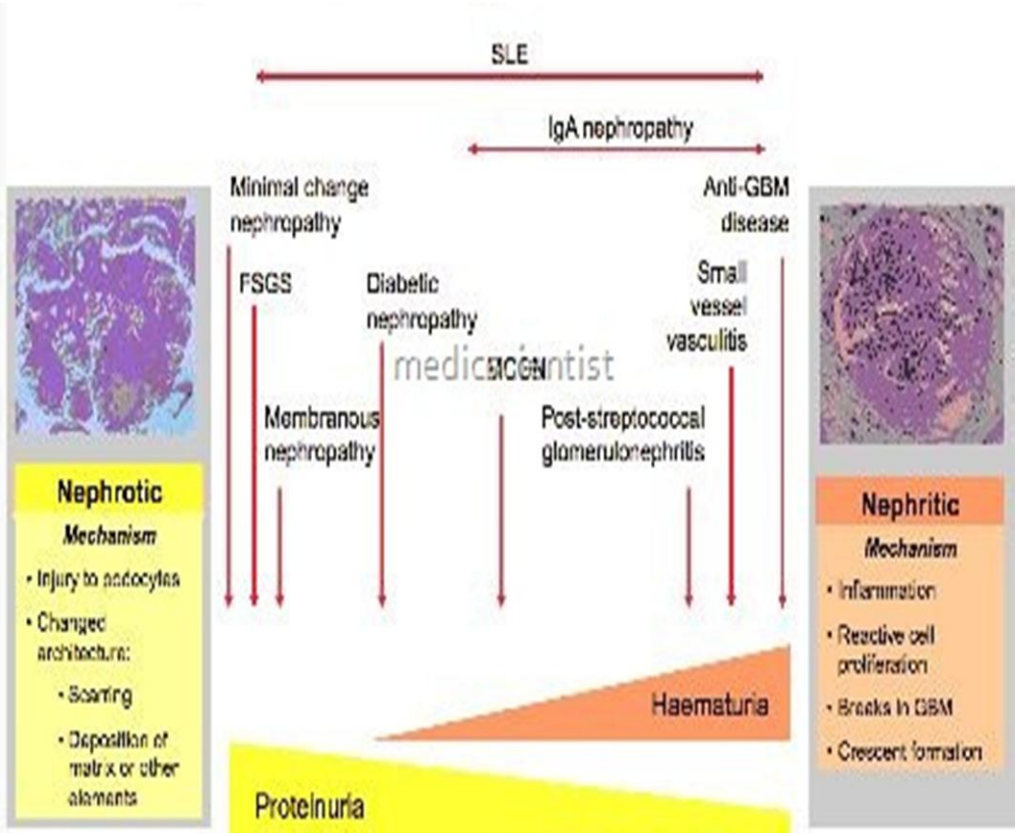


Figure 4. The spectrum of glomerular diseases



NEPHROTIC SYNDROME IN CHILDREN (NS)

Nephrotic Syndrome is a common renal disorder in children characterized by altered permeability of glomerular capillary wall results in massive loss of urinary protein. This can be acute or transient, may be chronic and progressive like FSGS. Some of disease may be remitting and relapsing like minimal change NS[12].

ACCORDING TO ISKDC (INTERNATIONAL STUDY OF KIDNEY DISEASE IN CHILDREN), **a child is said to have Nephrotic syndrome if,**

Proteinuria (more than 40mg /m^2 / Hr)

Hypoalbuminimia (less than 2.5g/dl).

Hyperlipidemia (more than 200mg/dl).

Edema

Figure 5. Nephrotic Syndrome Presentation I

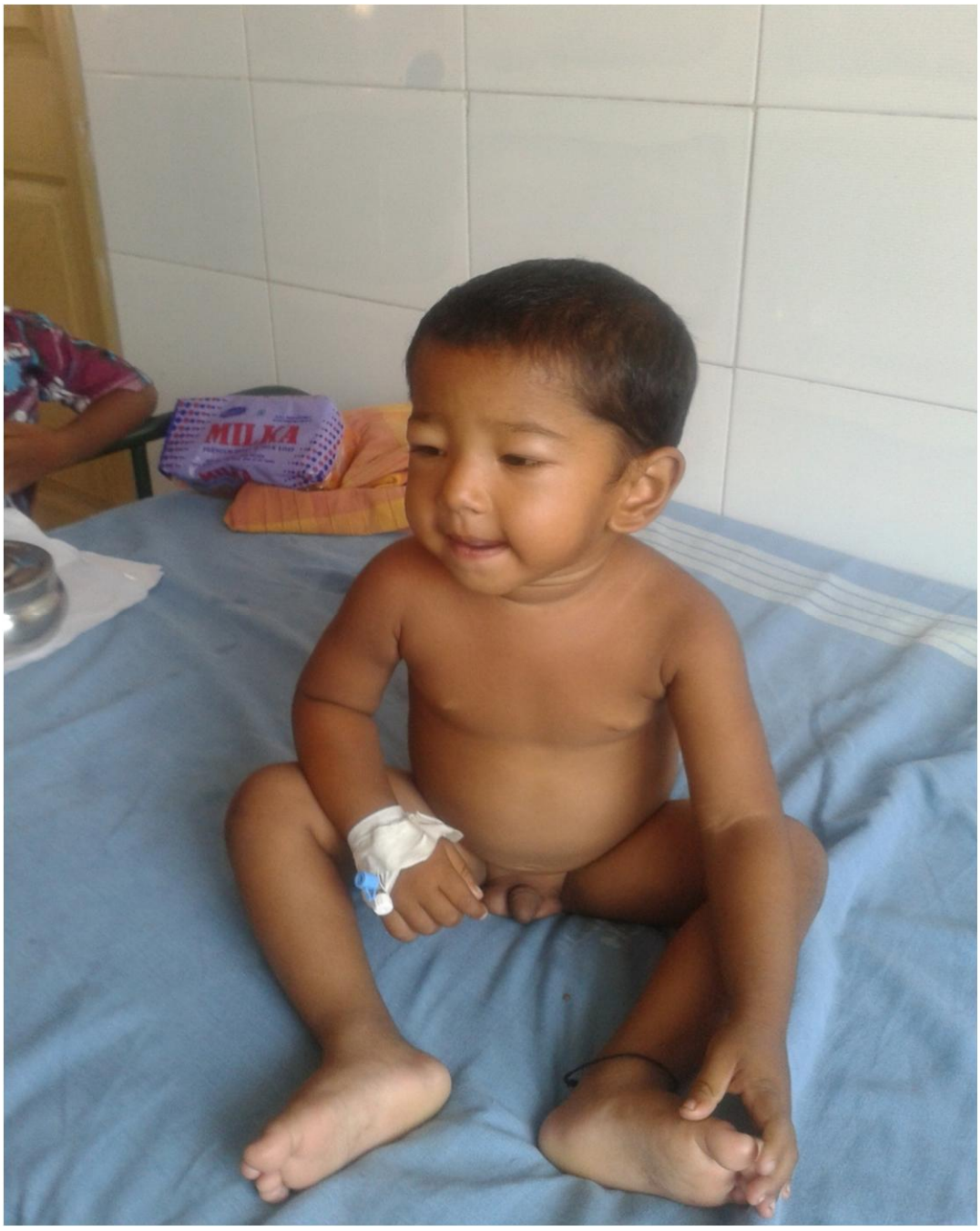
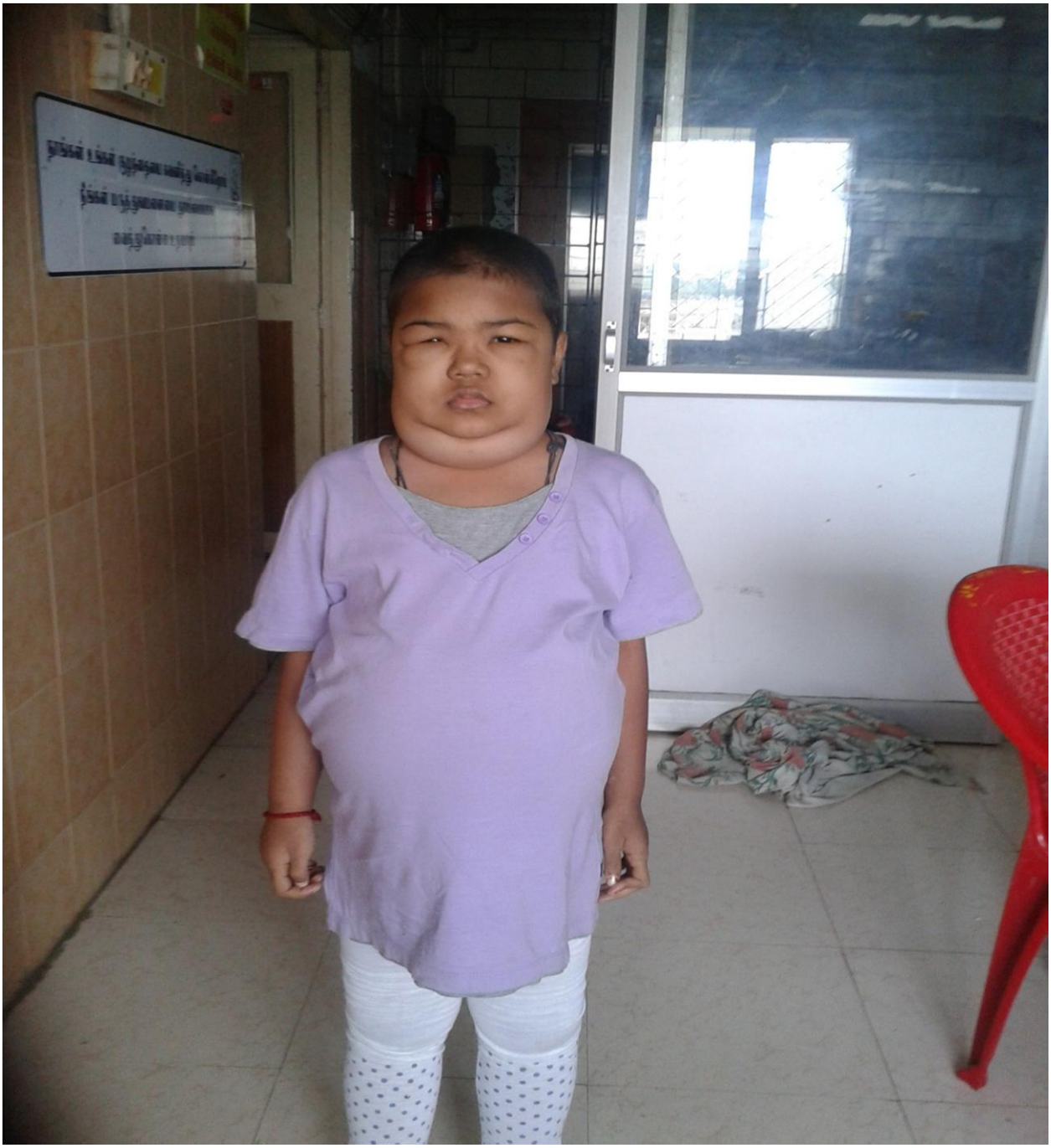


Figure 6. Nephrotic Syndrome Presentation II



EPIDEMIOLOGY

- Annual incidence ranges from 2 – 7 per / Lakh Children, prevalence 12 – 16 / Lakh[13].
- Higher incidence in South Asia[14] than Europe. Increased incidence of primary NS in India, Japan, south west Asia[15] . In Africa – primary NS is very rare. Secondary NS is more common .
- Male to female ratio is 3:2 in various studies in children less than8 years[16], in old children M:F is 1:1.

CLASSIFICATION

Primary

Secondary

Infantile.

Congenital

Primary NS – Intrinsic to kidney

- Minimal change nephrotic syndrome – Most common cause of NS in children.
- Focal segmental glomerulosclerosis.
- Membrano-proliferative GN.

- Membranous nephropathy.
- C3 GN.
- IgA nephropathy.
- Diffuse mesangial proliferation.

Secondary NS

- **Infection :** Hepatitis B& C , Toxoplasmosis, Cytomegalo virus , Congenital , Syphilis, Rubella, Malaria , HIV/ AIDS.
- **Drugs** – Lithium, NSAID , interferon, mercury, penicillamine, gold, heroin.
- **Systemic Disease** – Malignancies like lymphomas, leukemia, systemic lupus erythematosis ,Vasculitis, Wegeners Granmulomatosis, polyarthritis nodosa, microscopic polyangitis , Henoch scholein purpura and Churg – Strauss syndrome (eosinophilic granulomatosis) .
- **Immune complex associated** – post strepto coccal GN.

Infantile NS : It occurs before 3months of life.

Congenital NS : it occurs between 4-12 month of age.

Causes :

- Finish type congenital NS (NPHS1- Nephrin gene).

- Denys – Drash syndrome (wilms tumour suppressor gene WT1).
- Frasier syndrome (wilms tumour suppressor gene WT1).
- Diffuse mesangial sclerosis (WT, PLCE1, phospholipase C, epsilon 1 gene).
- Autosomal recessive, familial FSGS (NPHS2, podocin gene).
- Autosomal dominant , familial FSGS (ACTN4, α actinin 4, TRPC6).
- Nail patella syndrome (LMX1B).
- Pierson syndrome – (LAMB2).
- Galloway –Mowat syndrome.
- Schimke immune osseous dysplasia (SMARCAL1).

Two types of NS, based of response to steroids.

- Steroid sensitive NS (SSNS).
- Steroid Resistant NS (SRNS).

Common definitions to define the course of nephrotic syndrome

Nephrotic syndrome: Edema, nephrotic range proteinuria (>40 mg/m²/hr on timed sample, spot albumin to creatinine ratio >2mg/mg); hypoalbuminaemia (<2.5 g/dl)

Relapse

Urinary protein excretion >40 mg/m²/h; > 3+ by dipstick for 3 consecutive days.

Remission

Urinary protein excretion <4 mg/m²/h; nil or trace by dipstick on spot sample for 3 consecutive days.

Frequent relapse

Two or more relapses in 6 months of initial response; 4 or more relapses in any 12 months period.

Steroid dependence

Occurrence of 2 consecutive relapses during steroid therapy or within 2 week of its cessation.

Steroid resistance

Failure to achieve remission after 4 wk of daily therapy with oral prednisolone at a dose of 2 mg/kg/day.

Pathogenesis

The pathogenesis is unclear in MCD, but there is strong evidence of immune dysregulation, involving cell mediated immunity. This view in supported by the tendency of NS to manifest and relapse after viral

infections or an atopy, the association with HLA antigens and Hodgkin's lymphoma and its response to steroids and cyclosporine.

T cell function abnormality have been variably reported in a number of patients with MCD[17,18,19].

Cytokines bias

T Cells – Type I – (2 interferon, IL2) cytokines predominate in cell mediated immunity .

Type II - (IL4, IL10, or IL13) cytokines – atopy association.

B Cells - Production of Ig G4 and IgE[20].

Increased plasma levels of IgE1, normal IgG4, association with type 2 cytokine bias in subjects with MCD. Increased production of cytokines especially IL4 is reported[21].

In vitro studies shows that podocytes express receptors for IL_4 and IL_{13}[21]. Activation of these receptors, by respective cytokines disrurpts glomerular permeability resulting in proteinuria.

Vascular permeability factors

Factors like vascular endothelial growth factors, heparinase and hemopexin[22] play a role in increased glomerular permeability in patients with MCD and FSGS. Hoff et al[23] has showed dysregulated heparinase synthesis in children with steroid sensitive NS.

Podocyte injury

Recent evidence suggests, primary defect in idiopathic NS in at the level of podocyte, the glomerular visceral epithilial cell. Injury to podocytes occurs in many immune or non immune kidney diseases. This results in glomerular proteinuria. Viruses like HIV, Simian SV40, Parvo Virus B19 directly damages podocyte[24].

Mutations

Mutations in genes encoding proteins of podocyte results in familial nephrotic syndrome. Structurally defective podocyte and basement membrane protein results in loss of permeability and nephrotic range of proteinuria. These patients are less likely responds to steroids and progresses to end stage kidney failure[25].

The most common mutation of NPHS1 gene, encoding the protein nephrin, which is present in slit diaphragm between the podocytes. Mutation of these genes results in Congenital Finish NS[26].

Pathophysiology

Proteinuria[27,28] : Proteinuria > 150mg / 24hrs is abnormal.

Two types of proteinuria

Glomerular proteinuria due to leakage of protein through a glomerular filteration barrier.

Tubular proteinuria. Due to failure of tubular absorbtion .

Hypoalbuminimia

Massive proteinuria results in depletion of serum levels of albumin beyond protein synthesis of the liver, resulting in hypoalbuminemia . Increased renal catabolism of filtered albumin also leads to hypoalbuminemia.

Oedema

Due to decreased colloid oncotic pressure leads to accumulation of fluid in interstitial tissue.

Other factors are , sympathetic system stimulation, increased renin secretion, reduced natriuretic factors secretion[29].

Hyperlipidemia :

Is due to increased production of lipoproteins in liver, Decreased catabolism of lipoproteins[29].

Haematuria

Due to glomerular basement membrane damage RBCs escapes through urine.

Clinical features

Edema

- In 95% of children, is the main symptom, may be intermittent and insidious.
- First appears in the low tissue resistance areas (periorbital, scrotal and labial areas).
- It may progress to generalized edema.
- More noticeable in the face in morning, lower extremities later in the day typically dependent in nature[30].

Gross heamaturia

- More common in MPGN, FSGS than MCD.

Respiratory distress

- Due to massive ascites , frank pulmonary edema, effusions[30] or both.

Hypertension

- More common in children with FSGS and MPGN than MCNS[31].

Others

- Fever, lethargy, abdominal pain due to peritonitis or sepsis, anorexia, abdominal discomfort, irritability , fatigue, diarrhorea, ascites .

Treatment

Oral corticosteroids plays a major role in management of most children with nephrotic syndrome. The commonly used preparations are prednisone or prednisolone . Deflacort, an oxazotic derivative of prednisone has an anti inflammatory and immuno suppressive activity with fewer side effects but its non availability has restricted its use.

First episode

During 1970, ISKDC empirically recommended a protocol for NS[32,33,34]. The initial episode to be treated with prednisolone of 60mg /m^2 for 4weeks, daily, followed with 40mg /m^2 for 3 days for another 4weeks (intermittent therapy[32,33,34]).

Subsequently a study conducted by the Arbets gemeinschaft far paediatrische nephrologic (APN) therapy showed that follow up was therapy on alternate days was superior to intermittent therapy[35].

A study showed that prednisolone as a single morning dose was as effective like divided doses and as well as less side effects. Single dose is more convenient and better drug compliance. 70% of MCD patients achieve remission in 2 week. 75% showed relapses, or steroid dependence. In an APN study, relapse rate will significantly lower (36 VS 62%) who received 12 week compared to 8 week steroid therapy[36].

