"MAJOR INFECTIONS AND THEIR RISK FACTORS IN CHILDREN ADMITTED WITH NEPHROTIC SYNDROME IN A TERTIARY CARE CENTRE- ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY".

BY

(REG NO.BM0119004)

Dissertation

Submitted to the
KLE Academy of Higher Education and Research, Belagavi, Karnataka
In Partial Fulfillment of the requirements for the degree of

M. D. (Doctor of Medicine)

IN

PAEDIATRICS

DEPARTMENT OF PEDIATRICS,
JAWAHARLAL NEHRU MEDICAL COLLEGE
BELAGAVI, KARNATAKA

APRIL – 2022

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH,

BELAGAVI, KARNATAKA

Endorsement by the HOD, Principal/Head of the Institution

This is to certify that the dissertation entitled **"MAJOR INFECTIONS AND THEIR RISK FACTORS IN CHILDREN ADMITTED WITH NEPHROTIC SYNDROME IN A TERTIARY CARE CENTRE- ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"** is a bonafide research work done by **(REG No. BM0119004).**

Dr. MAHANTESH V PATIL M.D.
Professor & Head,
Department of Paediatrics,
J. N. Medical College,
Nehru Nagar,
Belagavi-590010

Date:
Place: Belagavi.

Dr. N.S. MAHANTASHETTI M.D.,
Principal
J.N.Medical College,
Nehru Nagar,
Belagavi-590010.

Date :
Place: Belagavi.

PLAGIARISM ACCEPTED LETTER

KLE
JAWAHARLAL NEHRU MEDICAL COLLEGE
(Recognized by Medical Council of India, New Delhi)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)
Nehru Nagar, Belagavi- 590 010, Karnataka, INDIA
0831 - 2471350 0831 - 2470759 www.jnmc.edu principal@jnmc.edu

Ref No: MDC/PG/ Date: 30-11-2021.

ACCEPTANCE LETTER

The softcopy of thesis entitled: **"MAJOR INFECTIONS AND THEIR RISK FACTORS IN CHILDREN ADMITTED WITH NEPHROTIC SYNDROME IN A TERTIARY CARE CENTRE- ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"** has been submitted for Anti-Plagiarism check through Turnitin software. The scan has been carried out and the scanned output reveals a match percentage of **09%** which is within the acceptable limits of **10%** as per the guidelines given by UGC.

Guide.

KAHER BELAGAVI J.N. MEDICAL COLLEGE

Dr. (Mrs.) N.S. Mahantashetti.
Chairperson-Antiplagiarism Committee &
Principal,
J. N. Medical College, Belagavi.

To,
Reg. No. BM0119004.
Postgraduate Student,
2019-20 Batch,
Department of Pediatrics,
J. N. Medical College, Belagavi.

LIST OF ABBREVIATIONS USED

NS	Nephrotic Syndrome
SRNS	Steroid Resistant Nephrotic Syndrome
SSNS	Steroid Sensitive Nephrotic Syndrome
MCNS	Minimal Change Nephrotic Syndrome
SDNS	Steroid Dependent Nephrotic Syndrome
FRNS	Frequently Relapsing Nephrotic Syndrome
FSGS	Focal Segmental glomerulosclerosis
MPGN	Mesangial Proliferative Glomerulonephritis
ISKDC	International Study of Kidney Disease in Children
MMF	Mycophenolate Mofetil
Hs-CRP	High sensitivity C Reactive Protein
GBM	Glomerular Basement Membrane
PEC	Parietal Epithelial cells
CD2AP	CD associated Protein
MAG1	Membrane Associated Granulate Kinase
TRPC	Transient Receptor Potential Cation Channel
UIP	Universal Immunisation Programme
NFHS	National Family Health Survey

ABSTRACT

BACKGROUND AND OBJECTIVES: Nephrotic syndrome is a relatively common childhood kidney disease affecting the glomerular basement membrane. Infectious complications in Nephrotic syndrome children may be a reason for onset of the disease or relapse. Changes in immunity are complex in the disease affecting both humoral and cellular balance impairing the response to infection. This study was aimed to understand the prevalence of major infection ,the type of infection and their risk factors in nephrotic syndrome cases admitted to our tertiary care centre.

MATERIAL & METHODS: This one-year cross sectional study was conducted in department of Pediatrics, KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Belagavi**.** All children admitted with Nephrotic syndrome between 1-18 years of age was included and screened for infections. Demographic data, type of infection, etiological microorganism, risk factors, predictive risk factor Hs-CRP value was collected and analyzed using R software version 4.1.1.

RESULTS: Among 72 children admitted with nephrotic syndrome 44 cases had major infections in which 72.73% were boys, mean age group of presentation was between 7.76± 5.28. 86. UTI was the most predominant infection 12 cases out of 44 (27.27%) and most common causative organism for major infection was E.coli(18.18%). Culture positive major infection was found in 59.09% of the cases while 18 out of 44 cases(40.91%) were culture negative suggesting a viral etiology for these infections. Most of the infectious episodes occurred during relapses (86.36%) where 37 out of 44 cases(84.09%) were on steroid treatment. Hs-CRP was a predictive risk factor indicative of risk of infection and mean values in cases of major

infection ranged between 83.93 ± 123.05 and 79.55% of the cases belonged to the high risk group.

CONCLUSION: Prevalence of major infections in admitted cases of Nephrotic syndrome in children between ages 1-18years is 61%. UTI was the predominant major infection and E.coli was the commonest pathogen isolated. Infection is a common cause of relapse in nephrotic syndrome and hence strong clinical suspicion and finding the focus of infection is important in reducing morbidity and burden of the disease.

KEYWORDS: Infection, Nephrotic syndrome, Hs-CRP, culture

TABLE OF CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF FIGURES

INTRODUCTION

Nephrotic syndrome is a common renal disorder. Its evolution from Hippocrates over 1000 years have undergone recent advances and effective treatment introduction during the 1900's. The advent of immunosuppressants, antibiotics and immunomodulators have brought in significant changes to the curve of mortality and morbidity in NS. Steroids used in the treatment of nephrotic syndrome was first isolated in 1936 and cortisone synthesis was attempted in 1946. ISKDC established in 1965 formulated definitions, pathogenesis and recommendations for management and therapy of Nephrotic syndrome which are standard protocols even today.[1]

It is the most common disease of kidney in childhood with an incidence of 2-16.9 per 1 lakh population.[2] The incidence is 20-70 cases per million in western countries, while in Asian countries the incidence is around 90-160 per million population.[3]

Minimal change disease is the most common underlying histopathological lesion (80-90%) and long term prognosis is mostly benign. 10% of the children have MPGN or focal segmental glomerulonephritis. Histology of the disease predicts the response to corticosteroids, with 93% of children having minimal change nephrotic syndrome and achieving remission following eight week course of prednisolone.[4]

Without adequate medical therapy, nephrotic children are more susceptible to mortality, more due to bacterial infection. Before the time of corticosteroids and antibiotic treatment, about 40% of children expired and 50% of these deaths were due to infection. Recently it has been proved that at least 50% of the active cases in paediatric onset NS are initiated by a common viral URTI, which may be secondary

to non specific response of the host to infection more than the reaction generated to the virus itself or their antibody.

Children diagnosed with nephrotic syndrome (NS) are exposed to multiple sources of infectious complications resulting in increased morbidity and further subsequent complication.[5] There is a lapse in literature regarding the clinical spectrum of deep seated morbid infections in childhood NS from developing countries like India in recent years and hence knowledge of these infections and their affection is therapeutically and preventively relevant

Complete remission of Nephrotic syndrome with corticosteroids has been taken as indicator of long term satisfactory outcome in pediatric nephrotic syndrome. Corticosteroid responsive MCNS was the most frequent diagnosis in pediatric age group. Response also predicted requirement for biopsy in corticosteroid sensitive group.[6]

The incidence of serious systemic infections in NS in India was estimated as 35%. Incidence from neighbouring countries varied from 20-30% of these infections in admitted cases of Nephrotic syndrome. When considering the minor infections the rate increased around 76-84%.[7]

The major infections in study were defined as “disseminated affecting the deep organs, requiring prolonged hospitalization (*e.g.* cellulitis, disseminated varicella) or potentially causing threat to life”. Specifically major infections were outlined by the Indian Academy of Pediatrics and Indian Pediatric Nephrology group which were defined and clinically identified for the study which included Peritonitis, Pneumonia, Sepsis, Urinary tract infection, Cellulitis, Meningitis and tuberculosis.[8]

Several factors together combine to cause an increased susceptibility to infections of bacterial etiology. The various factors include presence of decreased levels of immunoglobulin (IgG) due to improper synthesis in the blood and excessive urinary loss, edema fluid in the extracellular compartment which acts as a culture medium, deficiency of varied range of proteins specially decreased serum albumin, volume loss leading to decreased perfusion of spleen, loss of complement factor B and D which are primarily needed for phagocytic process of most encapsulated organisms, impaired and inappropriate T-lymphocyte functioning and effects of prolonged immunosuppressive and immunomodulatory therapy which are frequently employed in such children.[9]

According to Indian Academy of Pediatrics blood cultures in infants and children remain as a mainstay in the diagnosis of infections, even negative cultures have good predictive value and diagnostic importance as further probing into the causes of infections in wide spectrum can be evaluated.[10]

Understanding the background of infections is important for adequate treatment and decrease in the frequency of relapses thereby curbing the rising mortality and hospital admissions. As per the latest immunisation coverage survey NFHS-4 in the year 2015-16 the percentage of fully immunised children is 62%. Though the vaccination has been introduced in a phased manner in UIP since 2017 immunisation status remains poor with the children admitted with nephrotic syndrome which in turn contributes to the morbidity curve of the disease. Hence the present study is being conducted to understand the spectrum of prevailing infections in children with nephrotic syndrome and the risk factors associated with them.

OBJECTIVES

PRIMARY

1. To study the prevalence of major infections in Nephrotic syndrome.

SECONDARY

1. To evaluate risk factors for culture positive major infections in nephrotic syndrome and correlate them.
2. To understand the etiological spectrum of infections and their sensitivity pattern.