Based on current evidence and the need to reduce steroid toxicity, most nephrologists recommend prednisolone for 6 week daily and 6 week alternative days (total 12 week therapy) for the initial episode[13,37,38,39].

Frequent relapse steroid dependence

Almost 50 – 60% have frequent relapses or steroid dependence within first 6 months of initial therapy. Factors responsible are age younger than 3 years onset, delayed time to remission after 7-9 days and early relapse occurrence in the first 6months after initial treatment[40,41,42].

Long term alternative day oral prednisolone followed with slow tapering of prednisolone is done to maintain dose of 0.25 – 0.5 mg/kg on alternate days, for 9 – 12 months.

Levamisole

An antihelminthic drug with immune stimulatory effects, has been reported an effective as steroid sparing agents in number of case series with recent review[43].

In a study with levamisole administration at a dose of 2.5mg /kg on alternate day in 43 patient with SDNS, duration ranged 6 – 31 months, a significant reduction in relapse rate and steroid sparing effect was noticed[44].

The drug is well tolerated with few side effects leucopenia , vasculitis rash and liver toxicity.

Cyclophosphamide: (2-3 mg/kg)

It is an alkylating agent.Along with prednisolone(1mg/kg) on alternate day for 8 – 12 weeks induces remission in 25 – 60%. Patients with frequent relapses and steroid dependence needs 2 – 5 years follow up[45].

Adverse effects: bone marrow suppression, alopecia and hemorrhagic cystitis, bacterial infections[45], gonadal toxicity in pubertal boys .

Calcineurin inhibitors (CsA)

Cyclosporine A and tacrolimus act on intra cellular binding protein and inhibit calcium dependent signaling pathways involved in transcription of IL2 gene. About 80 – 85 % patients responds to CsA dosage[46] 4 – 5 mg/kg daily . It requires long term therapy 1 – 3 years .

Side effects: Nephrotoxicity, which may need renal biopsy.

Mycophenolate mofetil : (MMF)

Is hydrolyzed to its active metabolite Mycophenolic acid that inhibits, inosine monophosphate dehydrogenase, an enzyme involved in denovo synthesis. MMF at dose of 25 - 30 mg / kg /day, resulted in a significant reduction in relapse rates and marked corticosteroid sparing effect. Side effects were infrequent[47].

Mendoza regimen

- Combination of alternative day prednisolone for 2 weeks oral cyclophosphamide
- IV methyl prednisolone 30mg/kg / dose alternate day weekly for 8 weeks.
- Monthly for 8 Months.
- Alternate month for 1.5 to 2 years.
- Good results have been reported using high dose IV corticosteroid either alone or with alkylating agents.
- Complication : Hypertension, serious infections and delayed growth.

Rituximab

- Is an anticluster of differentiation 20 monoclonal anti body , very effective in children with SDNS.
- Mechanism is not known. 2 to 4 doses given at an interval of 1 - 2 weeks leads to gradual remission in 50% of children.

Table 2.Therapeutic protocols in children with steroid – resistance nephrotic syndrome[48,49,50,51,52]

Type of protocol	Complete response	Side effects	Comments
Methylprednisolone / triple therapy protocol	60%	Infections, cataract, growth retardation hypertension	82 weeks of therapy
Cycloporine, prednisolone	35%	Nephrotoxicity	2 years of therapy
Oral cyclophosphamide and alternate – day prednisolone (ISKDC)	27%	Hemorrhagic cystitis, seizures	1 Year poor response
Intravenous monthly cyclophosphamide and oral prednisolone	65%	Nausea, vomiting, alopecia	6 Months Economical
Tacrolimus and prednisolone	80%	Glucose intolerance, hypertension, nephrotoxicity	Less cosmetic side effects
Rituximab	44%	Infusion reaction, anaphylaxis	Expansive

Complications

Infections

This is due to loss of proteins, immunoglobulin, complement and properdin altered T cell function, immuno suppressive therapy and presence of edema. Peritonitis has an incidence of 2 – 6%, Cellulitis, pneumonias, upper respiratory tract infections[53].

In a study from china 54 patients with idiopathic NS were randomized to receive standard therapy with or without IV IG (dose 100-300 mg / kg/ day) for 2 – 3days. On follow up, the risk of nosocomial infection found lower in the cases compared to controls[54] (13.6% VS 46.8% P<0.05Varicella and pneumococcal (23-valent) vaccination is recommended for all children with NS in remission or off steroid therapy. Oral B pencillin V has been used as prophylaxis in all subjects with persistent anasarca[55].

Thromoboembolism

NS patients are at an increased risk 2–8% for venous and arterial thrombosis , but children are lesser risk than adults. Volume depletion, infections, diuretic use , venepucture and immobilization aggravate the risk of thromboembolism[56].

Evidence of thrombosis are treated with heparin followed with warfarin for 6months or longer. Prophylactic use is not recommended.

Hyperlipidemia

In SSNS, hyperlipidemia in transient[57] but in SRNS, it persists, contributes for cardiovascular morbidity and progression of FSGS[55]. Patients are advised to reach a normal weight for height, diet restriction in saturated fats. There is no guidelines for HMG COA reductase inhibitors use in children[58].

Osteoporosis

The risk of steroid induced osteoporosis has long term implications significantly. A prospective study[59] from India showed 22 out of 100 patients with NS had the features of low bone mass. Factors responsible for osteoporosis are older age , low calcium intake and cumulative steroid dosage[59]. A recent study from USA showed, high incidence of vitamin D deficiency in patients with NS even during remission[60].

Leonard et al[61] in his study concluded that intermittent use of glucocorticoid in children does not significantly alter bone mass. From the available evidence calcium supplementation in patients with frequent relapses, steroid dependence or resistance, who are likely to get long term steroid therapy is reasonable.

Outcome and prognosis

The outcome of patients with SRNS who fails to respond to high dose steroid, cyclophosphamide as CsA is unsatisfactory. Significant number of patients is at risk for progression to end stage renal disease. 20 – 25 % shows recurrence with FSGS in allografts.

ACUTE POST INFECTIVE GN (APIGN)

Other terms used are acute nephritic syndrome, post streptococcal GN, Acute GN.

Etiology

Long cope et al proposed no evidence could be obtained that the streptococcus caused by GN by actual invasion of the kidney, for blood cultures and urine culture were negative. Dick and Dochey stated that Beta- hemolytic streptococci were the pathogenic species in scarlet fever and which leads to APIGN.

Epidemiology

APIGN an important non suppurative complication of group A streptococcal infection [62].

- It may be sporadic or epidemic
- In world wide the incidence is 9.3 cases/ 1 lakh
- Male to female ratio in 2 - 3 :1.
- The risk of nephritis is 25% with pyoderma and of throat infection is 5%.
- Poor hygiene and lack of knowledge about medical care increase the risk in developing countries.
- Group A streptococci[63] are often typed by the surface M protein.

- ❖ Sero types for pyoderma – M47, M49, M55, M56, M57 and M60.
- ❖ Sero types for pharyngitis – M1, M4, M25 and M2 strains.
- ❖ Recently epidemics of APIGN with streptococci C, especially streptococcus, Zoo epidimics of unpasteurized milk of cows with mastitis has been noted.
- ❖ The incidence has been decreased in industrialized countries due to near eradication of streptcoccal pyoderma due to better hygiene and good medical care.

Table 3.Etiology of postinfectious glomerulonephritis

Bacteriae Gram – positive bacteria (streptococci, staphylococci, pneumococci, listeria monocytogenes) Gram – negative coccobacilli (Haemophilus). Gram – negative bacilli (Salmonella, Klebsiella, Serratia, Yersinia, Proteus, Pseudomonas). Other infections (legionellosis, brucellosis, bartonellosis) **Mycobacteria, Rickettsia, Mycoplasma, Chlamydia and spirochetes**	Tuberculosis and non – tuberculous mycobacterial infection Syphilis (Treponema pallidum) Leptospirosis (Leptospira interrogans) Rickettsial diseases (Coxiella burnetii) Mycoplasma pneumonia Chlamydia pneumonia

Fungi Candida albicans Histoplasma capsulatum Coccidioides immitis **Viruses** **DNA viruss** Hepatitis B, Varicella zoster and Epstein – Barr, Cytomegalovirus, parvovirus B19, Adenovirus **RNA viruses** HIV	Coxsackievirus, echovirus, hepatitis A Dengue virus, hepatitis C virus Mumps and measles **Parasitic infestations** Plasmodium falciparum, P. malariae Schistosoma haematobium, S. mansoni Toxoplasma gondii Filariasis, trichinosis and hydatid Disease Amebiasis (Entamoeba histolytica)

Pathogenesis

In early 20th century , schick and Von pirquit64, proposed the concepts of immune complex formation.

Theories proposed are

1. Glomerular trapping of circulating immune complexes.
2. Antibody mediated is situ immune complex formation.
3. Molecular biology.
4. Complement activation .

Recently two antigenic fraction have been noted as the main factors in pathogenisis[64].

Nephritis – associated plasmin receptors (NAPIr) noted as glyceraldehyde 3 P04 dehydrogenase(GAPDH) and the streptococcal pyogenic exotoxin B (SPEB).

And its zymogen precursor (ZSPEB).

NAP_1r[65] stimulates the alternate complement pathway and high antibody titers to NAP_1r is seen in 95% APIGN patients determined by western Blott.

NAP_1r facilitate glomerular immune complex deposits.

SPEB [66,67]is an extracelluar protein for about 90% of total protein .High antiSPEB antibody levels and renal deposits of SPEB are found in APIGN.

Immune complex deposition and complement activation

Vogt et al proposed that cationic antigen could be attracted to penetrate the negatively charged glomerular basement membrane which induces sub epithelial electron dense deposits and severe GN.

Complement activation is a mainfeature in APIGN the alternate pathway is preferably activated, as shown by low C3 and normal C4 levels. Immuno flurorescence pattern shows IgG, C3 and C5 deposition.

Cellular immune Mechanism

Macrophages and T helper cells infiltrate the glomeruli . The mediators IL-6, IL-8, TNF 2 plays an important role in the development and severity of inflammation.

Auto immune reactivity

Anti IgG antibodies are seen in severe and in glomerular deposits frequently. This auto immune reactivity may modulate the course of APSGN.

Pathophysiology

If the glomeruli gets damaged, it leads to reduction in GFR, leading to fluid retention. The mediators released by injured glomerlus , over expression of epithelial sodium channel and interstitial inflammatory cells also causes sodium and fluid retention by the distal tubule which in turn cause edema and hypertension.

Clinical manifestations

Median age at presentation at child hood is 6 - 8 years, rare prior to 2 years. This is attributed to the low rate of streptococcal pharyngitis and immature immune response . Males are more prone than females to 2:1 of unknown cause[68].

- APIGN characterized by gross hematuria , edema , hypertension,usually preceded by streptococcal pharyngitis or pyoderma.
- Latent period in 7 – 14 days in sore throat and while 2 – 4 weeks in pyoderma.
- Urine is classically reddish brown , smoky or cola coloured .
- Proteinuria, oliguria may be present.
- Hypertension occurs in 80 – 90 % of cases.
- Head ache, drowsiness, seizures, mental and visual changes occurs in 35 % of children.
- Dyspnoea, restlessness and pulmonary edema due to extra cellular volume expansion in over in 5% of patients.

Others: Fever ,rash, arthritis, purpura and,hepatospleenomegaly.

Investigations

- Urine microscopic – dysmorphic RBC, RBC cast suggest glomerular pathology low HB due to volume over load.
- Blood urea is increased 60- 65 %.
- ASO titre is higher in pharyngitis[69] .
- Elevated anti DNASE in pyoderma.

- Complement C3[69] in lowered but returns to normal levels with in 6weeks onset is foremost diagnostic importance.
- 80% shows streptozyme test positive (DNAase B, streptolysin B), hyalurinidase and streptokinase).

Renal biopsy

Indications:

- When resolution is delayed and nephritic – nephrotic features.
- Raised BUN, severe anaemia.
- Anuria requiring dialysis.
- Systemic diseases, fever , rash, joint pain and heart diseases.
- Persistent hypocomplementemia to rule out MPGN or lupus nephritis.
- Persistent Oliguria haematuria , hypertension , gross haematuria beyond 3 – 4weeks, azotemia beyond 2 weeks.

Light microscopy

Diffuse hypercellullarity of endothelial and mesangial cells with polymorpho nuclear cells. GBM is normal.

Immuno florescence

- Its show discrete granular deposits of IgG and C3 in the capillary loop and mensangium.

- ❖ Starry sky appearance.
- ❖ Mesangial pattern, Garland pattern.

Electron microscopy

Subepithelial humps is the hall mark finding

Management

Essentially symptomatic

- ❖ If infection is present at the time of diagnosis , Benzathine penicillin G given as single dose 6,00000 IU for less than 27 kg., oral pencillin V 250mg 2 – 3 times per day for more than 27 kg children for 10 days.
- ❖ Erythromycin is alternate for penicillin allergic patients .
- ❖ Restriction of fluids and sodium in take is advised .
- ❖ Diuretics - frusemide is needed for children with edema hypertension and circulatory congestion.
- ❖ Antihypertensives - Nifidipine (oral) or hydralazine (parentral) sodium nitroprusside is needed in hypertensive encephalopathy.
- ❖ Hemodialysis or peritoneal dialysis may be required for hyperkalemia , uraemia and severe circulatory congestion.

Course and prognosis

- APIGN has excellent prognosis.
- Edema , blood pressure , starts decreasing after the 1st week of treatment[70].
- Gross haematuria clears quickly , microscopic heamaturia may persist for many months even 6 – 12 months.
- Intermittent haematuria or proteinuria may exists which is in significant.
- Garland pattern[70] has poor out come.
- Death may occur due to hyperkalemia or pulmonary edema.
- Recurrence is rare .
- APIGN patients should be followed up for proteinuria and Blood pressure for several years.
- Renal biopsy is indicated in persistent proteinuria [70]and decline in renal function.

ALPORT SYNDROME (AS)

Is a heredity nephropathy[71,72] under classification as collagen IV nephropathy, initially present as haematuria.

Clinical presentation

- Micro and macroscopic haematuria,
- sensoneural hearing loss
- Ocular abnormalities.

Molecular biology

- Basement membrane of glomerulus is the effective filtration barrier supported by epithelial and endothelial cells, made up of type IV collagen[71,72].
- Six genetically distinct type IV collagen alpha chains α1-α6 are there, which is encoded as COL4A1 to COL4A6[73].
- α3-α6 are expressed in basement membrane of kidney, cochlea and eyes which is responsible for clinical features of AS.

Two forms

- X linked recessive 85% most common, involves X chromosomes, encodes COL4A5.

- ❖ AR or AD - COL4A3 or COL4A4 females are affected, responsible for thin BM nephropathy.

Clinical manifestations

- ❖ Microscopic haematuria – constant features of AS.
- ❖ Macroscopic haematuria .
- ❖ Proteinuria , hypertension.
- ❖ Bilateral progressive sensori neural hearing loss.
- ❖ Anterior lenticonus – pathognomonic of AS, Marker of severity of AS.

Renal biopsy

Light microscopy [73]: Podocytic hypertrophy and stiffness of capillary wall followed by focal and segmental thickening of the capillary walls.

Immunofluorescence [74]: Focal deposits of IgG ,IgM or C3.

Differential Dignosis

IgA nephropathy, Membranous nephropathy, mesangio capillary glomerular nephritis, thin BM nephritis.

Prognosis

- Depends on mode of inheritance, gender and genetic mutations[71].
- Juvenile form progress to ESRD[71] by 2-3 decades of years.
- Other form progress to CKD by 60years of age.

Treatment

- Symptomatic treatment for auditory and ocular symptoms and its complications.
- ACE inhibitors and ARB blockers[74] as renoprotective effects.
- Renal transplantation for ESRD.

MEMBRANO PROLIFERATIVE GLOMERULAR NEPHRITIS : (MPGN)

- Is an uncommon cause for chronic progressive GN in children and young adults.
- Synonyms: Mesangio capillary GN, Lobular GN, Hypocomplimentemia GN.

Epidemiology

- In adults it is a major cause for nephrotic syndrome.
- 0.2 – 20 % primary GN are due to MPGN in adults, 6.2% in children.

Classification

Based on immunofluroscence .

Idiopathic or Primary – TYPE I , II & III[75,76].

- Type I – Subendothelial electrondense deposits.
- Type II – Complement containing dense deposits of GM.
- Type III – Both subendothelial and subepithelial deposits.

Secondary forms

- Most common form of MPGN .

Table 4.Etiology of MPGN

MPGN type I	**MPGN type II (Dense deposit disease)**	**MPGN type III**
Idiopathic Familial **Secondary** Malignancy B-Cell lymphoma Chronic lymphoid leukemia Non – Hodgkin's lymphoma Immunologic SLE cryoglobuinemia Sjogren's syndrome Complement deficiencies Infections Hepatitis B, Hepatitis C HIV, malaria, Shistosomiasis Others Heroin abuse Partial lipodystrophy	**Idiopathic** Familial **Secondary** Complement deficiencies Partial lipodystrophy	**Idiopathic** Familial

Differential diagnosis

Lupus nephritis , hypocomplimentemia GN.

Investigations

- Complete Haemogram, ESR
- RFT,LFT, Electrolyte, Serum Cholesterol
- Complement levels C3,C4
- Antinuclear antibodies(ANA)
- Double stranded DNA(anti-ds DNA)
- Serology for HIV,HbsAg,HCV
- Renal biopsy- indicated in persistant low complement at 8 – 12 weeks in a child with PIGN[77,78]

Treatment

- Angiotensin II blockers for normal kidney function.
- Long term alternate day glucocorticoid therapy.
- Eculizumab anti C3 monoclonal antibody inhibitis C5 activation.

Outcome : Irrespective of type of MPGN

- 50% progressive to ESRD [78,79]by 10 years.
- 90% progressive to ESRD[78,79] by 20 years.

HENOCH SCHOLEIN PURPURA

It is a disease of skin , kidney, joints affecting children mostly.

Synonyms

Anaphylactoid Purpura ,Purpura Rheumatica, Scholein –Henoch purpura[80]. Usually preceded by throat infection.Involves skin causing palpable purpura and kidney causing hematuria,proteinuriamay progresses to chronic kidney diseases if left untreated. It is a systemic small vessel vasculitis[80] charecterised by deposition of IgA .

Epidemiology

HSP occurs more common in children[81] than adults.

Male:Female ratio is 2:1

Incidence[81] :1/ 5000

Most common systemic vasculitis in children

Etiology: Idiopathic

Infections: Beta hemolytic streptococci,hepatitis,Herpes simplex virus, ParvovirusB19, Coxsackievirus, Adenovirus, H.Pylori, Measles, Mumps, Rubella, Mycoplasma.

Drugs: NSAIDs, cefuroxime, ACEinhibitors, Vancomycin, Ranitidine, Streptokinase.

Pathophysiology

Deposition of IgA complexes on arterioles,capillaries,and venules[81]. Similar to IgA Nephropathy.