REVIEW OF LITERATURE

Nephrotic syndrome in childhood is the commonest kidney disease with a rate of incidence of 2-16.9 per 1 lakh population.[8,9] Idiopathic nephrotic syndrome is proven to be the most common type of nephrotic syndrome(NS) in children. It is two times more common in boys than girls. MCNS is more frequent in the age group ranging between 2-6 years. About 85% - 90% of childhood Nephrotic with first episode below 6 years of age present as MCNS. But only 20-30% of adolescents with first episode of nephrotic syndrome presents with MCNS. Commonest cause of nephrotic syndrome in older age group of about 12-16 years is found to be Focal Segmental Glomerulosclerosis (FSGS). Idiopathic nephrotic syndrome (INS) is rare in siblings. Placental transfer of proinflammatory cytokines have also been mentioned in the pathogenesis of idiopathic nephrotic syndrome in children.[11]

Eighty percent (80%) of children with nephrotic syndrome show good response to corticosteroid treatment. According to ISKDC guidelines kidney biopsy has not been mandatorily advised as 90% of the children with minimal change disease and 25-50% of children with mesangioproliferative glomerulonephritis achieve remission on corticosteroids. Long term prognosis including normal kidney function has proven to be good on corticosteroid therapy. Without treatment the risk of death was found to be 40% of which half constituted bacterial infection which has been significantly reduced to less than 1% with treatment.[12]

The treatment protocol of six weeks daily followed by six weeks alternate day was superior to then existing treatments, frequently relapsing patients were advised alternate day regimens, 20% proportion of them were prednisolone dependent. Cyclophosphamide was introduced in late 1960's, by the mid of 1980's levamisole was added which showed 50-60% efficacy in milder forms of Minimal change Nephrotic Syndrome(MCNS) and has sparing of steroid effect. Calcineurin inhibitors like cyclosporine and more recently tacrolimus has been beneficial to achieve remissions over prolonged period. By 2000's the role of mycophenolate mofetil has been proven to be successful in SDNS cases. Another new approach in SDNS management came during 2007 with monoclonal antibody against CD20 – Rituximab the functioning of which has been found to be beneficial in short term course.[13]

The nephrotic syndrome pathology in childhood is principally idiopathic or primary, remaining of which are found to be consequent response to glomerular and inclusive diseases or other infectious agents. Age is another factor which influences the presentation. Majority of cases present during first three months of life and are known as Congenital Nephrotic Syndrome (CNS) and is caused by genetic causes. Though the aetiology of these cases which occur later part in the decade(3-12months) are not clearly known, part of them has also been attributed to genetic factors.[14]

Gene	Protein	Inheritance	Locus	Phenotypes
Slit diaphragm and adaptor proteins				
NPHS1	nephrin	AR	19q13.1	CNS, SRNS (NPHS1)
NPHS2	podocin	AR	1q25–q31	CNS, SRNS (NPHS2)
PLCE1	phospholipase C, ε1	AR	10q23	DMS, SRNS (NPHS3)
CD2AP	CD2-associated protein	AD/AR	6p12.3	SRNS (FSGS3)
TRPC6	TRPC6	AD	11q21–q22	SRNS (FSGS2)
TRPC6	TRPC6	AD	11q21–q22	SRNS (FSGS2)
INF2	inverted formin-2	AD		SRNS (FSGS5), Charcot-Marie-Tooth disease with glomerulopathy
MYH9	myosin, heavy chain 9	AD	22q12.3–13.1	Macrothrombocytopenia with sensorineural deafness, Epstein syndrome, Sebastian syndrome, Fechtner syndrome
MYO1E	myosin IE	AR	15q22.2	Childhood-onset SRNS (FSGS6)
ARHGDI	rho GDP-dissociation inhibitor (GDI) α1	AR	17q25.3	Childhood-onset SRNS (NPHS8), seizures, cortical blindness
ARHGAP24	Arhgap24 (RhoGAP)	AD	4q22.1	Adolescent-onset FSGS
ANLN	Anillin	AD	7p14.2	(FSGS8)
GBM and basal membrane proteins and related components				
LAMB2	laminin subunit β2	AR	3p21	Pierson syndrome DMS, FSGS (NPHS5)
ITGB4	integrin-β4	AR	17q25.1	Epidermolysis bullosa, Anecdotic cases presenting with NS and FSGS
ITGA3	integrin-α3	AR		Epidermolysis bullosa, Interstitial lung disease, SRNS/FSGS
CD151	Tetraspanin	AR	11p15.5	Epidermolysis bullosa, Sensorineural deafness, CSRD
EXT1	glycosyltransferase	AR	8q24.11	SRNS
COL4A3,4	collagen (IV) α3/α4	AD/AR	2q36–q37	Alport syndrome, FSGS
COL4A5	collagen (IV) α5	XD	Xq22.3	Alport syndrome, FSGS

Fig 1 : Genes associated with childhood nephrotic syndrome[15]

Nephrotic syndrome is seen to affect the kidney almost exclusively and is depicted typically by podocyte foot processes effacement without deposition of glomerular process or inflammatory lesion. The defect along with other immunosuppressive factors like treatment makes the children susceptible to infections during therapy and leads to increase in morbidity of disease.[16]

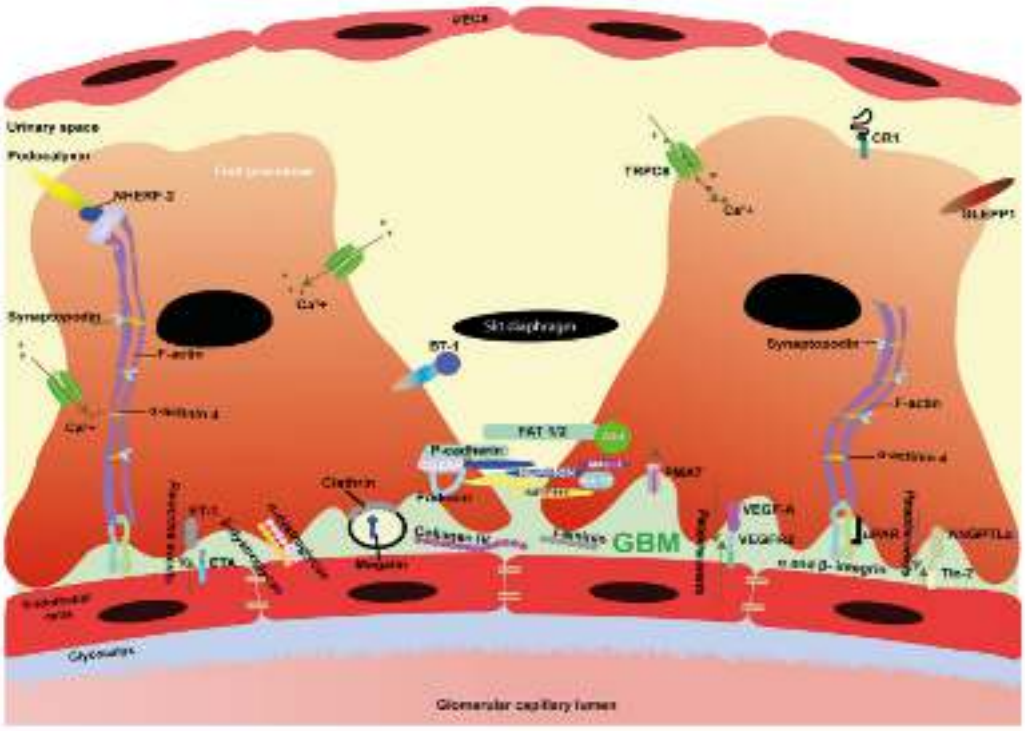


Fig 2 :Schematic demonstration of glomerular basement membrane and molecular overview of podocytes.[17]

EPIDEMOLOGY OF INFECTIONS IN NEPHROTIC SYNDROME

Deep seated infection is an important cause of severe morbidity and subsequent mortality in nephrotic children belonging to developing countries. Children with PNS have increased susceptibility to infections caused by bacteria which further may lead to steroid resistance or relapses or may by itself trigger the initiation of disease. Causative reasons of relapses in cases of steroid sensitive nephrotic syndrome is often infections of the upper airway passage or gastrointestinal tract. Estimated percentage of fifty two to seventy percentage of relapses among childhood incidences of NS in middle income countries chiefly follow infections of the upper airway tract. Common infections which are associated include acute upper and lower respiratory infections (ARI) which includes pneumonia with or

without (pus) empyema, infections of the dermis including cellulitis and impetigo , acute gastroenteritis or dysentery, renal tract infections or UTI and primary peritonitis.[2]

High rate of severe infections in Nephrotic syndrome (NS) children has been reported from developing countries like India, Pakistan and Bangladesh in various studies ranging almost 38-83%.[9] Study conducted in the setup of a level three care hospital among 720 cases of Nephrotic syndrome 450 were in relapse out of which 367 were due to infectious causes. The study by Khemchand N Moorani demonstrated highest frequency of Acute respiratory infections either during active disease or relapse and was followed by acute invasive or watery diarrhoea as the second most common infection.[2] Another study by Ajayan et al in 2013 evaluated 86 children requiring hospitalisation for Nephrotic syndrome among which 27 out of 37 children had major infections. Peritonitis was the most frequent infection encountered in the study followed by pneumonia.[5]

CLASSIFICATION OF NEPHROTIC SYNDROME:

It can be broadly classified as Steroid Resistant Nephrotic Syndrome (SRNS) and Steroid sensitive nephrotic syndrome (SSNS) based on the treatment response, of these only 20 % of cases belong to the class of (SRNS) steroid resistant nephrotic syndrome. Among the steroid sensitive nephrotic syndrome it can be further classified into Steroid dependent nephrotic syndrome(SDNS), Frequently relapsing nephrotic syndrome (FRNS) and infrequently relapsing nephrotic syndrome.(IRNS).[12]

PATHOPHYSIOLOGY OF INFECTIONS IN NEPHROTIC SYNDROME:

The old paradigm of pathogenesis which said NS as a disease due to abnormality of T-Cell function leading to increasing levels of permeability factor of lymphocyte in plasma was proposed in 1974. The massive proteinuria and hypoalbuminemia was thought to be due to the activation of T cell permeability factor by viral infection or allergens.[11]

Pathogenesis of increased permeability in nephrotic syndrome has been attributed to glomerular basement membrane defect, circulating factors and immunological factors.

The filtering of blood and products of blood at glomeruli, which comprises the most important function of GBM allows the permission of fluid and dirty products while retaining back the main chunk of blood proteins and all blood cellularity within the vascular space. The Glomerular filtration barrier is made up of specialised differential glomerular epithelial cells (podocytes), cells of the endothelium and glomerular basement membrane (GBM).[14]

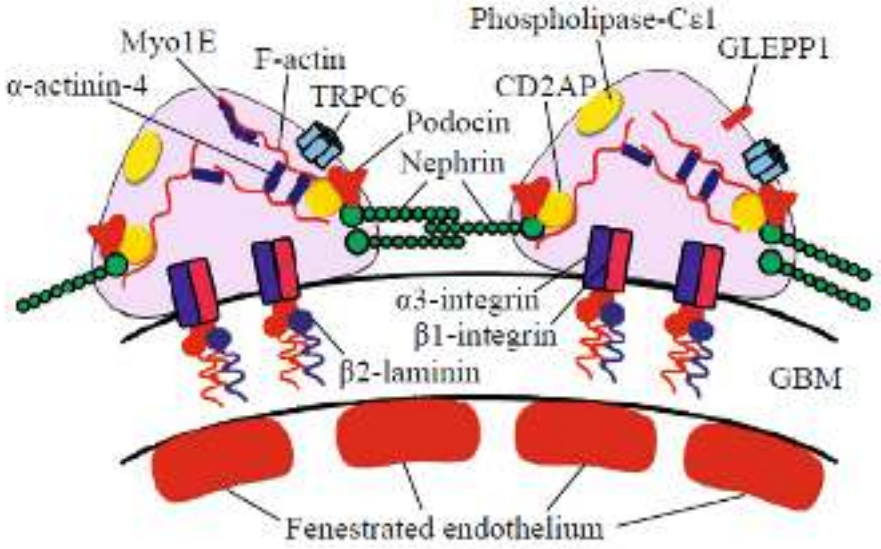


Fig 3 : Ultrastructure of the podocyte foot process proteins[11]

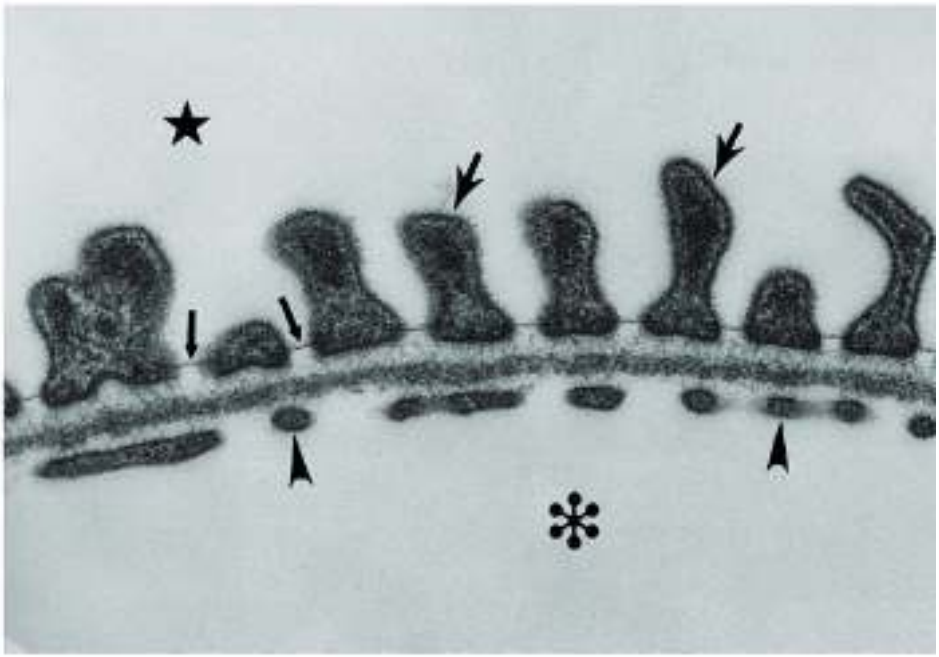


Fig 4 : Electron microscopic structure of glomerular basement membrane

The role of humoral and cellular responses in nephrotic syndrome is equally abnormal during an episode of relapse in nephrotic syndrome, though T lymphocyte function has been implicated more in most studies.[14]

Indicators of this proposition include increased sensitivity of variants of primary nephrotic syndrome to immunomodulators like mycophenolate mofetil, calcineurin inhibitors, corticosteroids and alkylating agents, all these drugs are inhibitors of T lymphocyte function. Childhood infections which are common like measles which slow down the cellular immunity are seen during remission phases of nephrotic syndrome.

The loss of immunoglobulins in addition to hematologic factors through urine puts children of nephrotic syndrome at risk for bacterial invasions specially encapsulated microorganisms like S.Pneumoniae, H.Influenzae, and Group B streptococcus.[18] Higher frequency of lower ARI (pneumonia) in nephrotic children may be due to absence of ability to localise infection and mechanical pressure on lungs due to massive ascites and pleural effusions leading to stasis of fluid in the lungs in these children.[2]

Infections in NS occur after respiratory and GI infections. Invasion by viruses can cause upregulation of TH1 cytokines cells which increase glomerular permeability of proteins. Initial surge of levels of pro-inflammatory cytokines is further accompanied by upsurge and anergy of monocytes and apoptosis of T-Lymphocyte. A period of immune paralysis maybe seen in remission which may cause serious bacterial infections.[19]

Pneumococcal vaccinations directed against capsular antigens is recommended to be administered in cases of Nephrotic syndrome, but immunisation should be given during the management with high doses of corticosteroids or when cytotoxic treatment is discontinued. Nephrotic children taking high-dose either of these agents within three months of its use are at

higher risk of infection by varicella, requiring varicella zoster immunoglobulin treatment. Infection is a disease related complication of NS in contrast to treatment associated complication.[20]

New pathogenesis mechanism also adds the possibility of factors like CD80, also known as B7 a T-cell costimulatory molecule which is found to have involvement in both activation and final termination of the T-cell response. Activation of CD80 on antigen-presenting cells (APC) and binding to the CD28 receptor on T-cells plays an important role in T-cell activation. In contrast, attachment and binding of CD80 to cytotoxic T-lymphocyte associated (CTLA)-4 terminates the stimulated T-cell response.[11]

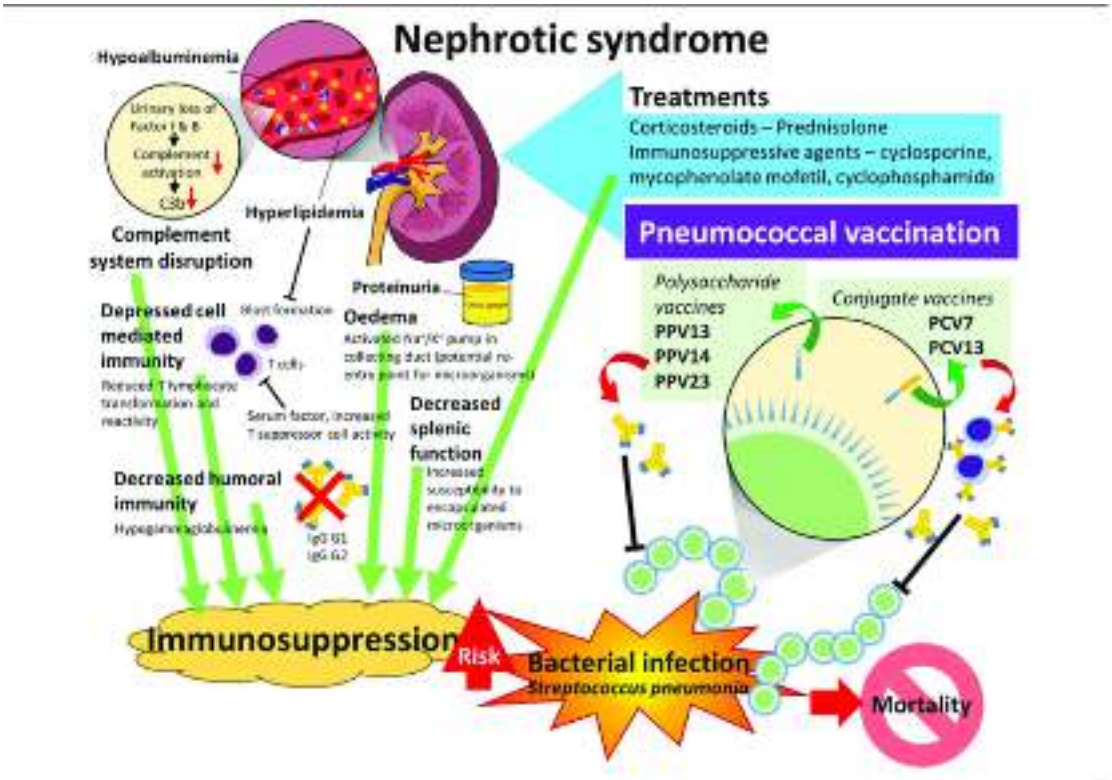


Fig 5 : Pathogenesis of nephrotic syndrome and role of pneumococcal vaccination.

STANDARD DEFINITIONS[21]

Nephrotic syndrome -Edema, protein/creatinine ratio more than 2 mg/mg, or more than or equal to 300 mg/dL, or 3+protein on urine dipstick, proteinuria exceeding 1000 mg/m2/day (24-h urinary sample), hypoalbuminemia ≤3 g/dL (≤25 g/L).

Remission-Urine protein excretion nil or minimal by urine dipstick on spot sample for 3 consecutive days morning sample.

Relapse- "Urine protein excretion more than 3 plus by urine dipstick on spot sample for 3 consecutive days on early morning specimens".

Frequent relapse nephrotic syndrome- "2 or more relapses within six months of initial response, or 4 or more relapses in any twelve month period or more than three relapses in any six months".

Steroid dependent nephrotic syndrome (SDNS)-"The occurrence of two consecutive relapses during alternate day of corticosteroid therapy or within two weeks of its termination in the absence of infections".

Steroid-resistant nephrotic syndrome-"Inability to achieve complete remission after six weeks of every day therapy with enteral prednisolone of 2mg/kg/day".

In the previous studies on the subject, children admitted with nephrotic syndrome were first subjected to investigation to fit in the criteria of nephrotic syndrome. Detailed investigation for the focus of infection depending on history was made and specific investigations for confirmation of the same was done.

Specific major infections were defined as follows:[8]

1. ***Peritonitis*:** "Abdominal pain, abdominal tenderness, distension of abdomen , diarrhoea, or vomiting, with ascitic fluid >100 leukocytes/mm3 and minimum 50% neutrophils and/or positive culture". It was found that among 1.4-3.7% of the children affected with spontaneous bacterial peritonitis as one of the major infection in NS,case fatality rate was around 9%. Both gram positive and negative organisms were implicated in the etiology.[22] Attacks of peritonitis usually occur during relapse periods and besides introduction of corticosteroids albumin levels of <2g/dl, defective humoral immunity and loss of small molecular proteins such as IgG, factor I and factor B leading to aterations in opsonisation may also add to pathogenesis.[23]

2. **Pneumonia**: rapid rate of breathing and chest wall indrawing with X-ray confirmation of chest pathology. In Indian studies the rate of pneumonia among children with NS is around 12-14% mostly comprising of community acquired acute respiratory infection.[11] Except during neonatal period Acute Respiratory illness contribute to highest cause of mortality and morbidity in the under 5 age group especially in developing countries.[24] Most of the upper respiratory and lower respiratory infections in children usually respond well to a course of appropriate antibiotics but when coupled with an immunocompromised state like Nephrotic syndrome they progress into life threatening pneumonia and further complications. Keeping in mind the common causes of ARI both hospital acquired and community acquired recent threats have been posed by the

SARS COVID -19 virus. The affinity of virus to the renal system in addition to the pulmonary system has been proven by the proteinuria, glomerulopathy and AKI that is seen in affected children.[25] Mainstay in management comprises of effective balance between the daily dosing of steroids aiming at reduction of immunosuppression to acceptable levels.[26]

3. **Urinary tract infection** (UTI)*: "*Colony count of bacteria more than 105 organisms/mL in a clean-catch midstream urine sample with fever (>38.5ºC), dysuria or increased urination frequency". UTI is often underdiagnosed during relapses of nephrotic syndrome. Observations reveal that more than the occurrence in first episode urinary tract infection contribute as causative agent for subsequent relapses.[27]

4. **Cellulitis**: Erythema of skin, localised warmth, edema of area, fever and local tenderness in any body part. Mild skin infections which initially trigger the relapse may become severe affecting the entire limb or region in few causes due to the immunosuppressive and hyperlipidemic status and progress into cellulitis and the disease course might ensue a morbid trajectory if not treated aggressively.

5. **Meningitis** : "Fever and one of the following: nuchal rigidity, altered sensorium, seizures with confirmation by cerebrospinal fluid cytology, biochemistry and culture". Susceptibility to encapsulated organisms remain a threat as children with nephrotic syndrome can progress to fatal complications like bacterial meningitis.[28]

Severe ascites was described as tense ascites or ascites with respiratory distress. Generalized distribution of edema (including edema of scrotum, vulval edema or severe ascites) was also counted as serious anasarca.