Clinical features

- Classical triad[82]- palpable purpura in all cases,arthritis(80%),abdominal pain(62%)
- Purpura usually involves legs and buttocks.
- Major joints are involved,Non erosive in nature.
- Hematuria,proteinuria,Nephrotic syndrome[83].1% progresses to chronic kidney disease.

Diagnosis:

Blood tests: Elevated RFT, Raised IgA 50%, Raised CRP & ESR, Platelets may be raised.

Biopsy of skin

- Microscopy: Hypersensitivity vasculitis[85]
- Immunofluorescence: IgA and C3 deposition[85] in vessel wall.
- Renal Biopsy: IgA deposition in mesangium[85]leading to formation of crescents.

Treatment

- ❖ Symptomatic.
- ❖ Steroids should be avoided.
- ❖ Depending upon biopsy,
- ❖ IV Methyl prednisolone, cyclophosphamide, dipyridamole.
- ❖ Other Regimens: Steroid/azathioprine, Steroid/ Cyclophosphamide, IVIG is rarely used.

Prognosis:

- ❖ Good prognosis 94% recovery[84] in children.
- ❖ HSP reoccurs after 4 months of initial episode[84] in children.
- ❖ In children it exhibits as nephritic /nephrotic features.
- ❖ Renal biopsy ranges from focal mesangial proliferative to marked cellular proliferation with crescents[85].

IgA NEPHROPATHY

The most predominant glomerulonephritis in the world is IgA nephropathy, also known as Berger's disease/Berger syndrome/ synpharyngitic glomerulonephritis. [86]

The disease is characterized by the deposition of IgA antibody in th glomerulus. While this is local, the systemic form is called the Henoch-Schonlein Purpura(HSP), which has a more benign prognosis than IgA which progresses to CKD in 20 yrs in about 30%of cases.

Pathogenesis

In around 50% of cases symptoms occur within two days of a non-specific upper respiratory tract infection (the reason for it being called synpharyngitic) not to be confused with post streptococcal glomerulonephritis (weeks after infection).

In a proportion, gastro intestinal or urinary tract infections can be the trigger. These infections activate the mucosal defense mechanisms and result in the production of IgA antibody which gets deposited in the glomerular mesangium .

Studies show that the degalactosylation of IgA, occurring in some in response to gut antigen exposures probably due to abnormal mucosal antigen handling leads to the polymerization of IgA in tissues, especially the mesangium[87]. Also studies are that the IgA deposited does not appear

to originate from MALT(which is the site of most URI) but from the bone marrow. This suggests an immune pathology rather than the direct interference by outside agents.

Some studies have shown the involvement of nuclear factor-kappa B(NF-kB) in the pathogenesis of glomerulonephritis and the increased expression of NF-kB in the tubular area may predict poor prognosis and decreased renal survival[88].

IgA receptor abnormalities (circulating IgA –soluble CD89 complexes and over expression of the mesangial IgA1 receptor,Transferrin receptor 1) might also be responsible[89].

Clinical features

- Hematuria within two days post an upper respiratory tract infection
- Loin pain
- Persistence of microscopic hematuria even after gross hematuria subsides.
- A proportion goes for acute renal failure.
- Some have proteinuria of <2g/day
- 5%of people present as nephrotic syndrome
- Rarely they present with chronic kidney disease.

- Complete remission occurs only in about 5% of cases, in case of adults. In contrast, 30-50% children show a normal urine analysis at the end of 10yrs.

Associated diseases

- Liver failure
- Coeliac disease
- Rheumatoid arthritis
- Reiter's disease
- Ankylosing spondylitis
- AIDS

Investigations

- History plays an important role to find out a prior URI OR UTI.
- Ultrasound of the kidney and cystoscopy are necessary to rule out other causes of hematuria, such as malignancies or calculi.
- Finally a renal biopsy might be necessary to confirm the disease. It shows the proliferation of the mesangium, mesangial widening and focal and segmental inflammation. It also shows an increase in the deposition of matrix proteins.

- Electron microscopy confirms electron dense deposits in the mesangium, sometimes extending to the sub endothelial regions of adjacent capillary walls.
- Mesangial deposition of IgA often with C3 and properdin and smaller amounts of IgG/IgM.
- Immunofluorescence also confirms IgA deposits in the mesangium.
- Protein electrophoresis and Ig levels assay reveals an increased IgA in around 50% of cases.
- Urine analysis shows RBCs as casts. Proteinuria may also be present.
- An increase in CRP, ESR, Complement levels, ANA, LDH may also be seen.

Treatment

- Patients with isolated hematuria and proteinuria <1g/day and a normal renal function are just followed up annually.
- The source of IgA (eg.tonsillitis) if identified can be treated but this did not show better results[90].

- To control hypertension, ACEI or ARBs can be used.Some studies show that 6 months of steroids reduces proteinuria and preserves renal function[91].

- Cyclophosphamide, due to its side effects of malignancy and sterility is not recommended but a combination of steroids and cyclophosphamide initially for 3 months and then azathioprine for the next 2 years resulted in a significant improvement in patients with a declining GFR[92].

- Some studies show that long term treatment with omega-3 fatty acids might reduce progress but without reducing proteinuria[93].

- Renal transplantations would prove beneficial but the disease recurred in transplanted kidneys too.

MEMBRANOUS NEPHROPATHY

It is a rare cause of asymptomatic proteinuria or NS in childhood.. Idiopathic type is more common in adults than in children.(<5%). It may also occur secondary to SLE, Hep B infection, secondary and congenital syphilis, malaria, EBV infection.

Incidence and prevalence in children

2/ 1lakh/ year incidence

16/ 1 lakh/ year prevalence

Gene associate with MN is HLA-DR3 in Caucasians[94].

Pathogenesis

Pododcyte injury and subepitehlial immune deposits of IgG ,c3[95]

Table 5: Etiology of Membranous Nephropathy

Etiology	Common cause	Uncommon cause
Autoimmune diseases	Systemic lupus erythematosus	Rheumatoid arthritis, sjogren's syndrome, mixed connective – tissue diseases, Graves' disease, Hashimotos thyroiditis, dermatomyositis, myasthenia gravis, dermatitis herpetiformis, primary biliary cirrhosis, bullous pemphigoid, Guillain- Barre' syndrome
Infections	Hepatitis B Congenital syphilis	Tuberculosis, Streptococcus, Cytomegalovirus, hepatitis C, Quartan malaria, schistosomiasis, filariasis, hydatid disease, leprosy.
Drugs and toxins	Non –steroidal anti-inflammatory drugs penicillamine	Captopril, gold, penicillamine, lithium, mercury,clopidogrel, probenecid, formaldehyde, hydrocarbons
Miscellaneous		Hematological malignancies like lymphoma and chronic lymphocytic leukemia, tumors, diabetes mellitus, sarcoidosis, sickle cell disease, hematopoietic stem cell transplant, postrenal transplant, C4 deficiency, selective IgA deficiency, selective IgA deficiency, Kimura's disease, sclerosing cholangitis, systemic mastocytosis, Gardner – Diamand syndrome

Pathology

Light microscopy

Histologic hallmark is diffuse glomerular capillary thickening[95,96]

Immunofluorescence

Uniform granular,capillary wall staining for IgG, C3

Electron microscopy

Subepithelial electron dense immune complex deposits[96,97]

Clinical features Asymptomatic proteinuria

Microscopic hematuria

Macroscopic hematuria

Table 6.Staging of membranous nephropathy based on LM and EM

Stage	**Light microscopy (LM)**	**Electron microscopy (EM)**
Stage I	Normal GBM in thickness	EDDs*-small, flat, but discrete
Stage II	Thickened GBM discernible	EDDs*-bigger, flanked by prominent
Stage III	Very prominent GBM	Spikes-bigger and intramembranous, irregular capillary wall
Stage IV	GBM irregularly thickened	Absent deposits, GBM vacuolated, electroluscent BM
Stage V	Return of GBM to normal	Residual GBM delicate and partially thickened

Investigations

- Complete urinanalysis
- Spot PCR
- LFT
- Lipid profile
- Renal biopsy
- Serum electrolytes
- Complement C3

Treatment

- ACE inhibitors for HTN
- HMGCoA reductase inhibitors for hyper cholesterolemia
- Immunosuppressants
- Ponticelli regimen[96]- daily i.v. methyl prednisolone pulses for 3 days followed by alternate months of prednisolone and chlorambucil.

CRESCENTIC GLOMERULO NEPHRITIS (RPGN)

It is a clinical syndrome characterized by extensive crescent formation in glomeruli resulting in rapidly progressing loss of renal function over a short period of time.

Crescents are defined as presence of two or more layers of epithelial cells in bowman's space. The constituents of crescents include coagulation proteins, macrophages, T cells, fibroblasts and parietal epithelial cells, IL-1 and TNF[98].

Classification&Etiology[98]

Anti-GBM GN

It is an example of cytokine- antibody mediated type 2 reaction.

Immune complex GN:

It is the most common type of crescentric GN seen in 75-80% of patients.

Pauci- immune GN:

15-20% contribute this type.80-90% show ANCA positivity.

Table 7.Classification and etiology of crescentic GN

Types	Etiology
Anti- GBM antibody GN	Anti-GBM nephritis, Goodpasture's syndrome
Immune complex GN	Postinfectious, poststreptococcal, infective endocarditis, visceral abscesses, other infections like HBV, HCV,HIV Systemic diseases-SLE, HSP Primary renal diseases-IgA nephropathy, MPGN, membranous nephritis
Pauci – immune GN	Microscopic polyangiitis, Wegener's granulomatosis (granulomatosis with polyangiitis),renal limited vasculitis

Clinical features

- ❖ Gross and microscopic hematuria
- ❖ Hypertension
- ❖ edema
- ❖ proteinuria
- ❖ joint pain and swelling
- ❖ seizure or altered sensorium

Investigations

- Peripheral blood smear- normocytic normochromic anemia.
- Elevated blood urea and creatinine
- Urine shows proteinuria, RBC or WBC casts.
- Decreased complement C3 and C4
- Raised ASO titre.
- ANA and Anti-DNA positivity
- ANCA positivity
- Renal biopsy.
- Light microscopy: crescents in bowman's space.

Immunofluorescence:

- granular and sub epithelial deposits of IgG and C3 in PIGN[98].
- Sub endothelial mesangial IgG and C3 deposits in MPGN
- Mesangial IgA deposits in IgA /HSP nephropathy
- A full house deposit along the capillary wall and mesangium in lupus nephritis.

Treatment

- Supportive therapy - anti hypertensives , peritoneal dialysis for fluid overload.
- Specific therapy.

Treatment of crescentic GN[98]

Treatment	Features
Supportive therapy	Dialysis, control of BP with antihypertensives, correctionof dyselectrolytemia
Specific therapy Induction of remission	Methylprednisolone pulses (20-30 mg/kg/day, 3-6 doses), followed by oral prednisolone, 1.5-2mg/kg/day for 4 week prednisolone is gradually tapered to 0.5 mg/kg/day by 3months. IV pulse cyclophosphamide (500-750mg/m^2), every 3-4 weekly for 6 pulses Therapeutic plasma exchange – double volume every alternate day for 2 week, in selected cases
Specific therapy Maintenance	Oral prednisolone 0.5 mg/kg every alternate day for 12-18 month Oral azathioprine (2-3 mg/kg/day) after pulse cyclophosphamide therapy, for 12-18 month

Outcome

- Depends on the cause & severity[98]
- Post streptococcal- good outcome
- Pauci immune- one or more relapses
- Cellular and fibrocellular crescents- good outcome

SYSTEMIC LUPUS ERYTHEMATOSIS – LUPUS NEPHRITIS

Lupus nephritis is a serious potential feature of systemic lupus erythematous (SLE).Systemic lupus erythematous is an autoimmune multisystem disorder which can affect numerous organs ranging from the kidneys, skin, pericardium, lungs, nervous system and others.

Renal involvement might be the first symptomatic finding within one year of diagnosis but sometimes within the first five years after diagnosis.

Pathogenesis

The presence of numerous autoantibodies with the formation of immune complexes immune complexes.In the kidney forms the main pathogenesis of lupus nephritis.

Classification

World Health Organization (WHO) morphologic classification of lupus nephritis ,modified in 1982.

Class I: Normal glomeruli

a. Nil (by all techniques)

b. Normal by light microscopy, but deposits by electron or immunofluorescence microscopy

Class II: Pure mesangial alterations (mesangiopathy)

a. Mesangial widening and/or mild hypercellularity

b. Moderate hypercellularity

Class III: Focal segmental glomerulonephritis (associated with mild or moderate mesangial alterations)

a. With “active” necrotizing lesions

b. With “active” and sclerosing lesions

c. With sclerosing lesions

Class IV: Diffuse glomerulonephritis (severe mesangial, endocapillary or mesangiocapillaryproliferation and/or extensive subendothelial deposits)

a. Without segmental lesions

b. With “active” necrotizing lesions

c. With “active” and sclerosing lesions

Class V: Diffuse membranous glomerulonephritis

a. Pure membranous glomerulonephritis

b. Associated with lesions of class II

c. Associated with lesions of class III

d. Associated with lesions of class IV

Class VI : Advanced sclerosing glomerulonephritis

Clinical features

Fever, hypertension or hematuria, edema of periorbital region, anasarca, presacral edema in the morning, symptoms of renal failure..

Treatment

The aim is to normalize renal function or to prevent further damage. Immunosuppressive therapy forms the main line of treatment. The American college of Rheumatolgy recommends that all lupus nephritis patients should receive therapy with hydroxychloroquine[99].

Class I requires only supportive and no specific therapy[100].

Class II requires prednisolone (20-40mg/day for 1-3months if there is proteinuria>1000mg/day.

Class III requires aggressive therapy with prednisolone 1mg/kg/day for a month followed by tapering to a daily maintenance dose of 5-10 mg/day for 2 yrs.methyl prednisolone in the dose of 1g/day for 3 days may be used in acutely ill patients.

In patients in whom corticosteroids are resistant or result in toxicity can be given immunosuppressants-cyclophosphamide (i.v. for 6 months and every 2-3 months thereafter ,depending on the response for 2-2.5 years.the dose is then adjusted based on hematologic response)[101],

Class IV :Mycophenolate mofetil 300-600mg/m2/dose dwice daily for 6months(to maintain control and to prevent relapses in induction therapy-responsive patients) [100,101]

Class V : patients are treated with prednisolone for 1-3 months, followed by tapering for 1-2 years. Studies show that some patients treated with corticosteroids and azathioprine had a complete remission, some partial and few resistant[101]

- ❖ Rituximab is being studied as a good choice for treatment.
- ❖ Other therapies under study are:
- ❖ Anti- CD20 monoclonal antibodies like ocrelizumab[99,100]
- ❖ Belimumab-anti-B lymphocyte stimulator.
- ❖ Atacicept- TACI-ig fusion protein
- ❖ Anticytokine therapies

Gucocorticoids should be given along with cyclophosphamide i.v. or mycophenolate mofetil orally for induction in ISN class III/IV disease. There is no need for immunosuppressants in class I/II patients.

GOOD PASTURE SYNDROME

It is a rare auto immune disease in which antibodies are produced against the basement membranes of the glomeruli and the alveoli causing diffuse pulmonary hemorrhage and acute or rapidly progressive glomerulonephritis.

The disease was first described by Ernest Goodpasture, an American pathologist[102].

Etiology

The cause is generally idiopathic but a disturbance in the alveolar capillary permeability is necessary to allow anti GBM antibodies act on the alveoli[102]. They are:

- Exposure to organic solvents like chloroform or hydrocarbons
- Exposure to tobacco smoke
- Infections such as influenza A.
- Cocaine inhalation
- Anti-lymphocytic treatment
- High content of oxygen
- Sepsis
- Metal dust inhalation
- Association with HLA-DR15 and DRB103, DRB*04[103].

Pathophysiology

The autoantibodies produced by the plasma cells bind to their reactive epitopes in the basement membrane and activate the complement cascade, resulting in tissue injury. This is a type II antigen antibody reaction. The auto antibody is directed against the alpha 3 chain of type 4 collagen[104]. T cells might also play a role in the pathogenesis by enhancing the B cell and antibody production.

Clinical features

- Malaise, fever, chills, arthralgia and other constituitional symptoms
- Hemoptysis
- Massive pulmonary hemorrhage
- Dyspnoea, cough, shortness of breath
- Hematuria, edema, hypertension, uremia
- Significant anaemia.

Diagnosis

Serological assay like RIA, ELISA, anti GBM antibodies – highly sensitive and specific.

- Western blotting on collagenase solubilised humanGBM.

- ❖ Recombinant antigen flourescence immune assay.
- ❖ Increase in IgG1 and IgG3 subclasses.
- ❖ Anti GBM antibodies against epitopes EA and EB and their correlation with disease severity
- ❖ ANCA testing.
- ❖ Chest radiograph and pulmonary function testing.
- ❖ Renal biopsy- linear deposition of immunoglobins along the GBM and crescentric glomerulonephritis.

Treatment

- ❖ Mainstay is plasmapheresis[105]. The plasma containing the antibodies is filtered out and the blood cells is recycled and given IV as a replacement fluid.
- ❖ Immunosupressants like cyclophosphamide, rituximab, prednisolone. Cyclophospahmide 2mg/kg orally and corticsteroids 1-1.5mg/kg.
- ❖ Renal transplantation, but post transplant anti GBM nephritis might result.

HEMOLYTIC UREMIC SYNDROME

HUS is a clinical syndrome characterized by progressive renal failure associated with microangiopathic hemolytic anaemia and thrombocytopenia. It is the most common cause of acute renal failure in children[106].

Most cases follow infections, sometimes bloody diarrhea. It is a medical emergency[106].

Types

- Shiga like toxin producing E.coli HUS –follows infection by E.coli, O-157:H7
- Shiga toxin secreting strains of Shigella dysenteriae.
- Pneumococcal HUS due to infections by Streptococcus pneumonia[107].
- Atypical HUS caused by genetic defects, resulting in chronic, uncontrolled complement activation.

Signs and symptoms

- Oliguria
- Hematuria
- Renal failure
- Thrombocytopenia

- ❖ Microangiopathic hemolytic anaemia
- ❖ Hypertension.
- ❖ In some cases, neurologic changes.[108].

Symptoms of thrombotic microangiopathy like abdominal pain, elevated LDH, decreased haptoglobin, anaemia, schistocytes, elevated creatinine, proteinuria, fatigue, confusion, nausea, diarrhea.

Pathogenesis

The primary event is damge to endothelial cells resulting in thrombotic micro angiopathy and RBC fragmentation. The binding of shiga toxin to gb3 receptors of glomerular endothelium. Signal of cascade of events leading to apoptosis and binding of leucocytes to endothelial cells which become thrombogenic and also cause the release of cytokines and chemokines. Also, a metalloproteinase called ADAM Ts13 is inactivated causing TTP which results in reduced blood flow to kidneys and CNS commonly.

Diagnosis

- ❖ By means of clinical symptoms
- ❖ A positive shiga toxin- EHEC test.
- ❖ Less than or equal to five percent of normal ADAMTS13 levels.

Treatment

- Usually dialysis is required.
- Some studies say antibiotics like fluoroquinolones may be beneficial.
- Monoclonal antibody like Eculizumab[109] can be used to treat atypical HUS.
- Plasmapheresis
- I.V immunoglobulins IgG
- Fibrinolytics
- Anti platelet agents
- Corticosteroids
- Anti oxidants
- Renal transplantation

Supportive therapy:

- Fluid and electrolyte balance
- B.P.control
- Prophylactic phenytoin for seizure control
- Azotemia control
- Optimizing nutrition
- Splenectomy as the last resort.

METHODS AND METHODOLOGY

STUDY DESIGN: Descriptive Study

STUDY PLACE: Paediatrics Department Chengalpattu Medical College and Hospital, Chengalpattu.

STUDY PERIOD: Sep. 2013 to Aug. 2014

STUDY POPULATION:

INCLUSION CRITERIA:

All children of 1-12 years with glomerular diseases admitted at Chengalpattu medical college.

EXCLUSION CRITERIA:

Children <1 years

Children>12 years

Congenital heart diseases

Acute severe respiratory diseases

Acute febrile illness

Acute poisoning

SAMPLE SIZE: 35

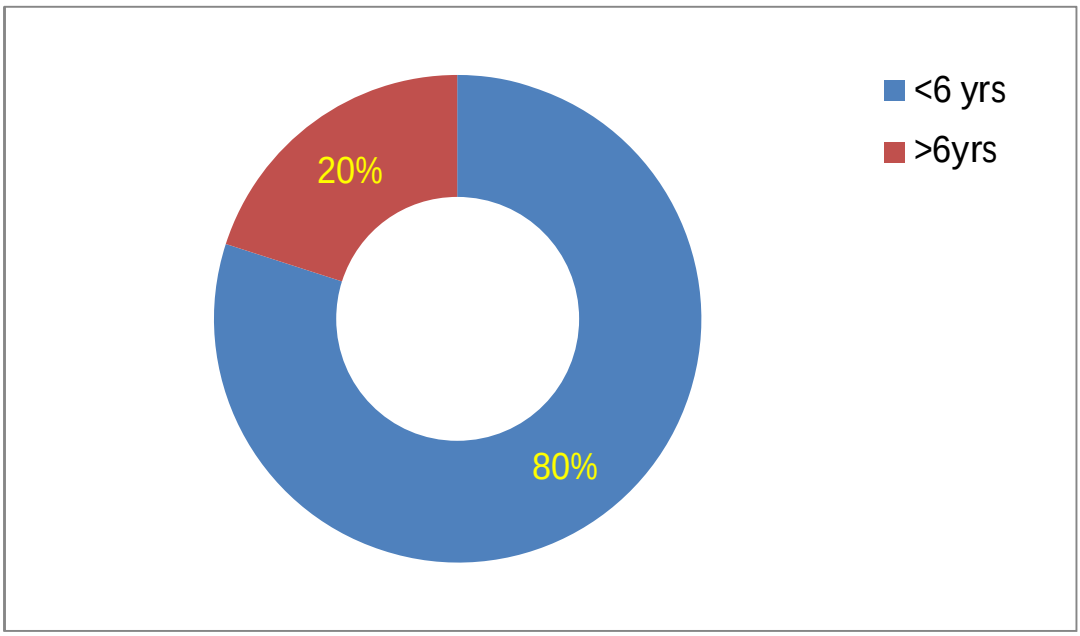
OBSERVATION

Table 8. Age Distribution

AGE AT PRESENTATION	NO. OF PATIENTS	PERCENT
<6 yrs	**28**	**80**
>6yrs	**7**	**20**
Total	**35**	**100**

Out of 35 patients 80%(N=28) were less than 6 years and 20%(N=7) were more than 6 years. The mean age of presentation is 4.87

Graph 1. Age Distribution



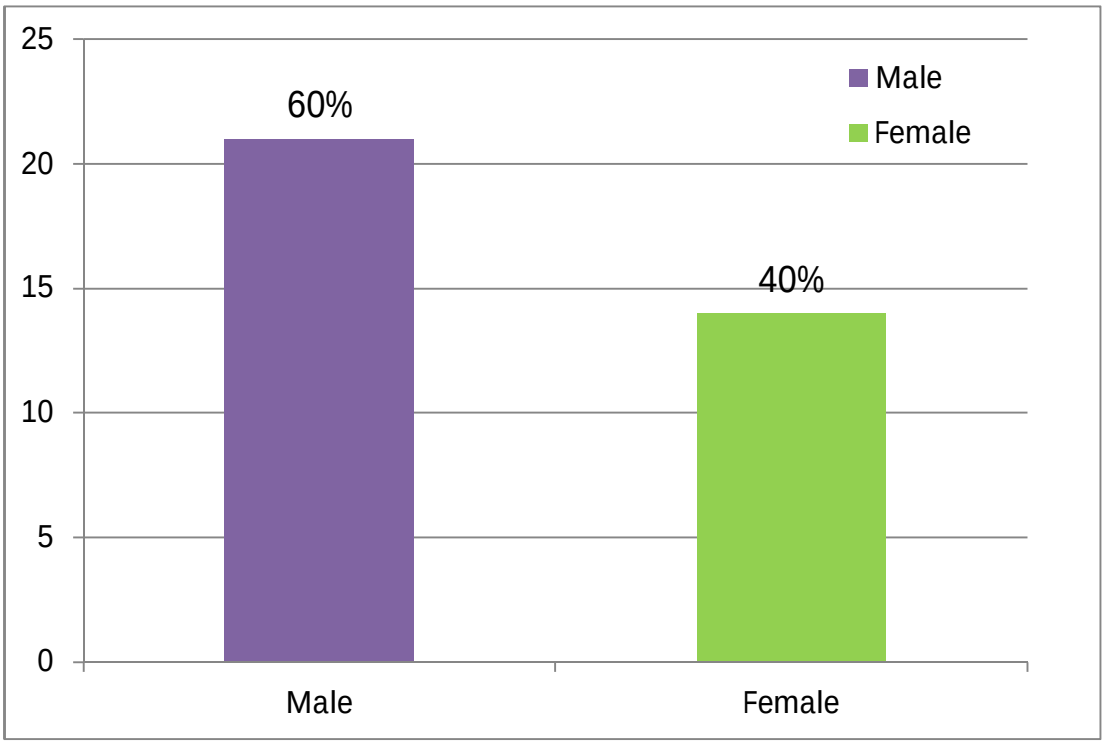
Shows the diagrammatic representation of age distribution of study group

Table 9. Sex distribution

SEX	NO.OF PATIENTS	PERCENT
Male	21	60
Female	14	40
Total	35	100

Out of 35 patients 60% (N=21) were males and 40%(N=14) were females. Male:Female ratio is 1.5:1.

Graph 2 Sex Distribution



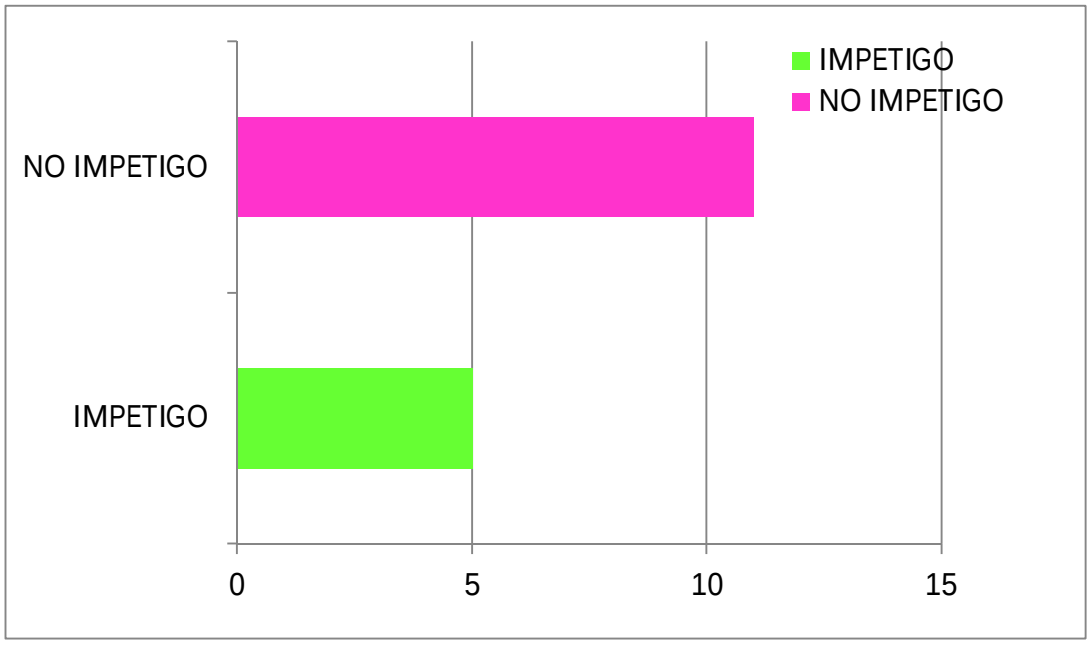
Shows the diagrammatic representation of sex distribution of study group.

Table 10. Past history-APIGN

PAST HISTORY	NO.OF PATIENTS	PERCENT
IMPETIGO	5	31.3
NO IMPETIGO	11	68.7
TOTAL	16	100

Out of 16 patients , 31.3% (N=5) were presented with Impetigo history among APIGN patients prior to admission.

Graph 3. Past history-APIGN



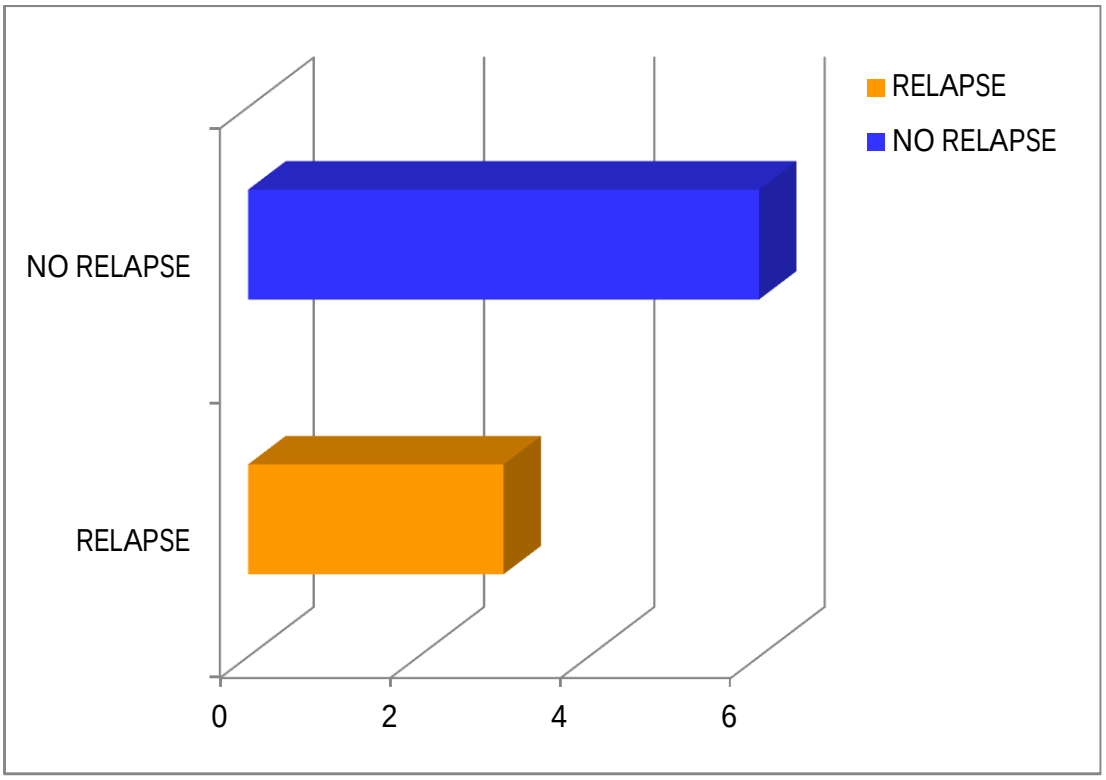
Shows the diagrammatic representation of Past History with Impetigo distribution of study group

Table 11. Past history – Nephrotic syndrome

PAST HISTORY	NO.OF PATIENTS	PERCENT
RELAPSE	3	33.3
NO RELAPSE	6	66.7
TOTAL	9	100

Out of 9 patients , 33.3% (N=3) were presented with Relapse history among NS patients prior to admission.

Graph 4. Nephrotic syndrome



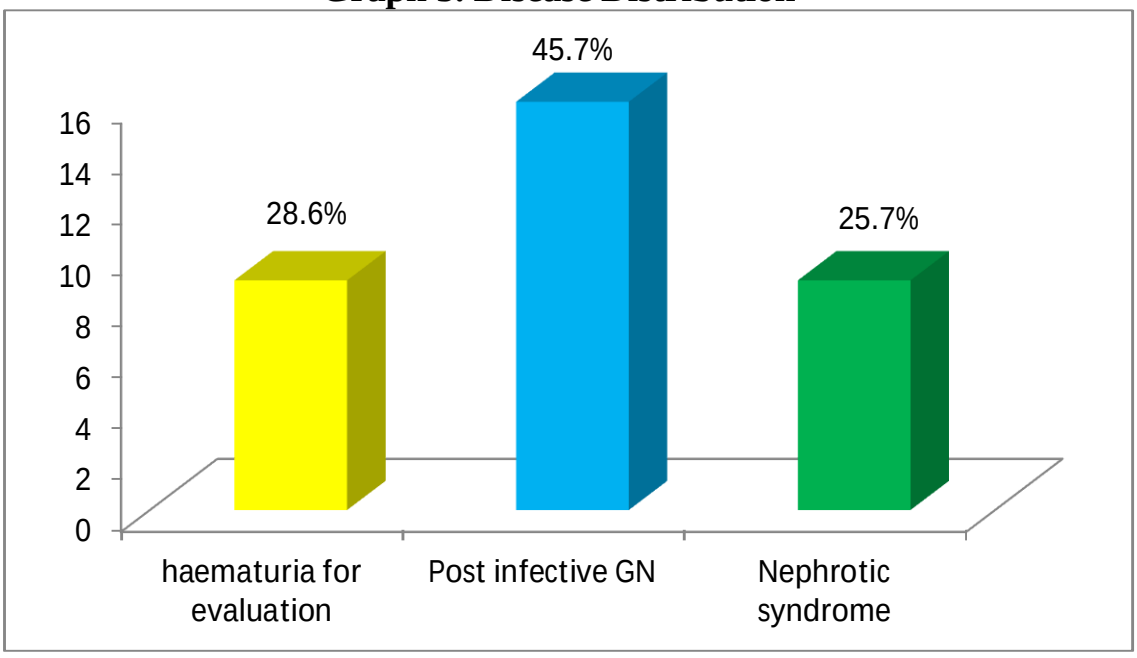
Shows the diagrammatic representation of Relapse History distribution of study group

Table 12. Disease Distribution

DISEASE DISTRIBUTION	NO. OF PATIENTS	PERCENT
HAEMATURIA FOR EVALUATION	10	28.6
POST INFECTIVE GN	16	45.7
NEPHROTIC SYNDROME	9	25.7
TOTAL	35	100

Out of 35 patients 45.7%(N=16) were Post Infective GN, 25.7%(N=9) were Nephrotic Syndrome , 28.6%(N=10) were Hematuria for evaluation.

Graph 5. Disease Distribution

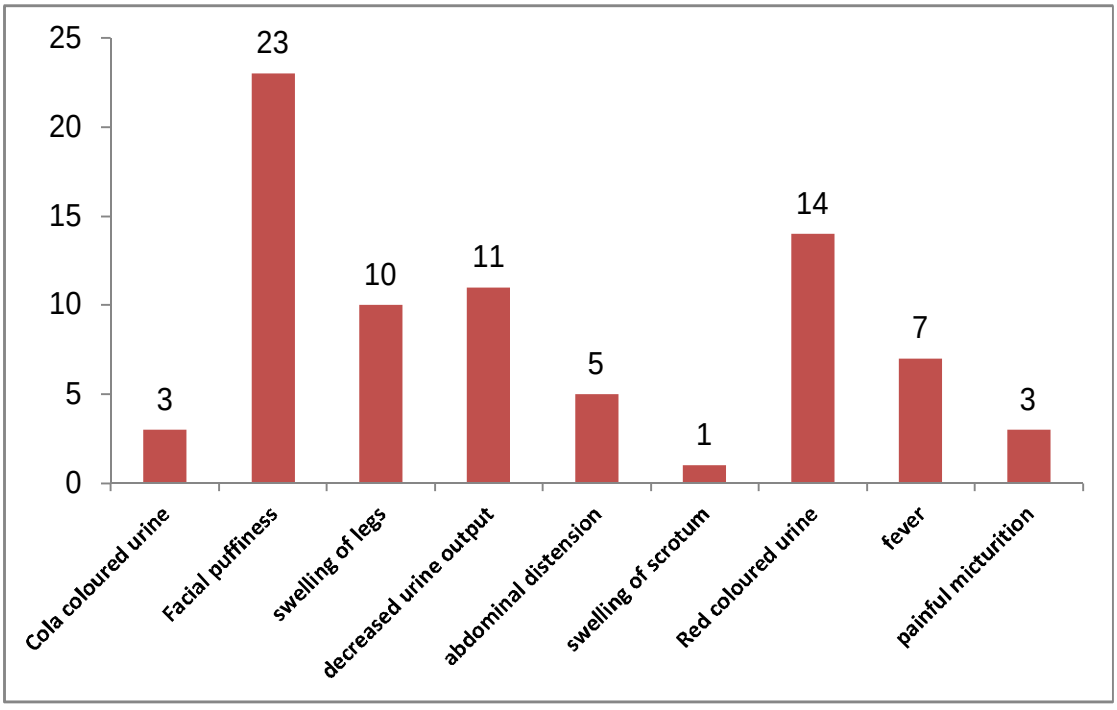


Shows the diagrammatic representation of disease distribution of study group

Table 13. Symptoms distribution

SYMPTOMS	NO.OF PATIENTS
Facial puffiness	23
Cola coloured urine	3
Swelling of legs	10
Decreased urine output	11
Abdominal distension	5
Red coloured urine	14
Fever	7
Painful micturition	3

Graph 6: Symptoms distribution



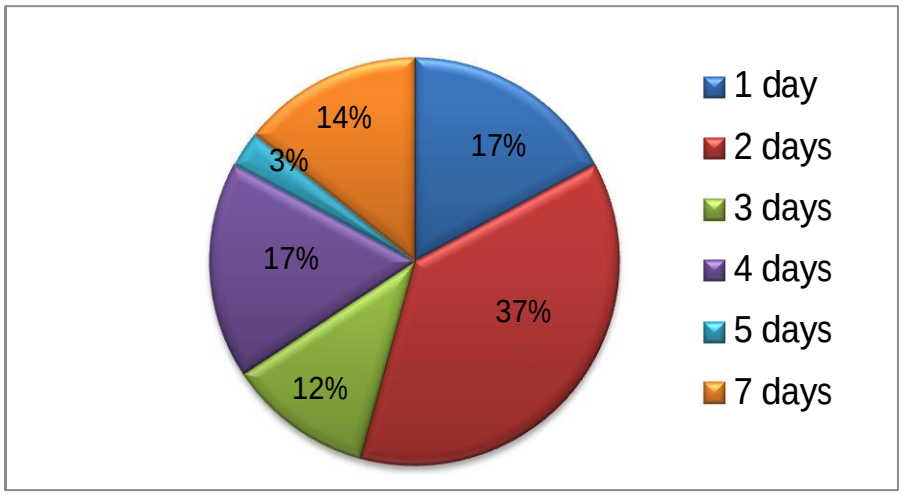
Shows the diagrammatic representation of Symptoms Distribution of

Table 14. Duration of disease

DAYS	NO.OF PATIENTS	PERCENT
1 DAY	6	17.1
2 DAYS	13	37.1
3 DAYS	4	11.4
4 DAYS	6	17.1
5 DAYS	1	2.9
7 DAYS	5	14.3
TOTAL	35	100

Out of 35 patients , 37.1%(N=13) were presented with 2 days,17.1%(N=6) were presents with 1 day and 4 days,14.3%(N=5) were presented with 7 days , 11.4% (N=4) were presented with 3 days and 2.9%(N=1) were presented with 5 days.