A study from neighbouring country of Pakistan based on 62 children with NS showed incidence of severe infections among which acute respiratory infections (29.27%) were the most common which presented in for admission followed by skin infections (27%) and acute diarrheal disease. Almost seventy eight percentage of the infections were associated with a relapse.[29]

In a previous study done by Ajayan P, Krishnamoorthy et al the incidence rate of deep seated episodes of infection was 36.6%. Among the severe infections, bacterial peritonitis and severe pneumonia combined accounted for 72.9%, while urinary tract infections (UTI) and cellulitis accounted for only 16.2%.[8]

In an institution based cross sectional study conducted in children with primary nephrotic syndrome admitted in a tertiary care hospital of Rajasthan a state of India. Infection was associated in 71.05% cases of relapses of nephrotic syndrome. The most common infections were acute respiratory tract infection (34.21%) [-URI-22.37% and pneumonia-11.84%] followed by urinary tract infection (26.32%).[30]

In a descriptive study including 199 children of Nephrotic syndrome hospitalised 260 episodes of infections were recorded. 61 had repeated attacks. Urinary tract infection was the commonest (46%) followed by peritonitis (25.8),

ARI (13.5%), Tuberculosis (5%), cellulitis (3.8%), Enteric fever (3.8%), hepatitis and exanthematous fever.[31]

In a study done by Krishnan C et al at Government Medical college, Kozhikode a district of Kerala, total of 246 children of nephrotic syndrome were enrolled, among whom forty six children developed forty eight (19.6%) episodes of major infections. Thirteen (27%) major infections had occurred in the initial episode and 35(73%) in relapse cases.Pneumonia (41.7%) was the most common infection, followed by urinary tract infection (UTI) (25%), generalised sepsis (16.7%), spontaneous bacterial peritonitis(8.3%), cellulitis (4.2%), perinephric abscess (2.1%) and pulmonary TB(2.1%).

Simultaneous onset of SARS-COV-2 with Nephrotic syndrome has been reported in a 3yr old Japanese boy who received induction therapy with prednisolone and achieved remission.[32]

Out of 231 nephrotic syndrome children admitted with 452 episodes of infection, predominant infection was peritonitis followed by sepsis. Organisms isolated included streptococcus pneumoniae and gram negative organisms like klebsiella, E.coli and Neisseria meningitidis.[33]

In a study conducted in 239 infection episode cases of 107 children admitted with NS, 35 spontaneous bacterial infections (14.6%) were diagnosed, including pneumonia (n = 12), generalised bacteremia or sepsis (n = 8), urinary tract infection(UTI)(n = 6), generalised peritonitis (n = 4), severe osteomyelitis (n = 2), bacterial enteritis (n = 2), and scarlet fever (n = 1). Thirteen cases (5.4% of admissions, 37.1% of SBI) were microbiologically culture proven.[(34)]

HS-CRP AS A DIAGNOSTIC TOOL IN INFECTION.

CRP is a pentraxin molecule described in 1930 is a regulator of innate immune system and am acute phase reactant.

C-reactive protein (CRP) is a complex protein molecule bound to plasma which is produced in hepatic cells and is composed of five apparently similar individual subunits which are arranged in pentameric cyclical symmetry surrounding a negatively charged core. Each subunit individually has a molecular mass of approximately 21.5 KD; the molecular mass of the protein differs from 110 to 144 KD. Inflammation of the blood stream is well recognized by serum CRP values. In both adults and pediatric age group, serum levels of CRP increase during episodes of bacterial infections.[35]

Concentration of HS-CRP increases in quick response to inflammation occurring with tissue destruction. Conventional C-reactive protein assays which are indicated for the evaluation of infectious process, tissue injury, and inflammatory disorders provide information for the clinical and final diagnosis, therapy, and monitoring of the inflammatory process. C reactive protein being one of the cytokine-induced “acute-phase” reactant, the blood levels of the same rise during a non specific response to infectious process and non-infectious inflammatory episode serving as an indicator of active immune response in the body.[36]

In a study done by Seema Patel, Manoj Kumar et al role of HS-CRP in children with Nephrotic syndrome associated with infections was studied. Serum High sensitivity C reactive protein level in healthy children ranged between 0.25

mg/L to 1 mg/L and cases had a range between 0.9- 9.7mg/L. Children who suffer from Nephrotic syndrome were shown with raised High sensitivity CRP and this observation positively correlated with increased cholesterol levels. Previous literature says hypercholesterolemia is present in such patients even after long period of remission. It has been proposed that regular monitoring of serum C reactive protein(Hs-CRP) level in such affected individuals may help in understanding the role of inflammation mediated atherosclerotic changes which poses greater risk of coronary artery disease during later part of pediatric age.[37]

Hs-CRP is a significant risk determining factor in the causative pathology of infection. Significant rise in level of this pentameric molecule can be seen in infections of bacterial origin. A serological test value higher than 100mg/L strongly suggests an active bacterial infection, whereas those below 10 mg/L indicates viral infectious etiology. In mycobacterium tuberculosis infection it is often seen that the value is between 10 to 100 mg/L.[38]

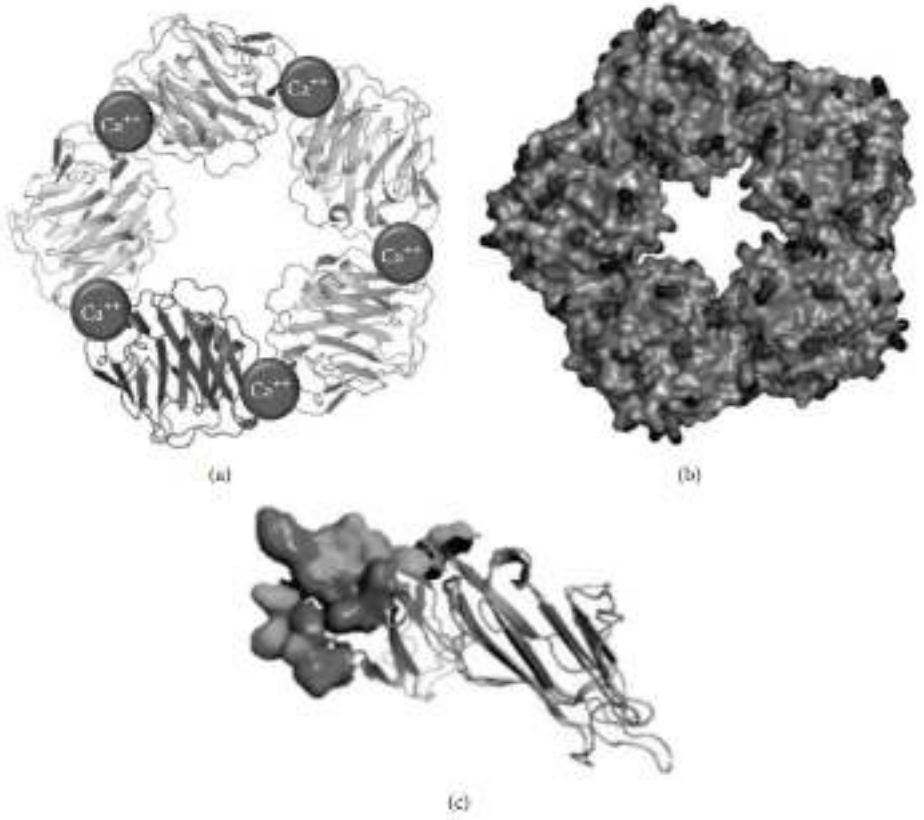


FIG 6 : **a) CRP molecule in pentameric form bound to calcium ions**

b) CRP molecule in spatial configuration

c) CRP molecule dissociated into monomeric form

METHODOLOGY

This study was conducted from January 2020 to December 2020 in the Department of Pediatrics, KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Belagavi. Due to the ongoing COVID 19 pandemic sample collection was extended to May 2021.

Study Design

Hospital based cross- sectional study

Study duration and period

January 2020 to May 2021

Place

This study was conducted in the Department of Pediatrics, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi a tertiary care teaching hospital attached to KAHER Jawaharlal Nehru Medical College, Belagavi.

Source of Data

All admitted cases of Nephrotic syndrome at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi.

The sample size was calculated using the formula as mentioned below.

N (sample size) =

$$\frac{Z^2 x_P x(1-P)/C^2}{1+\left\{\frac{Z^2 \times p(1-P)}{C^2 N}\right\}}$$

Where,

N= sample size

p=prevalence of infection in nephrotic syndrome in India, which was 13%.[16]

Q= 100-p when p is in percentage

Z=1.96 (constant)

$$n = \frac{13 \times (100 - 13) \times 1.96^2}{10^2}$$

$$n = 43.45 \approx 43$$

Calculated sample size was 43 and actual sample size was 44 .

Selection Criteria

Inclusion criteria:

All Nephrotic syndrome patients between 1 year and 18 years of age admitted in pediatric wards.

Exclusion criteria:

Atypical cases presenting with:

- Uncontrolled hypertension
- Hematuria
- Multisystem involvement

Any chronic kidney injury

Urogenital abnormalities

Method of collection of data

This study was conducted after the approval from the clinical ethical committee of the institution (Annexure ii), the parents of the children fulfilling he selection criteria were briefed about the nature of the study and a written informed consent was obtained from the parents/caregivers to participate in the study prior to the enrollment

(Annexure1). Parents/caregivers of the children who fulfilled the selection criteria were interviewed and detailed history including demographic details and course of the illness with the treatment history was procured and noted in the proforma.

At admission baseline presenting complaint was noted, vitals, anthropometry and detailed examination of the system affected in correlation with the symptoms were made in detail. All the findings were recorded on a pre-designed and pre-tested proforma. Further complete hemogram, mini renal profile, Serum albumin and blood cultures were collected at admission for the enrolled children. An attempt to delineate the focus of infection based o clinical history and examination was done and appropriate culture samples were sent in addition to routine investigations. All the investigations were processed in the standard lab under KAHER Dr Prabhakar Kore Charitable Hospital, Belagavi, Karnataka.

Case Definitions:

Peritonitis: Clinically suspected cases with abdominal pain, distension, vomiting, tenderness, and microbiologically >100 leucocytes/mm3 with atleast 50% neutrophils and or evidence of positive culture.

Urinary tract infection : Increased urinary frequency, burning micturition, lower abdominal pain, decreased urine output associated with or without fever with microorganisms >105/ml in midstream clean catch urine sample.

Pneumonia : Fast breathing according to age criteria by ARI control programme with chest Xray evidence.

Cellulitis : Erythema, warmth, swelling, local tenderness and local elevation of temperature

Sepsis : Fever with generalised infection involving multiple organs.

Statistical analysis:

Data was entered into Microsoft excel and analysed using R software version 4.1.1. Categorical variables are given in the form of frequency table. Continuous variables are given in Mean ± SD/ Median (Min, Max) form. Chi-square test is used to check the dependency between categorical variables. Two sample t-test used to compare the mean of variables over group. P-value less than or equal to 0.05 indicates significance.