Graph 7: Duration of disease



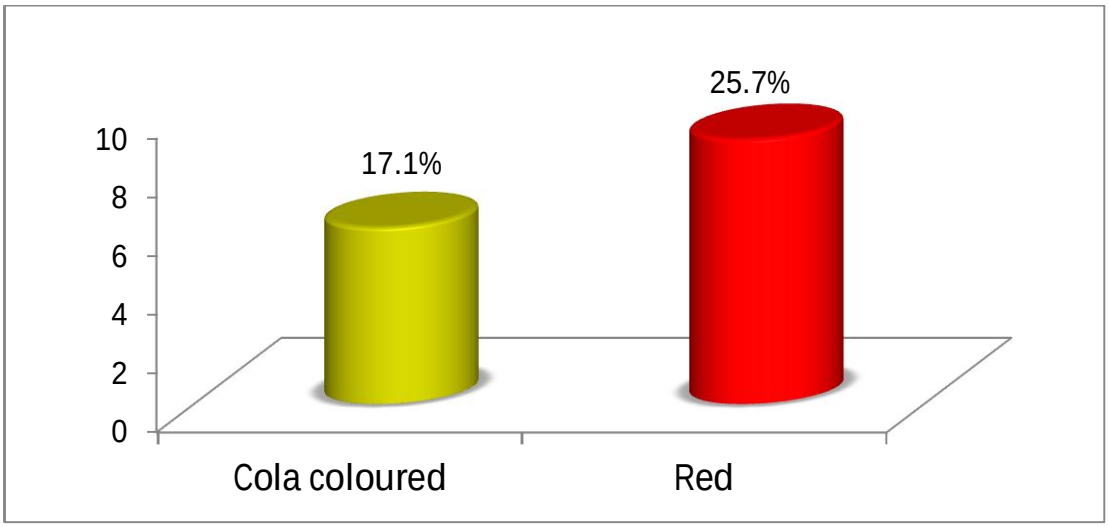
Shows the diagrammatic representation of duration of disease onset of study group

Table 15. Urine colour at presentation

URINE COLOUR	NO.OF PATIENTS	PERCENT
NORMAL	20	57.1
COLA COLOURED	6	17.1
RED	9	25.7
TOTAL	35	100

Out of 35 patients 25.7%(N=9) were presented with Red Coloured Urine and 17.1%(N=6) were presented with Cola Coloured Urine.

Graph 8: Urine colour at presentation



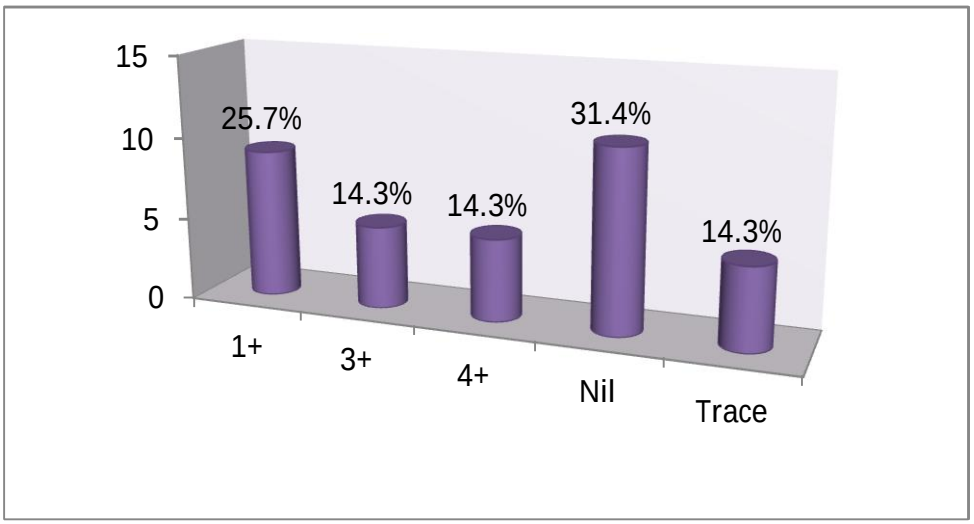
Shows the diagrammatic representation of Urine Colour distribution of study group

Table 16. Urine albumin

URINE ALBUMIN	NO. OF PATIENTS	PERCENT
1+	9	25.7
3+	5	14.3
4+	5	14.3
Nil	11	31.4
Trace	5	14.3
Total	35	100

Out of 35 cases, around 14.3% (N=5) had Urine Albumin 3 + , and around 14.3% (N=5) had Urine Albumin 4 + .

Graph 9. Urine albumin



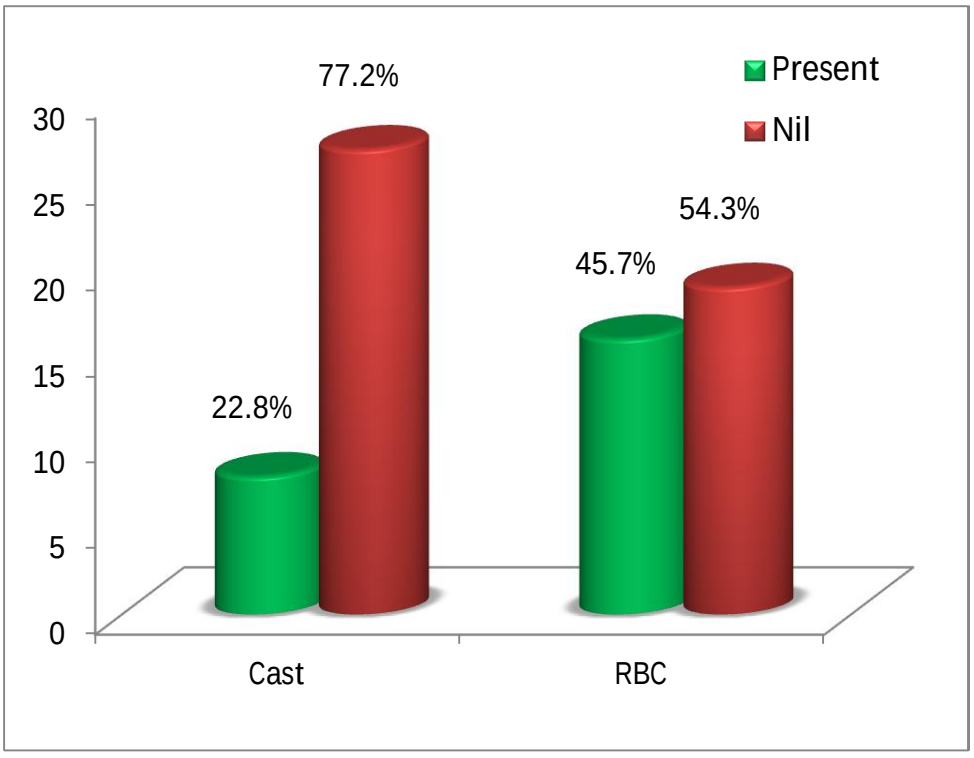
Shows the diagrammatic representation of Urine Albumin level of distribution of study group.

Table 17. Urine RBC/ CAST

URINE	NO.OF PATIENTS	PERCENT
RBC	16	45.7
CAST	8	22.8
NIL	11	31.5

Out of 35 patients 45.7%(N=16) were presented with Urine RBC and 22.8%(N=8) were presented with Urine cast.

Graph 10. Urine RBC/CAST



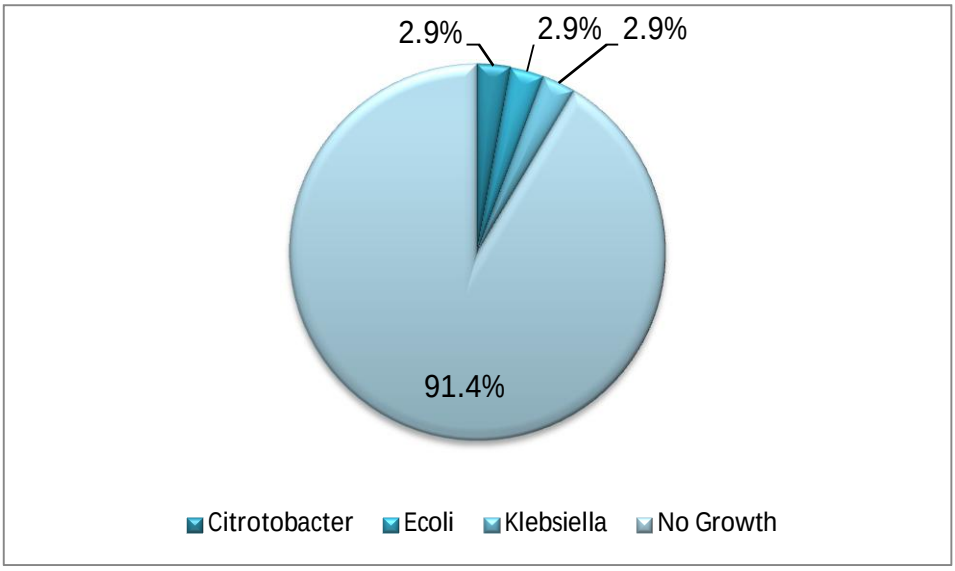
Shows the diagrammatic representation of Urine RBC/CAST distribution of study group.

Table 18. Urine culture & sensitivity

URINE CULTURE SENSITIVITY	NO.OF PATIENTS	PERCENT
CITROTOBACTER	1	2.9
ECOLI	1	2.9
KLEBSIELLA	1	2.9
NO GROWTH	32	91.4
TOTAL	35	100

Out of 35 patients, around 91.4% (N=32) were urine culture negative and 8.6%(N=3) were found positive.

Graph 11: Urine culture and sensitivity



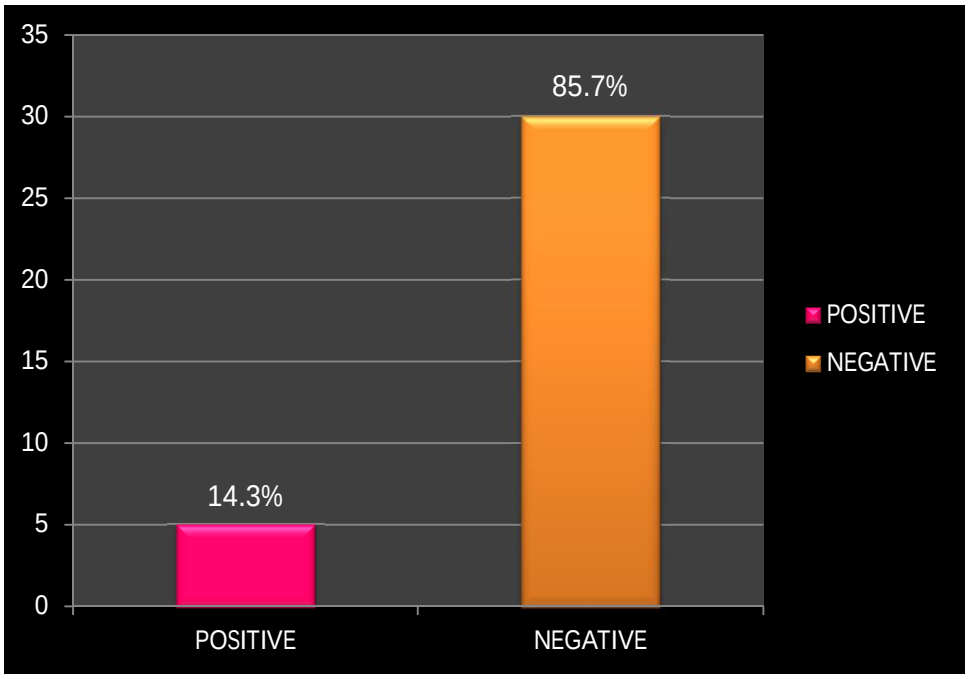
Shows the diagrammatic representation of urine culture growth distribution of study group.

Table 19. Aso titre

ASO TITRE	NO. OF PATIENTS	PERCENT
POSITIVE	5	14.3
NEGATIVE	30	85.7
TOTAL	35	100

Out of 35 patients, around 85.7% (N=30) were ASO titre negative and 14.3%(N=5) were found positive in PIGN patients.

Graph 12.Aso titre



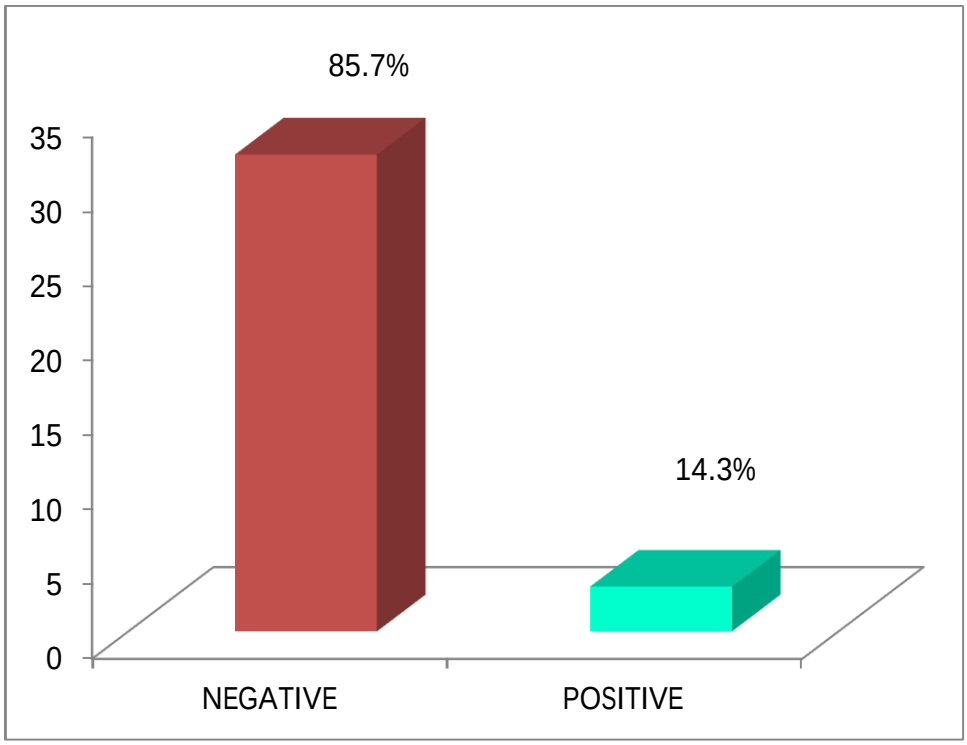
Shows the diagrammatic representation of ASO titre distribution of study group

Table 20. C-reactive protein

CRP	NO. OF PATIENTS	PERCENT
NEGATIVE	30	85.7
POSITIVE	5	14.3
TOTAL	35	100

Out of 35 patients, around 85.7% (N=30) were CRP negative and 14.3%(N=5) were found positive

Graph 13. C-reactive protein



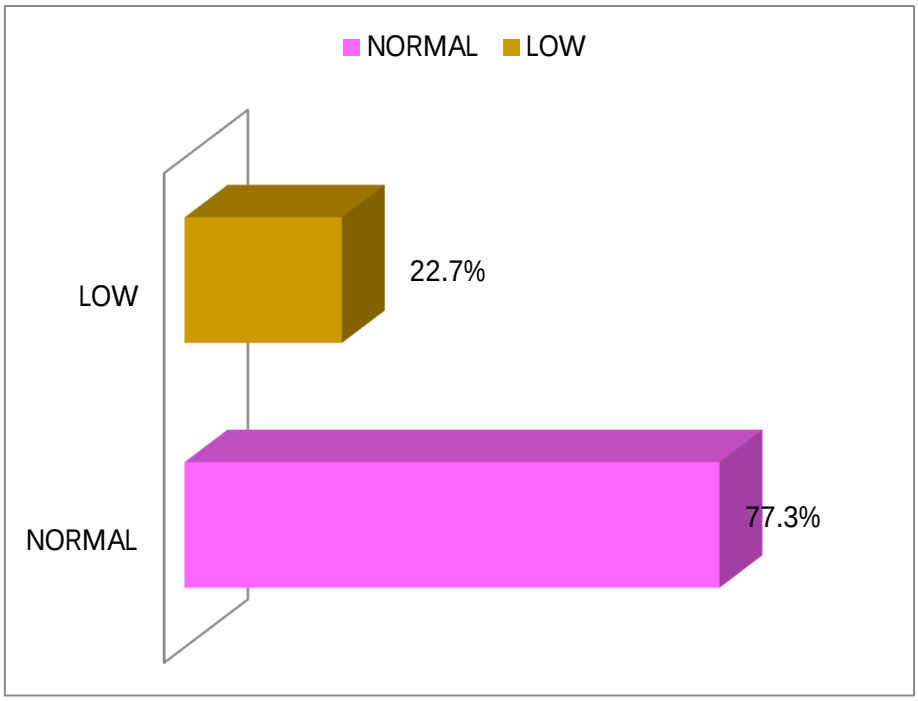
Shows the diagrammatic representation of C-Reactive Protein distribution of study group.

Table 21. Complement C3

COMPLEMENT C3	NO.OF PATIENT	PERCENT
NORMAL	17	77.3
LOW	5	22.7
TOTAL	22	100

Out of 35 patients 22 were done Complement C3 and found 77.3%(N=17) were normal, 22.7%(N=5) were found low Complement C3.

Graph 14. Complement C3



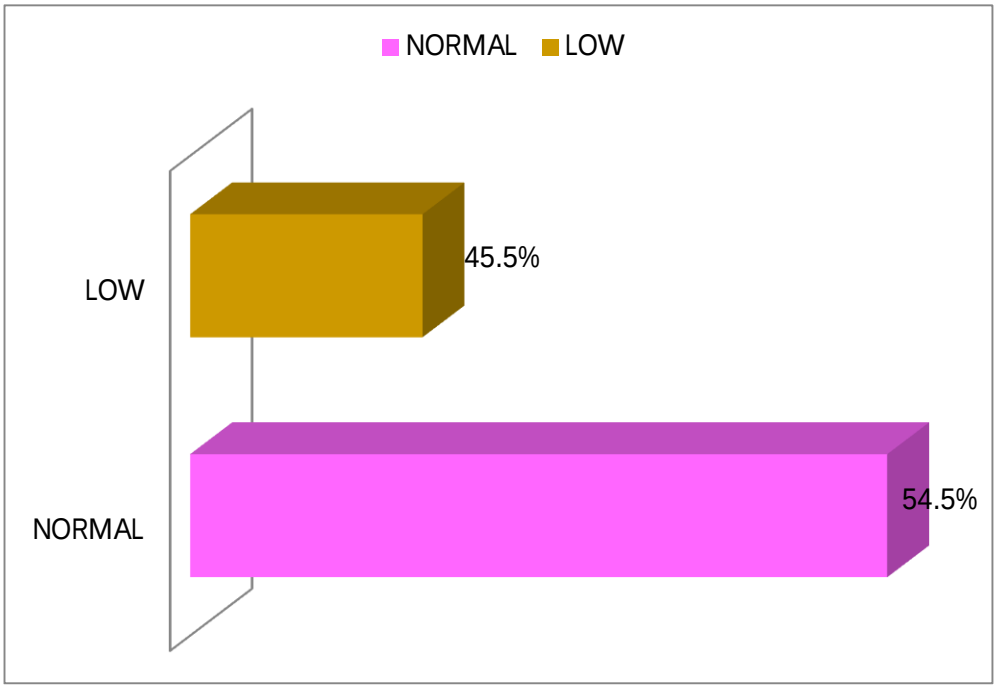
Shows the diagrammatic representation of Complement C3 distribution of study group.

Table 22. Complement C3 - PIGN

COMPLEMENT C3 - PIGN	NO.OF PATIENT	PERCENT
NORMAL	6	54.5
LOW	5	45.5
TOTAL	11	100

Out of 35 patients 11 were done Complement C3-PIGN and found 54.5%(N=6) were normal, 45.5%(N=5) were found low Complement C3.

Graph 15. Complement C3 - PIGN



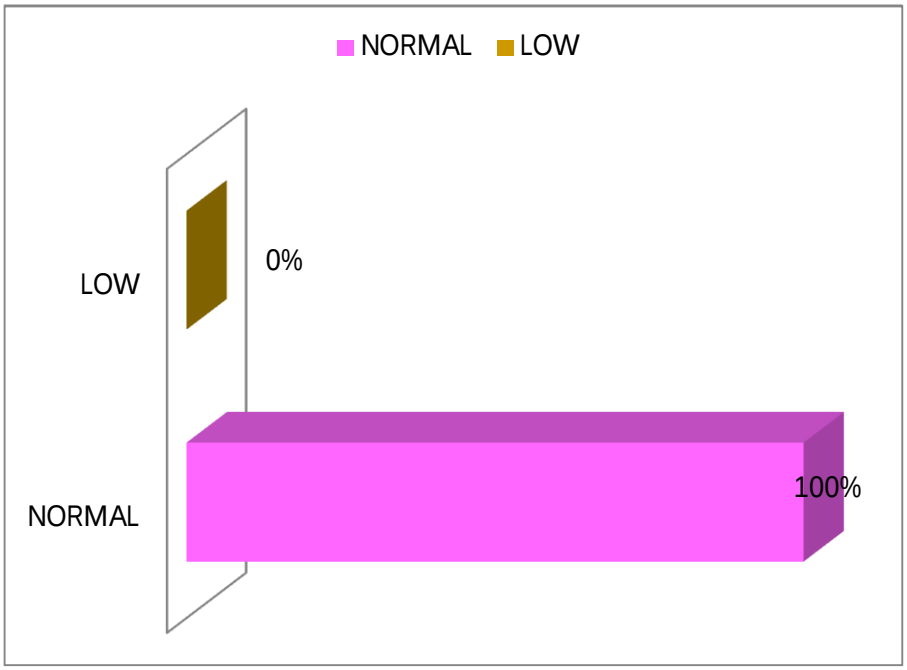
Shows the diagrammatic representation of Complement C3- PIGN distribution of study group

Table 23. Complement C3 - Haematuria

COMPLEMENT C3 - HAEMATURIA	NO.OF PATIENT	PERCENT
NORMAL	3	100
LOW	0	0
TOTAL	3	100

Out of 35 patients 3 were done Complement C3-Haematuria and found 100%(N=3) normal.

Graph 16. Complement C3 - Haematuria



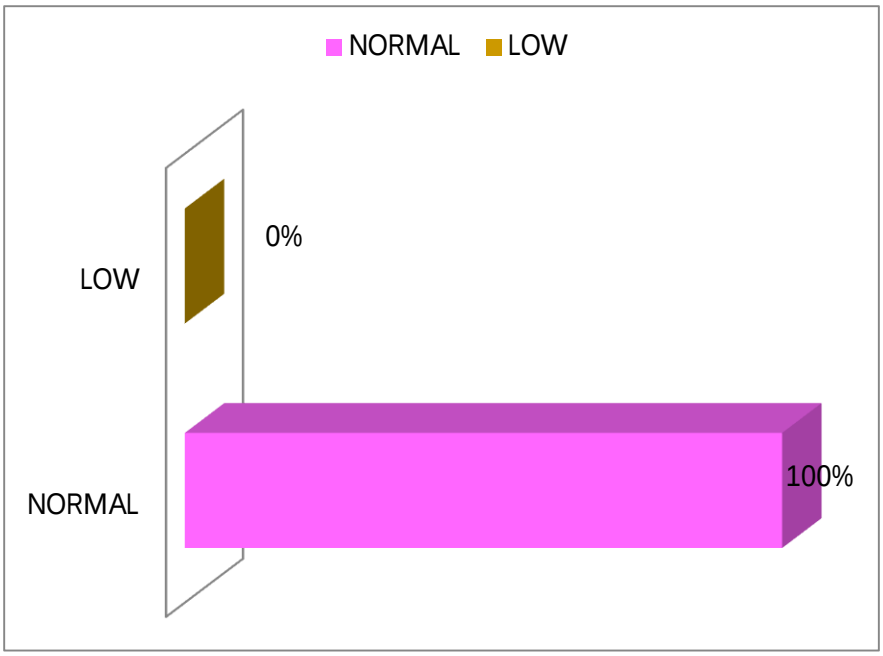
Shows the diagrammatic representation of Complement C3-Haematuria distribution of study group .

Table 24. Complement C3 - NS

COMPLEMENT C3 - NS	NO.OF PATIENT	PERCENT
NORMAL	8	100
LOW	0	0
TOTAL	8	100

Out of 35 patients 8 were done Complement C3 among NS patients and found 100%(N=8) were normal .

Graph 17.Complement C3-NS



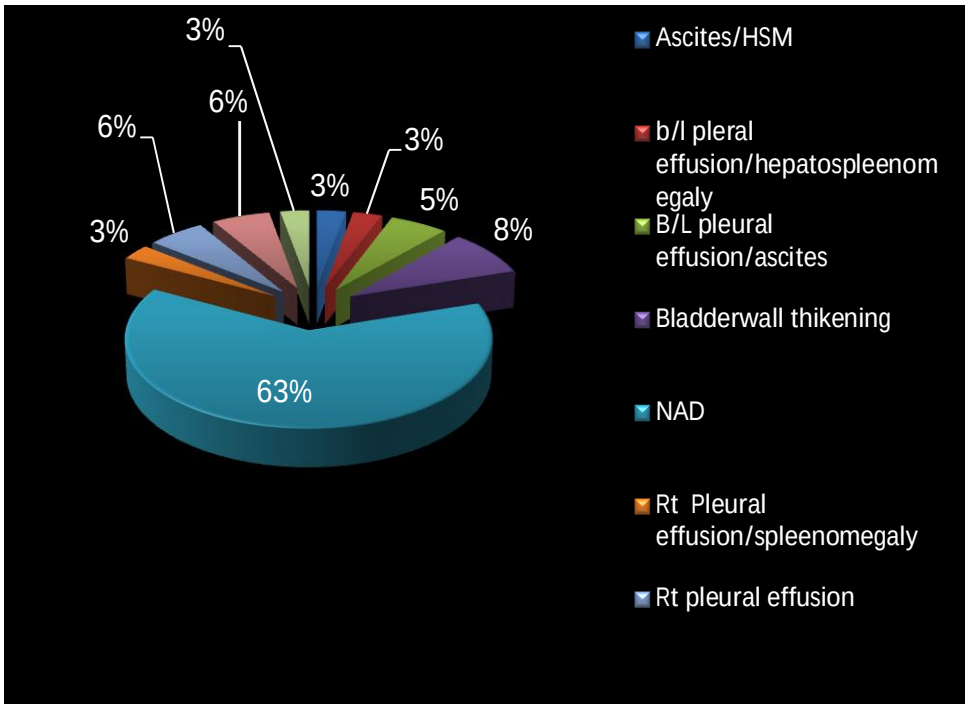
Shows the diagrammatic representation of Complement C3-NS distribution of study group.

Table 25. USG Abdomen

USG ABDOMEN	NO. OF PATIENTS	PERCENT
NORMAL	22	62.9
ABNORMAL	13	37.1

Out of 35 patients, around 62.9% (N=22) were Normal USG Abdomen and 37.1%(N=13) were found Abnormal.

Graph 18. USG abdomen



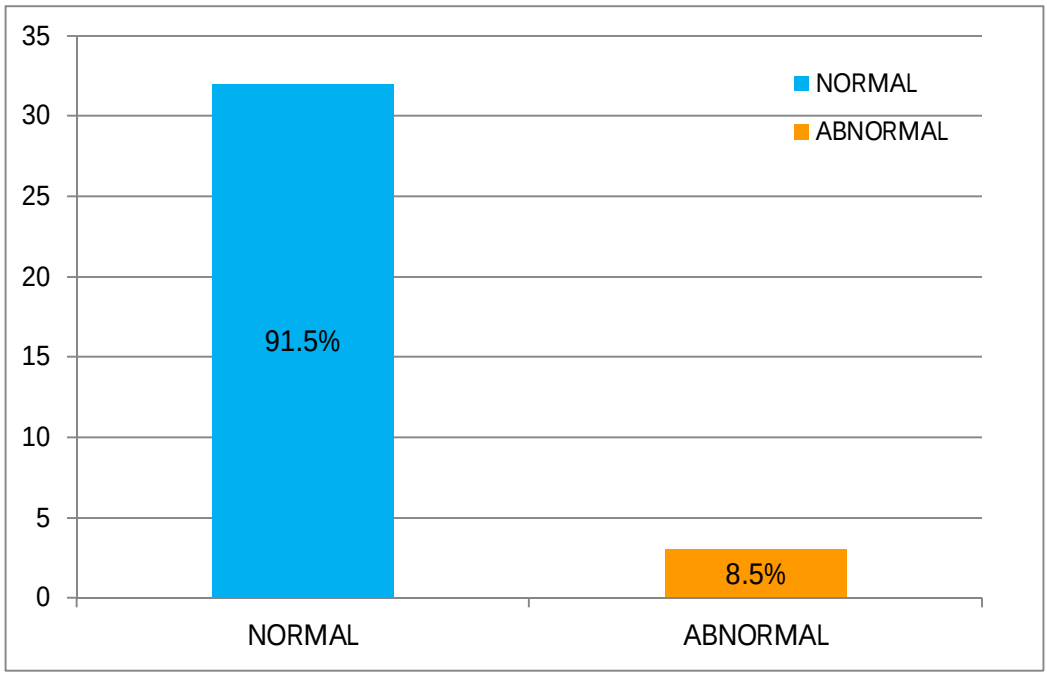
Shows the diagrammatic representation of USG Abdomen distribution of study group.

Table 26. CHEST X-RAY

CHEST X-RAY	NO. OF PATIENT	PERCENT
NORMAL	32	91.5
ABNORMAL	3	8.5
TOTAL	35	100

Out of 35 patients 91.5% (N=32) were Normal Chest X-ray and 8.5%(N=3) were found Abnormal.

Figure 19. Chest X-Ray

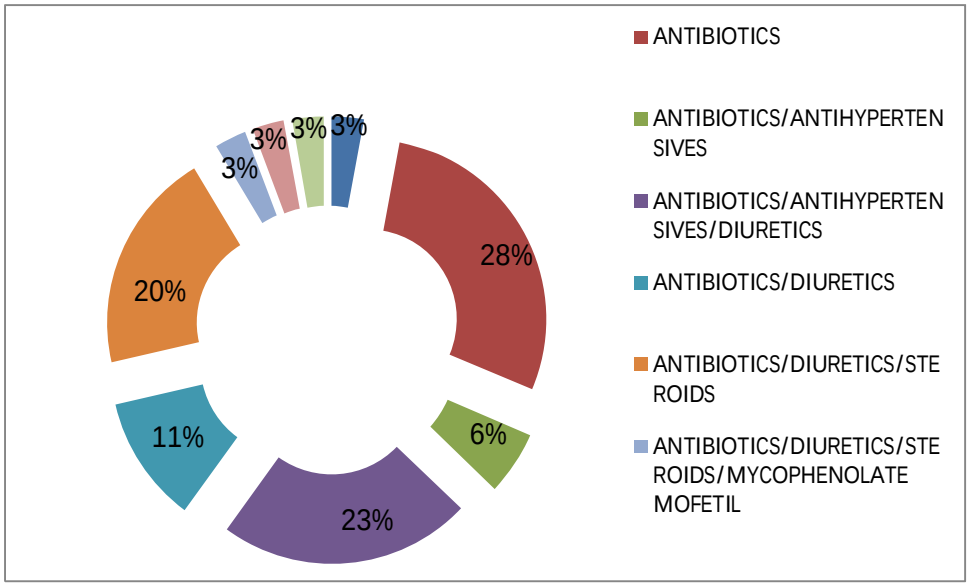


Shows the diagrammatic representation Chest X-ray distribution of study group.

Table 27. Improvement with treatment

IMPROVEMENT WITH	NUMBER OF PATIENTS	PERCENT
Nil	1	2.9
Antibiotics	10	28.6
Antibiotics/antihypertensives	2	5.7
Antibiotics/antihypertensives/diuretics	8	22.9
Antibiotics/diuretics	4	11.4
Antibiotics/diuretics/steroids	7	20
Antibiotics/diuretics/steroids/mycophenolate mofetil	1	2.9
Antibiotics/steroids	1	2.9
Plenty of fluids	1	2.9
Total	35	100

Graph 20. Improvement with treatment



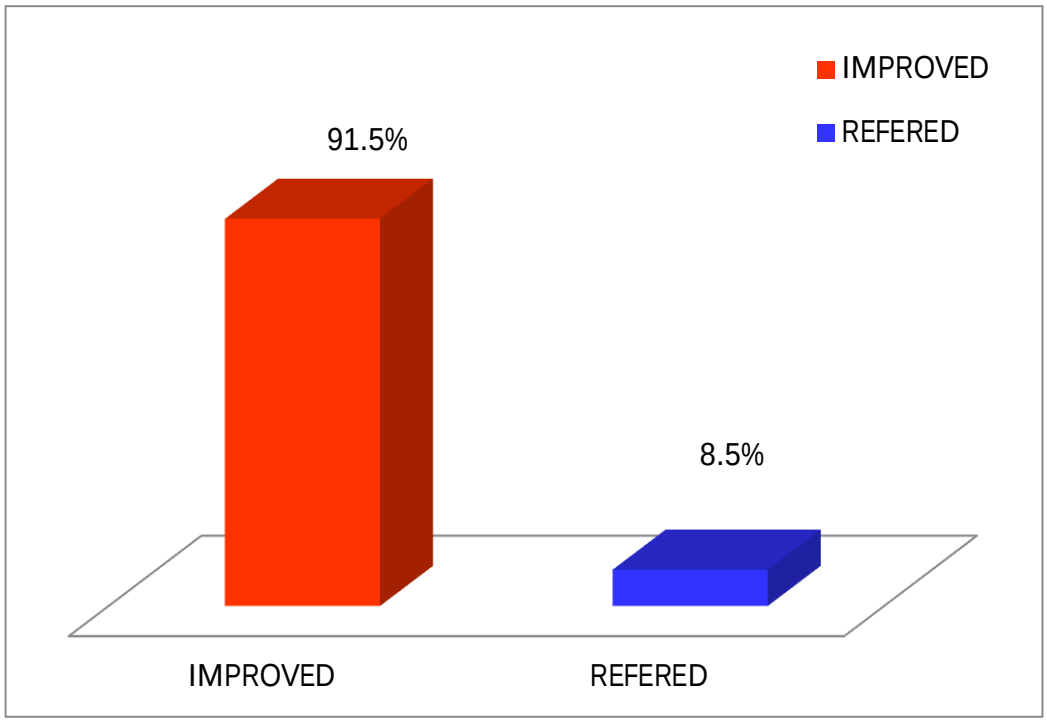
Shows the diagrammatic representation Improvement distribution of study group

Table 28.Prognosis Overall

PROGNOSIS	NO.OF PATIENTS	PERCENT
IMPROVED	32	91.5
REFERED	3	8.5
TOTAL	35	100

Out of 35 patients, around 91.5% (N=32) were improved Prognosis and 8.5% (N=3) were referred to higher institution.