Risk factors assessed during study :

1. Hs-CRP – Serum Hs- CRP values were analysed during day one of admission by collecting 2 ml blood in heparinised vacutainer and processed in KLE Hi-tech Lab.

2. Serum Albumin – Serum albumin values <1.5g/dl was considered as positive risk factor cut off. It was measured by collecting 2ml blood on day of admission in heparinised vacutainer and processed in KLE Hi-tech lab.

3. Immunisation status – Immunisation status as per the revised national immunisation schedule was outlined and any defaulter was considered as partially immunised for age.

4. Steroid status – Current steroid status of the child was accounted and recorded.

RESULTS

The cross sectional study was conducted from January 2020 to May 2021 in the Department of Pediatrics, KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Belagavi.

A total of 72 Nephrotic syndrome children were admitted during the study period of which 44 had infections (61%). Prevalence of Nephrotic syndrome in our study was observed to be 61%.

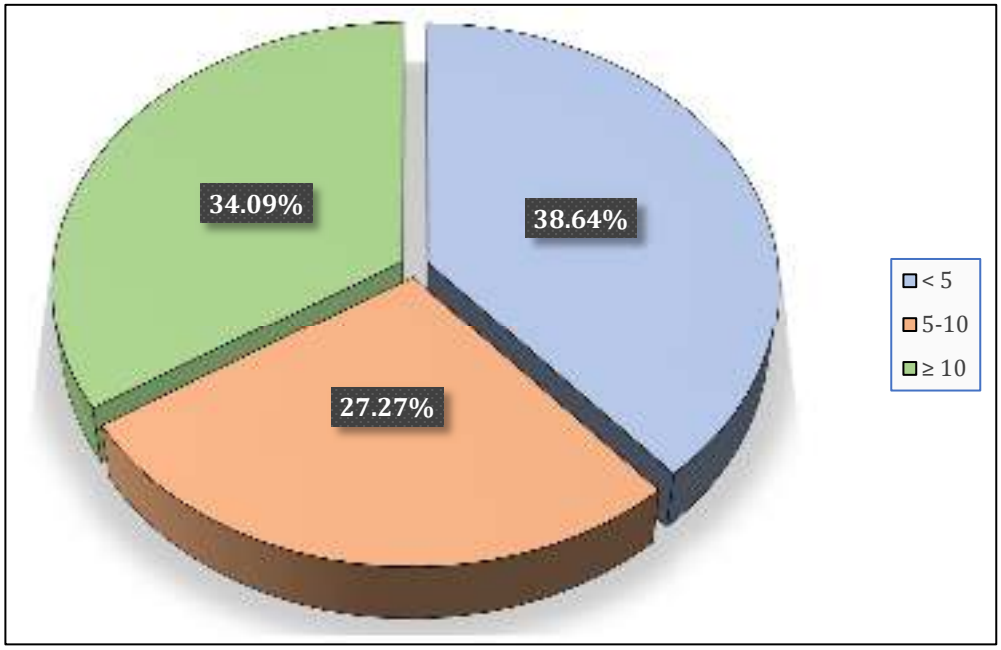
Demographical Characteristics:

Data contained measurements on 44 subjects whose age ranges from 1.5 years to 16.92 years with mean age 7.76 ± 5.28 years.

Table 1: Age distribution of nephrotic children enrolled in study

Age (In Years)	< 5	17 (38.64%)
	5-10	12 (27.27%)
	≥ 10	15 (34.09%)
	Mean ± SD Median (Min, Max)	7.76 ± 5.28 6 (1.5, 16.92)

Graph 1: Distribution of study subjects according to age

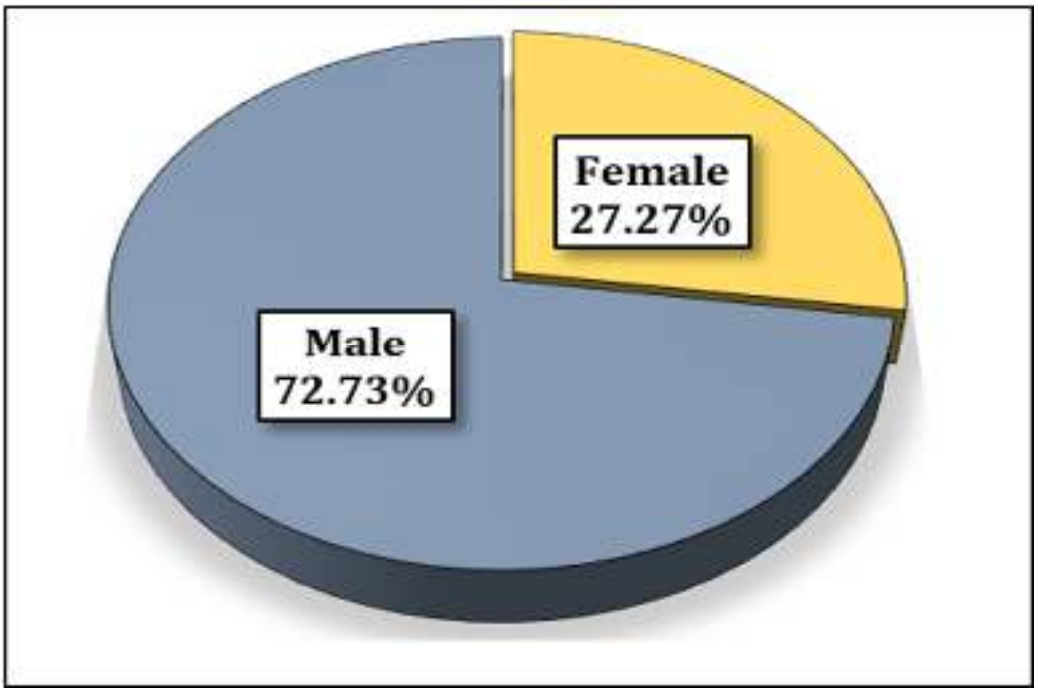


In the study 38.64% belonged to the under 5 age group while the lowest percentage of infection was found among 5-10 years. There was no significant difference in age of distribution of the cases.

Table 2: Distribution of subjects based on gender

Gender	**Female**	12 (27.27%)
	Male	32 (72.73%)

Graph 2 : Distribution of subjects based on gender



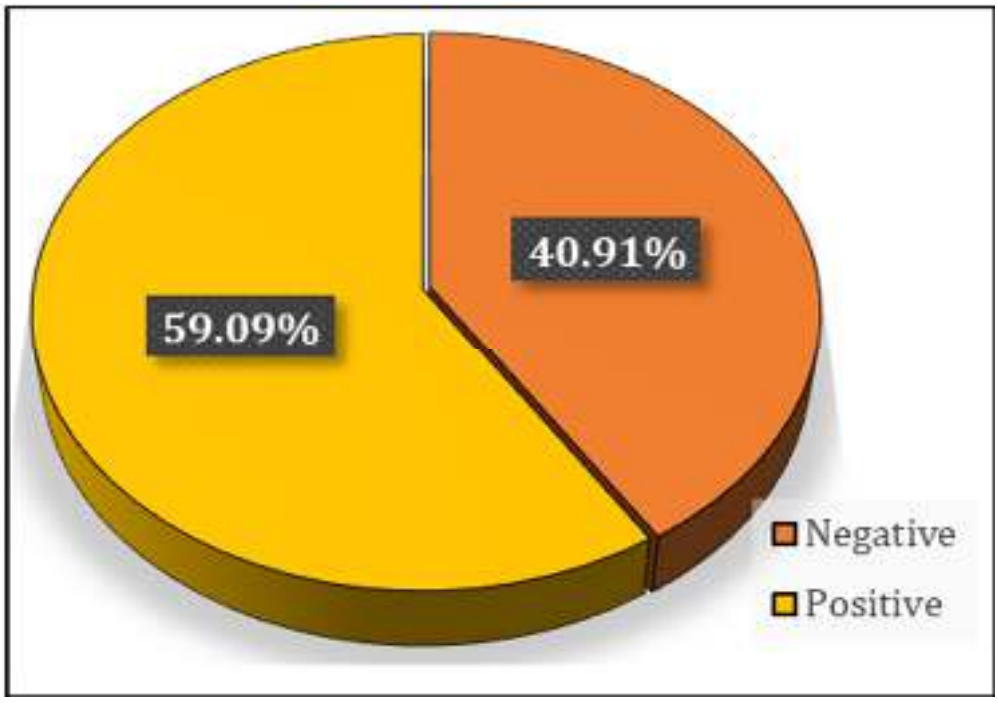
Out of the 44 subjects enrolled it was found that majority of subjects constituted of male gender 32 (72.37%) while females were 12(27.27).

Primary outcome:

Table 3: Distribution of subjects based on culture sample status

Culture	**Negative**	18 (40.91%)
	Positive	26 (59.09%)

Graph 3 : Distribution of culture sample status in subjects



Out of 44 cases in the study it was observed that 26 (59.09%) had culture positive major infections and 18 cases had culture negative infectious episodes. Culture samples were taken keeping in mind the clinical suspicion of focus of infection. Blood cultures were taken invariably in all cases.

Table 4 : Distribution of types of major infections in subjects

Diagnosis	**Acute Ge**	6 (13.64%)
	Acute Ge + Sepsis	1 (2.27%)
	Cellulitis	1 (2.27%)
	Fournier's Gangrene	1 (2.27%)
	LRTI	5 (11.36%)
	Peritonitis	11 (25%)
	Septicemia	6 (13.64%)
	Tuberculosis	1 (2.27%)
	UTI	12 (27.27%)

In our study we observed that predominant infection was UTI constituting 12 out of 44 cases (12.27%) followed by peritonitis (25%) Acute GE and sepsis each constituting 6% and cellulitis, fourniers gangrene and tuberculosis each 1%.