Graph 21. Prognosis Overall



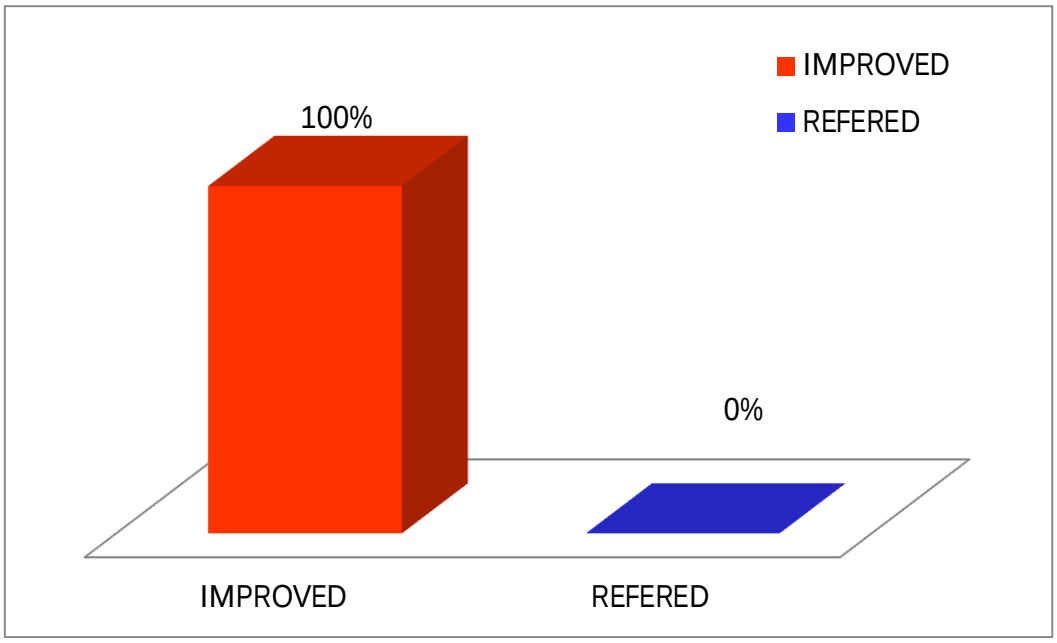
Shows the diagrammatic representation of Prognosis distribution of study group.

Table 29.Prognosis - PIGN

PROGNOSIS - PIGN	NO.OF PATIENTS	PERCENT
IMPROVED	16	100
REFERED	0	0
TOTAL	16	100

Out of 16 patients, 100% (N=16) were found improved Prognosis PIGN .

Graph 22. Prognosis - PIGN



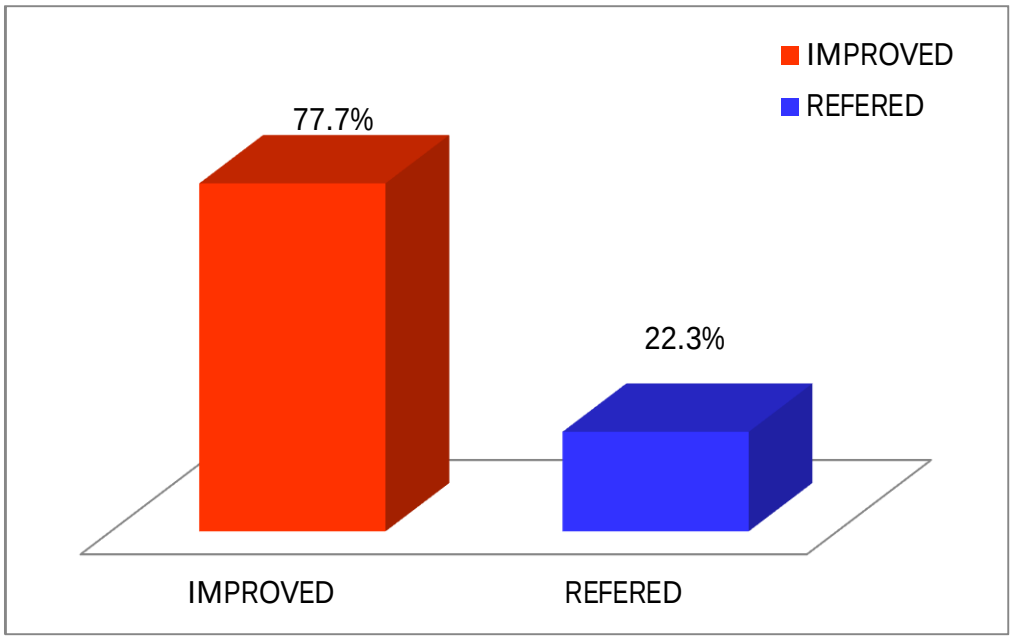
Shows the diagrammatic representation of Prognosis PIGN distribution of study group

Table 30. Prognosis - NS

PROGNOSIS - NS	NO.OF PATIENTS	PERCENT
IMPROVED	7	77.7
REFERED	2	22.3
TOTAL	9	100

Out of 9 patients, 77.7% (N=7) were improved Prognosis NS and 22.3%(N=2) were referred to higher institution.

Graph 23. Prognosis - NS



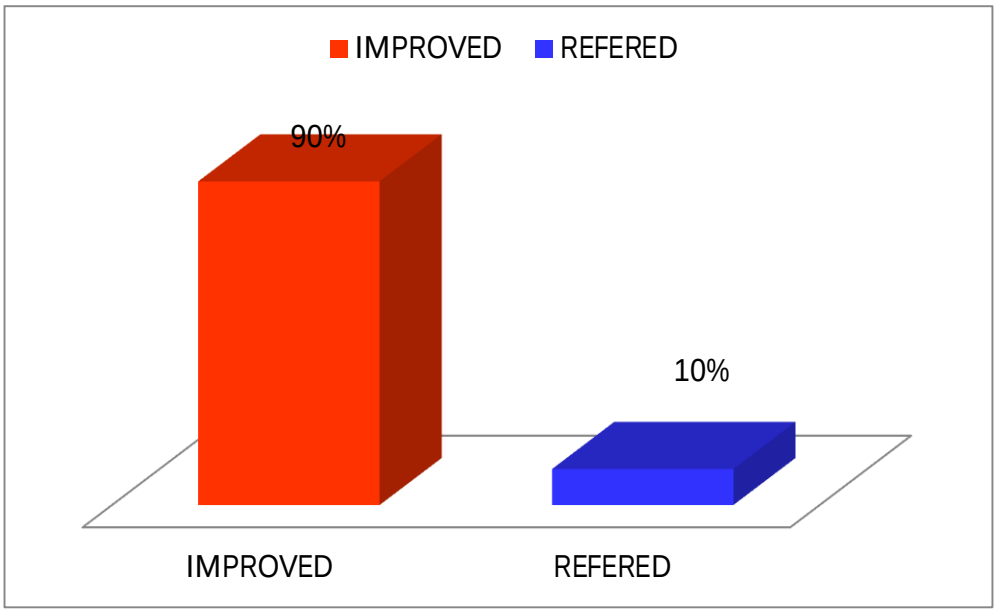
Shows the diagrammatic representation of Prognosis- NS distribution of study group.

Table 31. Prognosis - Haematuria

PROGNOSIS - HAEMATURIA	NO.OF PATIENTS	PERCENT
IMPROVED	9	90
REFERED	1	10
TOTAL	10	100

Out of 10 patients, 90% (N=9) were improved Prognosis-Haematuria and 10% (N=1) were referred to higher institution.

Graph 24. Prognosis - Haematuria



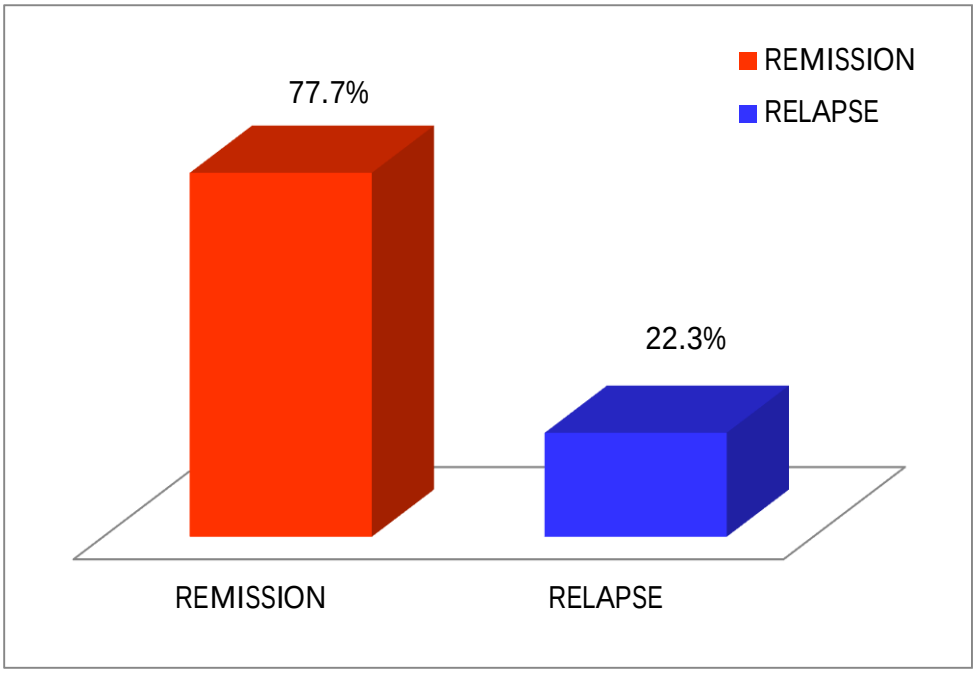
Shows the diagrammatic representation of Prognosis- Haematuria distribution of study group .

Table 32. Prognosis – NS on basis of steroid response

PROGNOSIS - NS ON BASIS OF STEROID RESPONSE	NO. OF PATIENTS	PERCENT
REMISSION	7	77.7
RELAPSE	2	22.3
TOTAL	9	100

Out of 9 patients, 77.7% (N=7) were Remitted Prognosis based on Steroid response and 22.3%(N=2) were referred to higher institution for Relapse.

Graph 25. Prognosis – NS on basis of steroid response



Shows the diagrammatic representation of Prognosis-NS basis on Steroid response distribution of study group.

DISCUSSION

1) AGE DISTRIBUTION

Out of 35 patients 80% (n=28) were less than 6 yrs and 20%(N=7) were more than 6 yrs .the mean age of presentation is 4.87.

In copp et al study[2],out of 432 children were less than or equal to 15 yrs, the mean age of presentation 8.96.

2) Sex distribution

Out of 35 patients 60%(n=21) were males and 40% (N=14) were females. Male :Female ratio is 1.5 : 1,

In fore man J.W chan JC study males accounted 54% and females 46%., male: female ratio is 1.2:1.

3) Past history

Out of 35 patients 31.3% among PIGN were presented with impetigo and 33.3%among NS were presented with relapse history.

4) Disease distribution

In our study out of 35 patients 45.7 %(N=16) were PIGN, 28.6%(N=10) were hematuria for evaluation,25.7(N=9)were Nephrotic syndrome.

5) Symptoms distribution

In our study ,out of 35 patients, most of the patients (N=23) were presented with peri orbital puffiness,14 were presented with red colored urine,10 were presented with swelling of legs, 11 presented with decreased urine output,3 were presented with cola colored urine ,7 were preseted with fever, 5 were presented with abdominal distension, 3 were presented with painful micturition.

6) Duration of disease

Out of 35 patients 37.1% were presented on day 2 of symptoms,14.3% were presented on 7^{th} day. Urine color at presentation out of 35 patients ,25.7% presented with red color urine,17.1% were presented with cola colored urine.

7) Urine Albumin

Out of 35 patients in our study 14.3 % (N=5) presented 4+ urine albumin , 14.3%(N=5) with 3+ urine albumin.

In Yong –hoog Park et al study, total 1044 school children were screened for proteinuria ,reported as 26.4% were found having isolated protenuria ,13.5 % were found having both protenuria and hematuria.

8) Urine culture and sensitivity:

out of 35 patient s 8.6% (N=3) were presented with positive urine culture found positive with Klebsiella,Ecoli,Citrotobacter. 91.4% were presented with no growth.

9) ASO titre

Out of 35 patients, 14.3% were presented with positive titre among PIGN,85.7% were presented withnegative titre,no positive titre was found among NS/Haematuria for evaluation.

In Schoff et al study , 150 cases were studied for a period of 3 years elevation of ASO titre was significantly higher to 96% in PIGN .

10) C reactive protein

Out of 35 patients 85.7% (N=30) were found CRP negative and 14.3% were found positive CRP among PIGN.

11) USG abdomen and chest xay

Out of 35 patients 62.9% (N=22) were found normal USG abdomen and 31.7%(N=13) were found abnormal with pleural effusion, hepatospleenomegaly among NS patients, bladder wall thickening for hematuria evaluation .

Chest xray showed 8.5%(N=3) were found abnormal and 91.5 %(N=32) were found normal with pleural effusion among NS patients.

12) Complement C3

Out of 35 patients, 22 were done serum complement,among this 77.3%(N=17) were found normal in both NS and PIGN patients. 22.7%(N=5) were found low complement values among PIGN pteints. After 6 weeks,repeat complement C3 test was done,Low complement patients were found normal C3 values in 100% patients. In Schoff et al study , 150 cases were studied for a period of 3 years c3 values are lower in 88% of children of PIGN and returned to normal in 95%.

13) Improvement with treatment

Out of 35 patients,28.6% were improved with antibiotics,5.7% were improved with only antihypertensive alone,11.4% were improved with diuretics alone,22.9% were improved with antihypertensives and diuretics, 2.9% steroids alone, 20% were improved with diuretics and steroids, 2.9% were improved with diuretics, steroid and mycophenolate mofetil,2.9% were improved only with fluids.

14) Prognosis

Out of 35 pateints,91.5% were improved with proper management, 8.5% were referred to higher institution for follow up care. Among PIGN patients, (N=16) patients were improved with antibiotics, antihyper tensives and diuretics. None were referred.

Among NS,77.7% were improved with diuretics and steroids and found remitted. 22.3% were found steroid dependent. Among haematuria for evaluation,90%were improved with proper management.10% were referred to higher institution as that child had recurrent haematuria and he was evaluated for ? IgAnephropathy for whom renal biopsy is advised.

SUMMARY

In our study, 35 patients who admitted or complaints of glomerular symptoms were taken. Out of this, 16 patients were diagnosed as PIGN,9 were NS and 10 were found haematuria for evaluation.

Among 16 PIGN patients, all patients were improved.7 out of 9 patients were found remitted among NS patients, 2 were referred to higher institution, they were found to be steroid dependent NS.

Among 10 haematuria for evaluation cases 9 were improved, only one was referred to higher institution for recurrent haematuria for whom renal biopsy was advised. On following up that child they have not done renal biopsy till now.

CONCLUSION

Based on the results of our study we conclude that,

- Our clinical profile is concordant with glomerular diseases in children.
- Both PIGN &Minimal change NS in children can be properly evaluated and treated promptly which shows better outcome in our study.
- Early diagnosis, proper treatment, and regular follow up care prevents end stage kidney disease among children.

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ANNEXURE

ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு : செங்கல்பட்டு மருத்துவமனை கல்லூரியில் சிறுநீரக (மயிர்துளைபந்து) பிரச்சனைகளுக்காக சேரும் குழந்தைகளின் மருத்துவக் குறிப்புகள் மற்றும் விளைவுகள் சம்பந்தமாக ஆராய்ச்சி.

பெயர் : தேதி :

வயது : ஆராய்ச்சி சேர்க்கை எண்.:

பால் :

- இந்த ஆராய்ச்சியின் விவரங்களும், அதன் நோக்கங்களும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது.
- எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்துகொண்டு எனது சம்மதத்தை தெரிவிக்கிறேன்.
- இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின்பேரில் நான் பங்கு பெறுகிறேன் மற்றும் நான் இந்த ஆராய்ச்சியிலிருந்து எந்நேரமும் பின்வாங்கமாட்டேன் என்பதையும், அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் நான் புரிந்துகொண்டேன்.
- இந்த ஆராய்ச்சியின் விவரங்களை கொண்ட தகவல் தாளை பெற்றுக் கொண்டேன்.
- நான் என்னுடைய சுயநினைவுடன் மற்றும் முழு சுதந்திரத்துடன் இந்த மருத்துவ ஆராய்ச்சியில் என் குழந்தையை சேர்த்துக் கொள்ள சம்மதிக்கிறேன்.

பெற்றோர் கையொப்பம்

ஆராய்ச்சி தகவல் தாள்

- செங்கல்பட்டு அரசு பொது மருத்துவமனையில் குழந்தைகள் நலப்பிரிவில் சிறுநீரகம் சம்மந்தமான நோய்களுக்கான ஆராய்ச்சி நடைபெற்று வருகிறது.

- இதில் மருத்துவமனைக்கு சிறுநீரக (மயிர்துளைப்பந்து) பிரச்சனைகள் சம்மந்தமான நோய்களுக்காக சேரும் குழந்தைகளின் மருத்துவ குறிப்புகள் மற்றும் விளைவுகள் பற்றி ஆய்வுகள் மேற்கொள்ளப்படுகிறது.

- உங்கள் குழந்தையும் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். இதனால் உங்கள் குழந்தைக்கு எந்த பாதிப்பும் ஏற்படாது என்பதை தெரிவித்துக் கொள்கிறோம்.

- முடிவுகளை அல்லது கருத்துக்களை வெளியிடும்போது அல்லது ஆராய்ச்சியின்போது தங்களது குழந்தைகளின் பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்மோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

- இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின்பேரில்தான் இருக்கிறது. மேலும் உங்கள் குழந்தை எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறேன்.