Graph 4: Distribution of types of major infections in NS

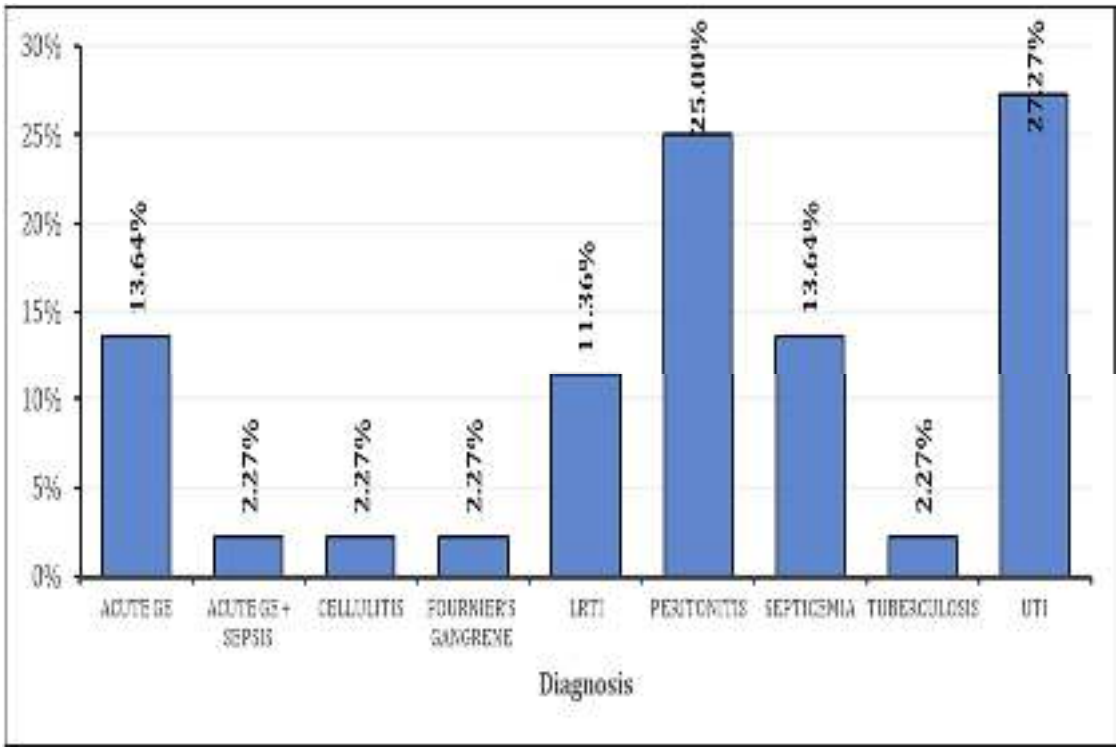
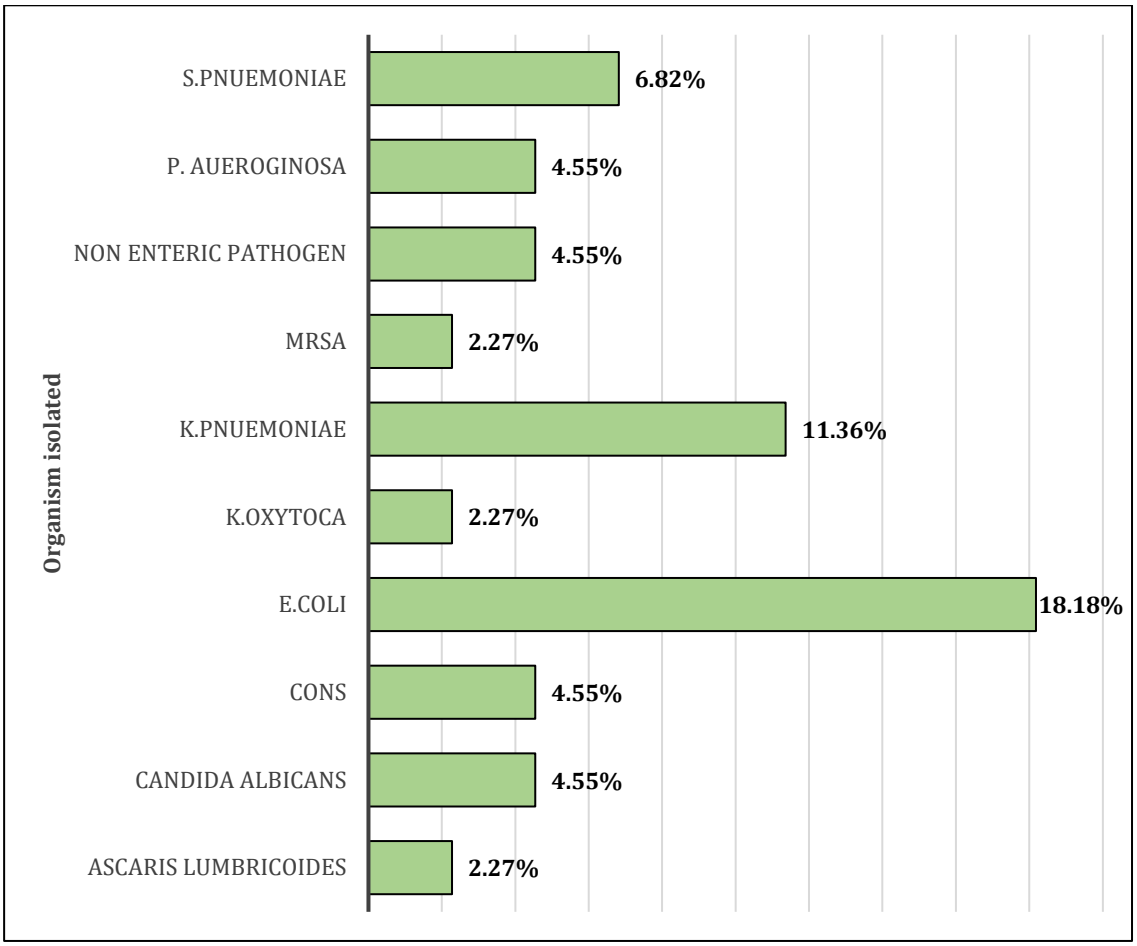


Table 5: Distribution of subjects according to organisms isolated from culture samples

Organism Isolated	**Ascaris Lumbricoides**	1 (2.27%)
	Candida Albicans	2 (4.55%)
	Cons	2 (4.55%)
	E. Coli	8 (18.18%)
	K. Oxytoca	1 (2.27%)
	K. Pneumonia	5 (11.36%)
	MRSA	1 (2.27%)
	Non-Enteric Pathogen	2 (4.55%)
	P. Aeruginosa	2 (4.55%)
	S. Pneumonia	3 (6.82%)

Graph 5 : Distribution of subjects according to organism isolated from culture samples

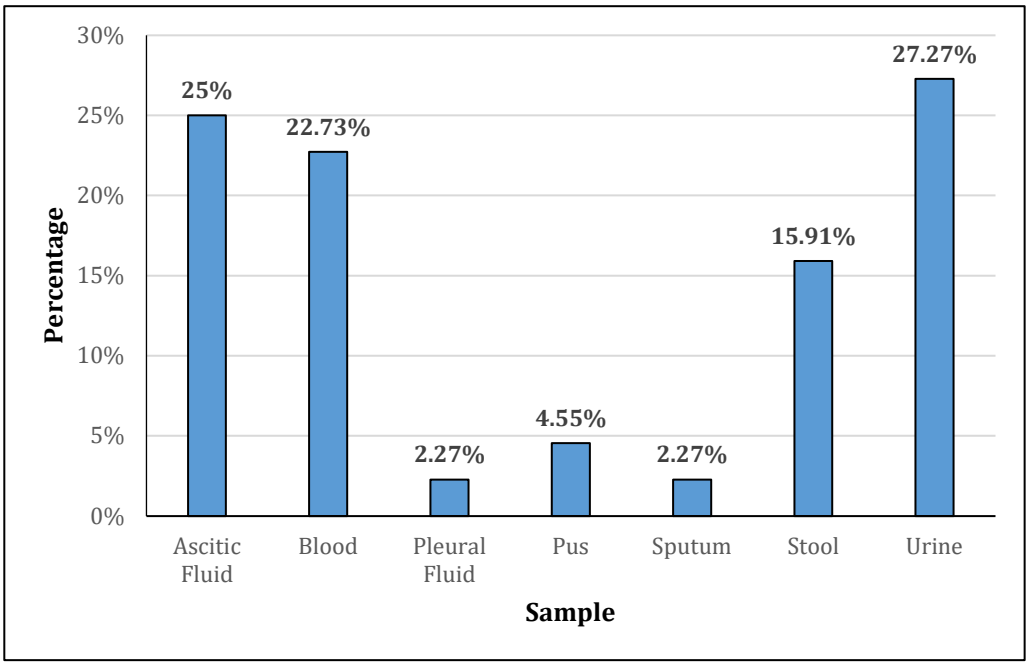


Of 44 patients enrolled, and 26 culture positive cases (59.09%) 18.8% isolated E.coli as causative organism for the infection followed by Klebsiella pneumoniae which constituted 11.36%. Streptococcus pneumoniae was isolated in 6.82% and CONS, Candida, Pseudomonas and Non enteric pathogen constituted 4.45% of the organisms.

Table 6 : Distribution of culture specimen taken in subjects presenting with infection.

Culture specimen	**Ascitic Fluid**	11 (25%)
	Blood	10 (22.73%)
	Pleural Fluid	1 (2.27%)
	Pus	2 (4.55%)
	Sputum	1 (2.27%)
	Stool	7 (15.91%)
	Urine	12 (27.27%)

Graph 6 : Distribution of culture specimen taken in subjects presenting with infection.



In the present study the specimen for culture was determined on the basis of clinical suspicion based on history and examination and maximum cultures have been sent of urine (27.27%) followed by ascitic fluid(25%).

Table 7: Distribution of diagnosis based on culture status of the cases.

		Culture -ve	Culture +ve	P value
Diagnosis	**Acute Ge**	1 (5.56%)	5 (19.23%)	**0.007^{MC*}**
	Acute Ge + Sepsis	0	1 (3.85%)	
	Cellulitis	0	1 (3.85%)	
	Fournier's Gangrene	0	1 (3.85%)	
	LRTI	3 (16.67%)	2 (7.69%)	
	Peritonitis	9 (50%)	2 (7.69%)	
	Septicemia	0	6 (23.08%)	
	Tuberculosis	1 (5.56%)	0	
	UTI	4 (22.22%)	8 (30.77%)	

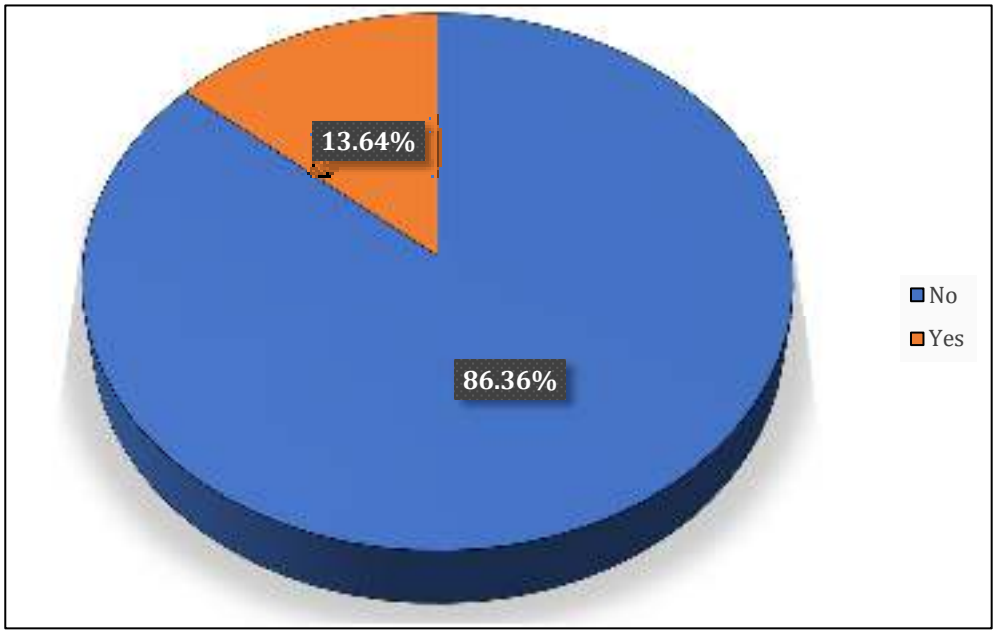
It was observed that in our study 30.77% of Culture positive infection was due to UTI, 23.88% due to sepsis and 19.23 % was due to acute GE. There was a positive correlation with p value 0.07 between clinical diagnosis and culture positive infection which was significant in our study.