- இந்த சிறப்பு பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின்போது அல்லது ஆராய்ச்சியின் முடிவின்போது தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

CASE PROFORMA

I.P.NO:

NAME	**:**
AGE	:
SEX	:
ADDRESS	:
PH No.	:
DATE OF ADMISSION	:
DATE OF DISCHARGE/REFERRAL	:
INFORMANT	:
REFERRED FROM	:
PRE HOSPITAL TREATMENT	:
NATIVE TREATMENT	:
IN PATIENT	:
OUTPATIENT	:
REFERRAL DIAGNOSIS	:
PROVISIONAL DIAGNOSIS	:
FINAL DIAGNOSIS	:
CHIEF COMPLAINTS	:

HISTORY OF PRESENTING ILLNESS

GASTRO INTESTINAL	YES	NO	DURATION
VOMITING			
JAUNDICE			
ABDOMINAL PAIN			
SWELLING IN ILIAC			
LOOSE STOOLS			
ABDOMINAL			
BLOOD IN STOOLS			
BLOOD IN VOMIT			
CONSTIPATION			

RENAL SYSTEM	YES	NO	DURATION
FACIAL PUFFIN ESS			
NOT PASSED URINE			
RED COLOURED URINE			
WHITE COLOURED			
PAINFUL MICTURITION			
POLYURIA/POLYDIPSIA			
NOCTURNAL			
FOULSMELLING URINE			

RESPIRATORY SYSTEM	**YES**	**NO**	**DURATION**
FEVER			
COUGH/COLD			
DIFFICULTY IN BREATHING			
CHEST PAIN			

CARDIOVASCULAR SYSTEM	**YES**	**NO**	**DURATION**
CHEST PAIN			
DYSPNOEA			
ORTHOPNOEA			
PND			
PALPITATION			

CENTRAL NERVOUS SYSTEM	**YES**	**NO**	**DURATION**
HEADACHE			
FACIAL WEAKNESS/ HEMIPLEGIA			
LOSS OF CONSCIOUSNESS			
CONVULSIONS			
ALTERED SENSORIUM			
BLINDNESS			
VOMITING			

OTHERS:	**YES**	**NO**	**DURATION**
IRRITABILITY			
FAILURE TO THRIVE			
BONY DEFORMITIES			

PAST HISTORY:	**YES**	**NO**	**DURATION**
SIMILAR ILLNESS			
SORE THROAT			
SKIN INFECTION			
JAUNDICE			
FEVER WITH RASH			
UTI			
H/O S/O INFECTIVE ENDOCARDITIS			
GUM BLEEDING/BONE PAIN			
FEVER WITH ARTHRALGIA			

FAMILY HISTORY:	**YES**	**NO**	**DURATION**
SIMILAR ILLNESS			
TB CONTACT			

BIRTH HISTORY : LN/LSCS :

ADMISSION IN NICU :

DEVELOPEMENTAL HISTORY :

IMMUNISATION HISTORY :

CLINICAL EXAMINATION:	**YES**	**NO**
CONSCIOUS		
ALERT/LETHARGIC		
FEBRILE		
WELL/MALNOURISHED		
FACIAL PUFFINESS		
ANAEMIA		
CLUBBING/CYANOSIS		
JAUNDICE		
IMPETIGO/RASH		.<,
LYMPHADENOPATHY		
PEDAL EDEMA		
TONSILLITIS		
PETECHIAE/PURPURA		

VITALS **ANTHROPOMETRY:**

HR:	HEIGHT:	MAC:
RR:	WEIGHT:	HC:
JVP:	AT ADMISSION:	AC
TEMP:	AT DISCHARGE:	CC
BP:		

SYSTEMIC EXAMINATION:	**YES**	**NO**
CVS: SI S2		
MURMUR		
OTHERS/GALLOP		
RS: BAE		
ADDED SOUNDS		
P/A: SOFT		
DISTENSION		
HEPATOMEGALY		
SPENOMEGALY		
FLUID THRILL		
SHIFTING DULLNESS		
CNS:TONE		
PERL		
NEUROLOGICAL DEFICIT		
GENITOURINARY: ULCERS		
PHIMOSIS/PARA PHIMOSIS		
SWELLING		
SCROTAL/VULVAL EDEMA		
INGUINAL NODES		
B/LCRYPTORCHIDISM		

INVESTIGATIONS:

DATE:				
CBC:TC DC ESR HB PCV PLATELET				
PERIPHERAL SMEAR				
URINE: SUGAR				
ALBUMIN				
DEPOSITS				
MACROSCOPIC EX: COLOUR				
MICROSCOPIC EX: RBC				
WBC				
CASTS				
URINE PROTEIN : SPOT PCR				
24 HR URINE PROTEIN				
URINE C/S				
BLOOD UREA				
SERUM CREATININE				
SERUM ELECTROLYTES				
SERUM CHOLESTEROL				
TOTAL PROTEIN				
ALBUMIN				
GLOBULIN				
ASO TITRE				
ANTI DNASETEST				
MANTOUXTEST				
CRP				
C3 LEVEL				
C4 LEVEL				

IMAGING STUDIES:

DATE:				
PLAIN XRAY CHEST				
USG ABDOMEN				
IV PYELOGRAM				
MCU				
RADIONUCLEOTIDE IMAGING				

RENAL BIOPSY				
ECG				
ECHO				
CT SCAN				
OTHERS				

MANAGEMENT : **DURATION**

BED REST :

SALT RESTRICTION :

FLUID RESTRICTION :

T.FUROSEMIDE :

T.NIFEDIPINE :

ANTIBIOTICS-PENICILLIN :

ERYTHROMYCIN :

STEROIDS-PREDNISOLONE :

CONDITION AT DISCHARGE :

CLINICAL PROFILE AND OUTCOME OF GLOMERULAR DISEASES IN CI

									BP	
S. No	Name	Age	Sex	Diagnosis	Symptoms	Duration	Past / Family History	Signs	AD	DIS
1	Praveen Kumar	3 1/2	M	H.E	Red coloured urine	1 Day		Peri orbital puffiness	90/70	90/70
2	Naresh	4	M	PIGN	Red coloured urine , facial puffiness ,abdominal distention	1 Day	Impetigo 10 days back	Peri orbital puffiness/healed impetigo scars legs	130/100	100/70
3	Deepika	4 1/2	F	NS	Facial puffiness/ swelling of legs	2 Days	Similar history 6 months back	Peri orbital puffiness/ B/L pedal edema	90/70	90/70
4	Krishka	1 1/2	F	NS	Facial puffiness/ swelling of legs	2 Days		Periorbital puffiness/b/l pedal edema	90/70	90/70
5	Vignesh	9	M	HE	Cola coloured urine/fever	1 Day	Similar history 18 months back/treated for PIGN	Peri orbital puffiness/swelling of legs	90/70	90/70
6	Varadharaj	4	M	PIGN	Facial puffiness/ swelling of legs/decreased urine o/p	3 Days		Peri orbital puffiness/lt submandibular node	100/90	90/70
7	Thavasree	3	F	HE	Red coloured urine	3 Days			90/60	80/60
8	Deepak	6	M	PIGN	Facial puffiness/swelling of scrotum	3 Days		Peri orbital puffiness/impetigo legs	130/90	100/60
9	Ramachandran	11	M	PIGN	Facial puffiness/swelling of legs/decreased urine o/p	2 Days		Peri orbital puffiness/impetigo legs	128/90	90/60
10	Elangovan	6	M	HE	Red coloured urine/pain during micturition	7 Days		Peri orbital puffiness	94/70	90/60
11	Kavisree	6	F	PS	Facial puffiness/red coloured urine	7 Days		Peri orbital puffiness	94/70	90/60

12	Malini	5	F	SDNS	Facial puffiness/decreased urine o/p/swelling of legs/abdominal distension	1 Day	Similar history 6 months back	Peri orbital pufiness/B/L pedal edema	90/60	80/60
13	Kamelesh	3	M	PIGN	Red coloured urine/facial puffiness/decreased urine o/p	2 Days		Peri orbital puffiness	120/70	90/60
14	Ajay	10	M	PIGN	Facial puffiness	7 Days		peri orbital puffiness	120/80	100/70
15	Rithika	5	F	PIGN	Facial puffiness/red coloured urine	4 Days		Peri orbital puffiness	140/100	90/70
16	Likesh	2	M	PIGN	Facial puffiness/swelling of legs	4 Days		Peri orbital puffiness/B/L pedal edema	120/80	90/70
17	Jothipriya	6	F	PIGN	Facial puffiness/decreased urine o/p	4 Days		Peri orbital puffiness/B/L pedal edema	140/90	100/70
18	Kishore	4	M	PIGN	Facial puffiness	4 Days		Peri orbital puffiness/B/L pedal edema	100/70	90/60
19	Vijay	8	M	NS	Facial puffiness/decreased urine/abdominal distension	4 Days	Fever with rash 2 weeks back	Peri orbital puffiness/healed impetigo scars legs	110/70	100/70
20	Dharshan	3 1/2	M	HE	Red coloured urine/painful micturition	2 Days			90/60	
21	Dilipan		M	HE	Red coloured urine	1 Day			90/50	
22	Stalin	9	M	NS	Facial puffiness/decreased urine o/p/swelling of legs/fever	4 Days		Peri orbital puffiness/b/l pedal edema/b/l scrotal swelling	120/80	100/60
23	Raja	2	M	NS	Facial puffiness/decreased urine o/p/swelling of legs/fever	5 Days	H/o dog bite 1week back	Peri orbital puffiness/b/l pedal edema	120/80	90/70
24	Suriya	7	M	PIGN	Cola coloured urine/fever	3 Days		Healed impetigo legs	100/70	90/70

25	Prathesh	6	M	PIGN	Facial puffiness/decreased urine o/p/swelling of legs/fever	2 Days	Impetigo 1 week back	Peri orbital puffiness/healed impetigo scars legs	90/70	80/70
26	Vigneshwaran	3 1/2	M	NS	Red Coloured urine/facial puffiness	2 Days		Peri orbital pufiness	100/70	90/80
27	Deepika	6	F	PIGN	Cola coloured urine/fever	2 Days		Healed impetigo legs	130/50	90/70
28	Jeevan	2 1/2	M	HE	Red coloured urine	2 Days			90/60	90/70
29	Gopika	6	F	HE	Red coloured urine	2 Days			90/70	90/70
30	Setharaman	7	M	PIGN	Facial pufiness/fever/painful micturition	7 Days		Periorbital puffiness	100/70	90/70
31	Jesintha	3	F	NS	Facial puffiness/abdominal distension	1 Day		Periorbital puffiness	90/70	90/70
32	Hemavathy	3	F	SDNS	Facial puffiness/abdominal distension/swelling of legs/decreased urine output	7 days	Similar illness 1 yr back	Periorbital puffiness,abd.distension,b/l pedal edema	90/70	90/60
33	Manisha	1.6	F	HE	Red coloured urine	2 days			90/70	90/60
34	Abinaya	2	F	HE	Red coloured urine	2 days			90/60	90/70
35	Padmapriya	4	F	PIGN	Red coloured urine/facial puffiness/decreased urine o/p	2 days	Impetigo legs 10 days back	Periorbital puffiness, healed impetigious lesions	130/80	100/80

HILDREN ADMITTED--SEP2013-AUG2014----MASTER CHART

Weight			Urine						Blood				
AD	Dis	Hb %	Macro	Albumin	Deposits	Spot PCR	24 Hours	Culture Sensitivity	Urea	Creatinine	Serum Electolytes	Serum Cholestrol	NEC
12	12	12.1	Red	1+	4-6 EPI/5-6RBC s	0.3	370	Klebsiella	18	1.1	N	161	No Growth
14	12.5	9.9	Cola coloured	Nil	1-2 Puscells/Cast/6-8 RBC s	2.6	280	No Growth	46	1.1	N	139	No Growth
15	13	12.3		4+	1-2 Puscells	8.5	870	No Growth	19	0.8	N	207	No Growth
9	7.5	10.0		4+	2-3 Puscells	27.5	920	No Growth	22	0.8	N	326	No Growth
24	24	10.4	Red	Nil	2-3 Puscells/Cast+/ 4-5 RBCs	2.5	250	No Growth	29	1.0	N	120	No Growth
14	13.5	8.0		Trace	2-3 Puscells/2-4 RBC s	0.2	180	No Growth	19	0.7	N	160	No Growth
12	11.5	9.9	Red	Trace	4-8 Puscells/5-10 RBC	0.3	90	No Growth	21	0.8	N	168	No Growth
18	17	8.8		1+	4-5 Puscells/4-5 RBCs	1.8	120	Citrotobacter	55	1.1	N	128	No Growth
24	24	11.0		1+	1-2 EPI	0.4	64	No Growth	24	0.7	N	100	No Growth
18	18	11.5		Trace	2-3 Puscells/5-6 RBCs	0.5	320	No Growth	22	1.0	N	132	No Growth
17	16	11.2		1+	2-3 Puscells/2-3 RBC	1.3	168	No Growth	54	1.5	N	148	No Growth

20	17	12.6		3+	6-8 Puscells	3.7	1290	No Growth	24	0.8	6.5/5.1	341	No Growth
12	12	9.9	Cola coloured	1+	RBC Cast	1.4	300	No Growth	55	0.9	N	128	No Growth
25	25	10.0		Nil	1-2 Puscells	0.5	190	No Growth	20	0.8	N	100	No Growth
16	15	10.4	Cola coloured	Trace	2-3 Puscells/4-5RBCs	0.1	200	No Growth	28	0.8	N	174	No Growth
10	9	9.4		Nil	1-2 Puscells/Cast/6-8 RBC s	0.2	128	No Growth	27	0.5	N	166	No Growth
18	17	11.2		1+	1-2 Puscells/Cast/4-6 RBC s	0.4	350	No Growth	37	0.6	N	126	No Growth
14	13	10.9		1+	2-4 Puscells/cast/5-6 RBCs	0.6	98	No Growth	20	0.8	N	132	No Growth
24	23	14.1		3+	1-2 Puscells	3.6	1528	No Growth	17	0.7	N	320	No Growth
13	13	11.0	Red	Nil	1-2 Puscells/4-5 RBCs	0.4	90	No Growth	33	0.8	N	120	No Growth
8	8	10.8	Red	Nil	1-2 Puscells?3-5 RBCs	0.2	100	Ecoli	27	0.7	N	100	No Growth
26	23	14.8		4+	2-3 puscells	4.8	1640	No Growth	21	0.8	N	478	No Growth
10	9	11.0		4+	1-2 Puscells	3.0	670	No Growth	49	0.6	N	387	No Growth
20	20	9.6		1+	2-3 Puscells/8-10 RBC	1.8	108	No Growth	23	1.1	N	128	No Growth

18	17	11.4	Cola coloured	Nil	2-3 Puscells/ cast	0.4	128	No Growth	40	0.9	N	140	No Growth
13	12	13.0		3+	4-5 Puscells	7.1	920	No Growth	23	0.6	N	398	No Growth
17	15	11.2	Cola coloured	3+	2-3 Puscells/ cast	2.1	312	No Growth	28	0.8	N	154	No Growth
13	13	10.0	Red	1+	4-5 Puscells	2		No Growth	19	0.6	N		No Growth
20	20	13.8	Red	Trace	4-5 RBC	0.4		No Growth	19	0.5	N		No Growth
20	20	9.8		Nil	1-2 Puscells	0.5	120	No Growth	59	1.0	N		No Growth
13	10	10.6		3+	1-2 Puscells	8.3	1220	No Growth	15	0.6	N	315	No Growth
16	13	8.2		4+	6-8 pus cells	3.8	1430	no growth	29	0.9	N	320	No Growth
10	10	12.0	Red	Nil	2-5 pus cells			No Growth	30	0.9	N		
11	11	10.8	Red	Nil	4-8 pus cells	0.8	168	No Growth	26	0.8	N	132	No Growth
15	14	12.0	Cola coloure	Nil	2-3 pus cells	2	198	No Growth	52	1.4	N	148	No Growth

					Imaging Studies				
LFT	ASO	CRP	Compliment C3		USG Abdomen	Chest X-ray	PROGNOSIS	improvement with	duration
7/3.6/3.4	N	N			Bladderwall thikening	NAD	Improved	Antibiotics	D5-D12
6/3.2/2.8	400 IU	N			Rt Pleural effusion/spleenomegaly	NAD	Improved	Antibiotics/Antihypertensives/Diuretics	D1-D14
6.6/3.6/3.0	N	N	114 (N)		Rt pleural effusion/ascites	NAD	Improved	Antibiotics/Diuretics/Steroids	REMITTED
7/4.8/2.2	N	N	132 (N)		NAD	NAD	Improved	Antibiotics/Steroids	REMITTED
	N	N			NAD	NAD	referred	Antibiotics	D1-D10
6.8/3.5/3.3	N	N			NAD	NAD	Improved	Antibiotics	D1-D7
5.6/3.0/2.6	N	N			NAD	NAD	Improved	Antibiotics	D1-D5
6.4/3.9/3.5	N	N			b/l pleral effusion/ascites	RT Pleural Effusion	Improved	Antibiotics/Antihypertensives/Diuretics	D1-D10
	N	N	122 (N)		NAD	NAD	Improved	Antibiotics/Antihypertensives/Diuretics	D1-D7
6.2/3.2/3.0	N	N			NAD	NAD	Improved	Antibiotics	D2-D6
6.4/3.9/2.5	400 IU	N	154 (N)		NAD	NAD	Improved	Antibiotics/Antihypertensives	D2-D7

6.8/2.4/4.4	N	N	142 (N)		NAD	NAD	Refered	Antibiotics/diuretics/Steroids/Mycophenolate mofetil	SEROID DEPENDENCE
7/3.8/3.2	N	N	106 (N)		NAD	NAD	Improved	Antibiotics/Antihypertensives/Diuretics	D1-D14
6.4/3.2/3.2	N	N			Rt pleural effusion	NAD	Improved	Antibiotics/Diuretics	D1-D7
5.3/3.8/1.5	N	N	85	130	B/L pleural effusion/ascites	NAD	Improved	Antibiotics/Antihypertensives/Diuretics	D1-D7
6.5/3.9/2.6	N	Positive	102.3 (N)		b/l pleral effusion/hepatospleenomegaly	NAD	Improved	Antibiotics/Antihypertensives/Diuretics	D1-D10
6.3/4.3/2	N	N	91.4 (N)		NAD	NAD	Improved	Antibiotics/Antihypertensives/Diuretics	D1-D8
5.6/3.2/2.4	N	N	19.8	121.4	NAD	NAD	Improved	Antibiotics/Diuretics	D1-D8
6.5/3.2/2.4	N	N	102 (N)		Rt pleural effusion/ascites	LT Pleural Effusion	Improved	Antibiotics/Diuretics/Steroids	REMITTED
6.5/3.8/2.7	N	N			NAD	NAD	Improved	plenty of fluids	
	N	N			NAD	NAD	Improved	Antibiotics	D1-D7
6.8/2.1/4.7	N	N	123 (N)		Ascites/HSM	NAD	Improved	Antibiotics/Diuretics/Steroids	REMITTED
6.6/2.8/3.8	N	N	98.7 (N)		NAD	NAD	Improved	Antibiotics/Diuretics/Steroids	REMITTED
6.5/3.6/2.7	400 IU	N	71.1	93.7	NAD	NAD	Improved	Antibiotics/Diuretics	D1-D12

6.1/4.0/2.1	N	Positive			Spleenomegaly	NAD	Improved	Antibiotics/Diuretics	D1-D7
6.6/2.2/4.4	N	N			NAD	NAD	Improved	Antibiotics/Diuretics/Steroids	REMITTED
6.5/4.4/2.1	400 IU	N	81.4	180.1	NAD	NAD	Improved	Antibiotics/Antihypertensives	D1-D7
					Bladderwall thikening	NAD	Improved	Antibiotics	D1-D5
6.8/4.0/2.8			103.5 (N)		Bladderwall thikening	NAD	Improved		
6./3.0/3.7	N	N	89.7 (N)		NAD	NAD	Improved	Antibiotics	D1-D7
6.9/2.8/4.1	N	N	169.5 (N)		NAD	NAD	Improved	Antibiotics/Diuretics/Steroids	REMITTED
6.6/2.0/4.6	N	N	108(N)		Rt side pleuraleffusion	CITES/HEPATOMEGA	Refered	Antibiotics/Diuretics/Steroids	SEROID DEPENDENCE
		N	99.3		NAD	NAD	Improved	Antibiotics	D1-D7
6.0/3.2/2.8		N	125(N)		NAD	NAD	Improved	Antibiotics	D1-D7
6.8/3.5/3.3	400IU	positive	64.7	120	NAD	NAD	Improved	Antibiotics/Antihypertensives/Diuretics	D2-D8