RISK FACTORS ASSOCIATED

Table 8 : Distribution of subjects based on the status of primary diagnosis.

First Episode	**No**	38 (86.36%)
	Yes	6 (13.64%)

Graph 7: Distribution of subjects based on status of primary diagnosis.



In the study it was observed that 86.36% were established cases of nephrotic syndrome who presented in relapse with infection and 13.64% were newly diagnosed cases of Nephrotic syndrome presenting with infection.

Table 9: Distribution of culture status of subject and status of primary diagnosis.

		Culture -ve	Culture +ve	P value
First Episode	**No**	13 (72.22%)	25 (96.15%)	0.0405^{MC}
	Yes	5 (27.78%)	1 (3.85%)	

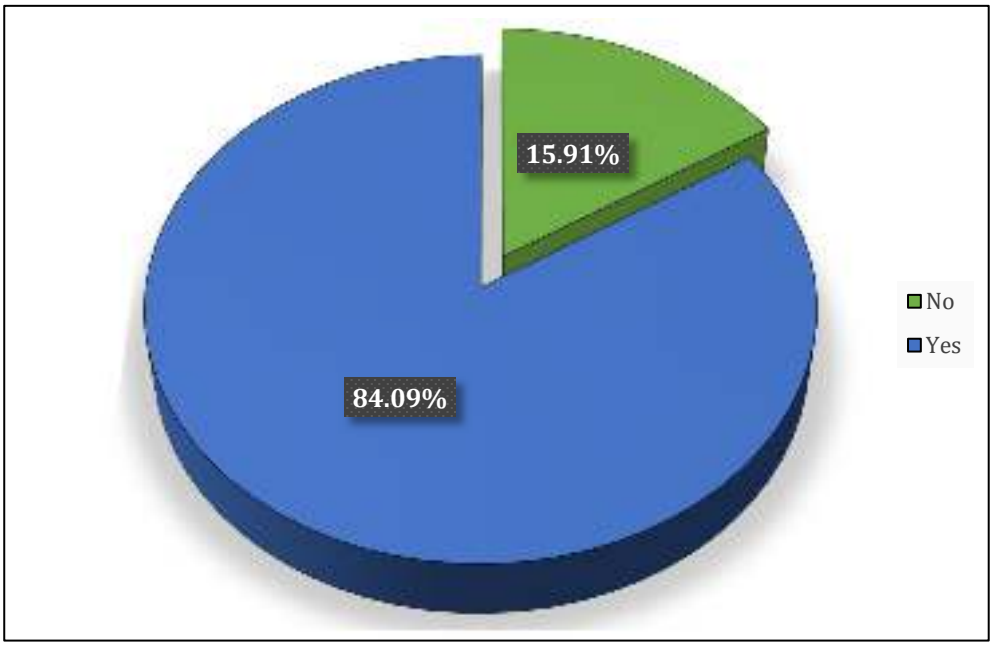
From the study it was observed that 96.15 % of the culture positive cases were episodes of relapse following infection on already diagnosed cases of nephrotic syndrome while 1% of the culture positive case was newly diagnosed. This association had a p value of 0.0405 and hence denoting a significant relationship between diagnosis status and culture positive incidence of infection.

Further the established diagnosed cases were classified into steroid sensitive and steroid resistant based on clinical history and response to treatment.

Table 10: Distribution of subjects based on current status of steroid consumption.

On Steroids	**No**	7 (15.91%)
	Yes	37 (84.09%)

Graph 8: Distribution of subjects based on status of steroid therapy



In the study it was observed that out of 44 cases 37 cases were on steroid therapy (84.09%) at the time of presenting with infection, while 15.91% i.e 7 cases were not on steroids, 6 were new cases and one case was in remission.

Table11 : Distribution of steroid status on culture positive and culture negative cases of infection

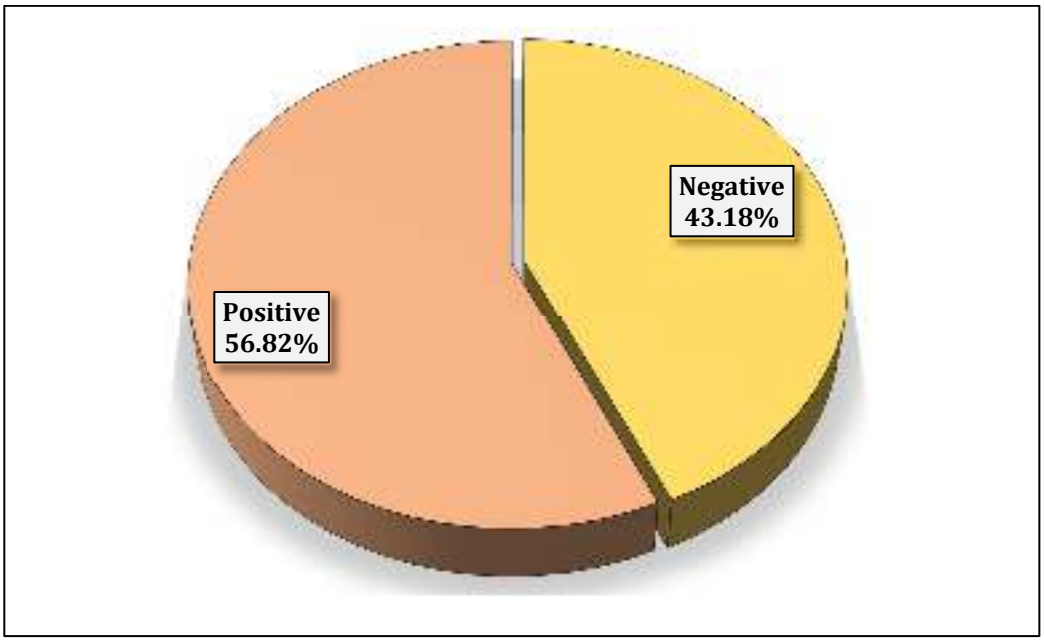
		Culture -ve	Culture +ve	P value
Steroid	**No**	5 (27.78%)	2 (7.69%)	0.1074^{MC}
	Yes	13 (72.22%)	24 (92.31%)	

From the study it was observed that 13 out of 18 cases of culture negative infection was on steroid therapy at the time of presenting with infection and 24 out of 26 cases of culture negative infection was on steroids at the time of presenting with infection with a p value of 0.1074 which was not significant.

Table 12: Distribution of subjects on the basis of Serum albumin levels at the time of admission with infection.

S.ALBUMIN	**Negative(>1.5g/dl)**	19 (43.18%)
	Positive(<1.5g/dl)	25 (56.82%)

Graph 9: Distribution of subjects based on Serum albumin values at the time of presentation with infection.



In our present study out of the 44 children 56.82% had a serum albumin value less than 1.5g/dl which was proposed as a risk factor for infection in children with nephrotic syndrome.

Table 13 :Distribution o serum albumin with respect to culture status of subjects.

		Culture +ve	Culture -ve	P value
Serum Albumin	**Negative**	7 (38.89%)	12 (46.15%)	0.6324[C]
	Positive	11 (61.11%)	14 (53.85%)	

Table 14: Distribution of children with infection in nephrotic syndrome on the basis of immunisation status.

Immunisation	**Fully immunised**	35 (79.55%)
	Partially immunised	9 (20.45%)

In our present study 79.55% of the children were fully immunised for age and there was no significant correlation with the incidence of infection.

Table 15 : Distribution of immunization status among culture positive and negative infections

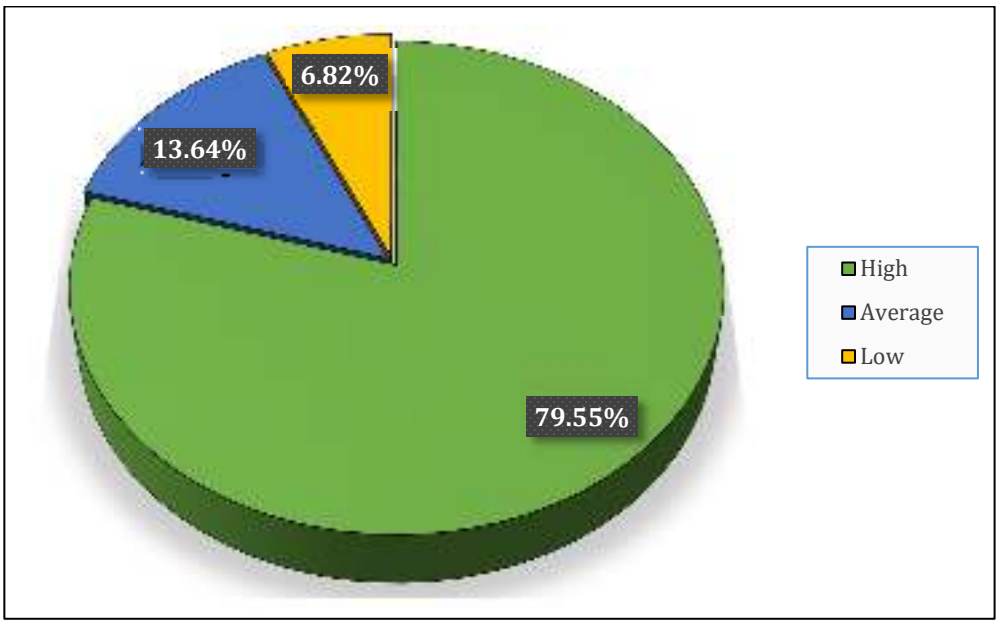
		Culture -ve	Culture +ve	P value
Immunisation	**Fully**	12 (66.67%)	23 (88.46%)	0.1399[MC]
	Partially	6 (33.33%)	3 (11.54%)	

In the study it was observed that there was no significant correlation between the immunization status among culture positive and culture negative cases, with p value 0.1399.

Table 16 : Distribution of Hs-CRP values based on predictive risk for infection.

HsCRP Values	**High Risk (≥ 3)**	35 (79.55%)
	Average (1-3)	6 (13.64%)
	Low (< 1)	3 (6.82%)
	Mean ± SD	83.93 ± 123.05
	Median (Min, Max)	20 (0.2, 617)

Graph 10: Distribution of Hs-CRP values based on predictive risk for infection.



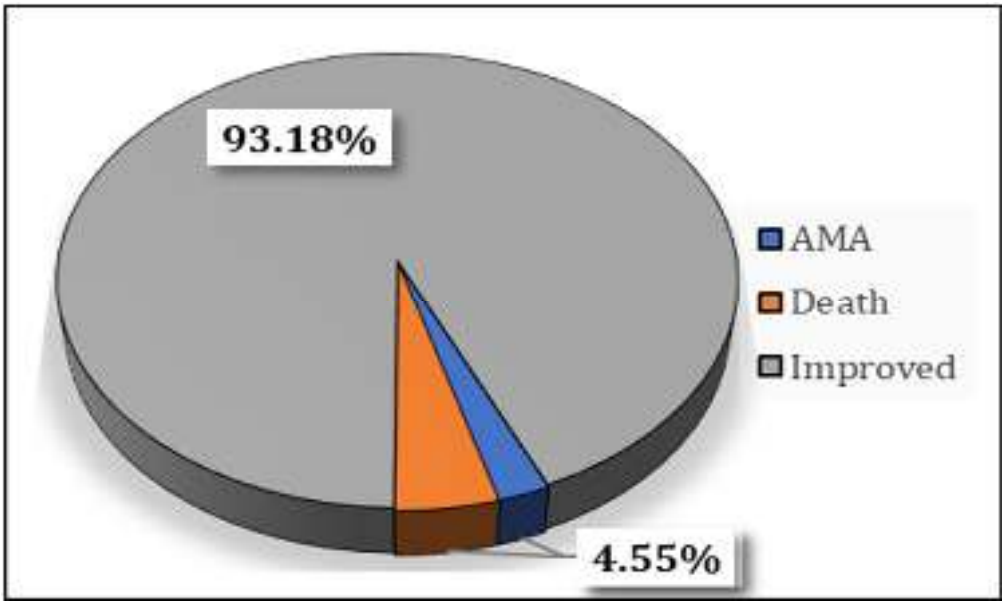
From the study it was observed that 79.55% of the total cases belonged to the high predictive risk group of infection based on serum Hs CRP values, 13.64 had moderate risk and 6.82% had low risk for infections. The mean value of Hs-CRP ranged between 83.93 ± 123.05

Table 17: Distribution of subjects based on Hs-CRP predictive risk and culture status

		Hs-CRP (>3)	Hs-CRP(<3)	P value
Culture	**Negative**	13 (37.14%)	5 (55.56%)	0.4723^{MC}
	Positive	22 (62.86%)	4 (44.44%)	

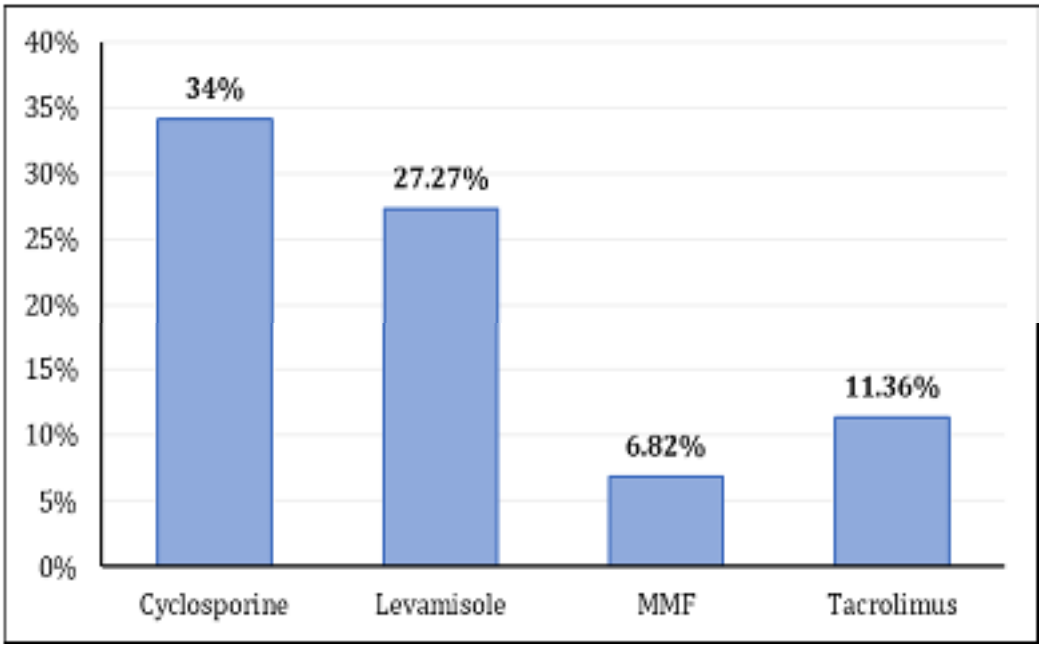
In our study there was no significant association between distribution of Hs-CRP values among culture positive and culture negative major infections with p value of 0.4723.

Graph 11: Distribution of subjects based on clinical outcome after admission and treatment



In our study it was observed that 93.88% had a good clinical outcome and was discharged successfully while 4.55% each succumbed to death or left against medical advice from our care.

Graph 12: Distribution of subjects based on the immunomodulator drugs intake



In our study of 44 subjects it was observed that 15 were on cyclosporine, 12 were on Levamisole, 3 on MMF and 5 on Tacrolimus while the rest were not on any immunomodulators. However we could not establish a positive correlation between immunomodulators and culture positive status of the infected children.

DISCUSSION

Infection triggered relapses requiring hospitalisation are an important risk factor for morbidity in pediatric age group affected with nephrotic syndrome.

The incidence of Nephrotic syndrome in global scenario is 2-16.9 per lakh population and in Asian countries 90-160 per million population.[3]

Peritonitis, pneumonia, urinary tract infections, cellulitis, meningitis and tuberculosis has been reported as major infection in children hailing from northern parts of India.[7] The present study was an attempt to find out the major manifested infections among children admitted with nephrotic syndrome (NS) and to assess the risk factors which has been studied in previous literature associated with the disease. An attempt was made to delineate the role of Hs-CRP molecule as a reliable marker of infectious etiology and to support the clinical diagnosis with appropriate microbiological culture evidence.

The cross sectional study was conducted from January 2020 to May 2021 in the department of Pediatrics, KAHER Jawaharlal Nehru Medical College and Hospital, Belagavi. During the study period a total of 72 children were admitted in the ward of which 44 had major infections. All of them were enrolled in the study and delineated for the cause and etiology of the episode.

General Characteristics:

In our present study the mean age of distribution of children was found to be 7.76 $\pm$ 5.28. The mean age of distribution observed in the study by Krishnan C et al was 5.69 $\pm$ 2.84 which was done in South India among the same age

group.[40] Another study done by Ajayan P et al showed a mean age group distribution of 6.8 $\pm$ 3.5.[8] The percentage of children below 5 years who presented with morbidity due to infection was 38.64% in this study.

In the study, majority of the children affected with major infections were boys which was consistent with the study done by Kumar M et al (53%),[7] Lebel et al (58%),[39] Ajayan et al (63%).[8] But in contrast to this study it was mentioned by Lebel et al that serious bacterial infections were found to be more in females(60%).[39] Though there is no ethnic or gender predisposition as per observational studies, the prevalence of nephrotic syndrome in children has a ratio of 2–1 male-to-female in most previous studies.[43]

Admission weight observed in this study was another demographic parameter that was recorded in the preformed proforma but as the edema associated with the disease poses to false positive results, analysis of the relationship of weight or nutrition status could not be associated with the infective state. A positive association between weight, BMI to the culture positive status was observed in the study but was not taken into account due to above mentioned lapse.

Bioelectric impedance analysis (BIA) and dual energy x-ray absorptiometry (DEA) are two modalities that accurately measure the body water and mineral composition and hence help in calculating the actual weight of the children.[44] Dry weight calculation was not done as the clinical assessment was done at the time of presentation with infection.

PRIMARY OBJECTIVE

In the present study primary objective was to identify the deep seated infections that were present in our tertiary care setup in children with nephrotic syndrome. After clinical evaluation the appropriate cultures revealed growth of micro-organism which supported our preliminary diagnosis. The important tool that we employed for this study was blood and body fluid culture and sensitivity. There was a significant association observed between the clinical diagnosis of major infections and culture of organisms in the sample p value of 0.0265. (<0.05).Thus clinical suspicion and focus directed sampling is essential in delineating an infection.

The major infection of maximum frequency in our study was Urinary tract infection which constituted 27.27% of the total. This result was consistent with the study done by Krishnamurthy et al which showed prevalence of urinary tract infection around 25%.[40] Most of the UTI episodes have been observed during periods of relapse rather than as a presenting infection in initial episode. Though not the most common infection UTI has been found in around the same prevalence and a little lesser in other developing countries around India.[42,45] Another observation in the study was the etiological agent associated with urinary tract infection.

The present study showed that E.Coli was the most common pathogen isolated in the culture samples which was consistent with studies done by Tanuka B et al which showed around 50% of UTI infections had E.Coli as the causative organism followed by Klebsiella and Proteus.[46] 62% of the Urine samples tested positive for E.coli. As urine analysis has no optimal sensitivity and the

nonspecific clinical signs of urinary tract infection has low diagnostic value urine culture has been considered as gold standard for diagnosis in children.[47]

The samples in our study has been collected keeping the Guidelines from The National Institute for Health and clinical Excellence which recommends the clean catch urine technique of the midstream urine for the culture analysis thereby preventing contamination.

The second most common infection associated in our study was peritonitis which had the similar prevalence when compared to the studies done in North India with The same sample size. This was consistent with the study done by Nermin et al which showed a prevalence of 16% of peritonitis patient in a 5 year study done in a tertiary care center.[23]

SECONDARY OUTCOME

The present study showed that the percentage of subjects who presented with first episode of nephrotic syndrome was 13.64% and the relapsed cases were 86.36%.There was increased frequency of infectious episodes in relapse cases in comparison to the initial episodes. This was in contrast to the study done by Gulati s et al which showed infection as presenting symptom of NS 38.7% cases of newly diagnosed nephrotic syndrome.[9]

In our study out of the culture positive cases we observed that 92.3% were on high dose of steroid and were diagnosed cases of steroid dependent nephrotic syndrome. This observation was different from the study observed by Ajayan et al where first episode of nephrotic syndrome had more frequency of infection than SDNS and SRNS.[40]

In our study we had included Hs-CRP as a predictive risk factor for infection, we observed that higher values of the serological marker was found in patients who had active major infection but could not find a positive correlation between the higher values and clinical outcome. This was consistent with the study done by Eran et al in 2016.[48] Sing radioimmunoassay kits Hs-CRP aids in diagnosing bacterial infections. If supported by Procalcitonin and serial values of treatment it can also be used as an indicator of treatment response. This was depicted in the study done by Vijay Kamble et al among children with infection in the year 2018.[49]

In our study no positive correlation was observed between the serum albumin value and incidence of infection. It was observed that albumin value <1.5g/dl did not increase the risk for deep seated infection which was against the observation by Gulati et al.[9] where low serum albumin levels and hypercholesterolemia was studied as a risk factor for infection.

In our study 79.5% of the children who had major infections were on immunomodulators like cyclosporine (34.09%), Levamisole (27.27%), MMF (6.82%) and Tacrolimus (11.36%). There was no observed correlation between the incidence the incidence of infection and type of immunomodulator that the child was currently on.

STRENGTHS & LIMITATIONS

1) Our study had a higher prevalence of major infections than previous similar studies due to the status of our institution as a reference centre with the availability of pediatric nephrologist and tertiary care ICUs.

2) Sample size was a limitation in our study as the prevalence of infection in nephrotic syndrome in North Karnataka was lesser than the previous studies done in other parts of South India.

3) In few of the cases even with HsCRP value high and infection rate high there was no organism isolated signifying viral etiology but Viral cultures were not employed in our study.

4) The antibiotic sensitivity pattern from the microbiology lab was inconclusive due to the limited testing depending upon community sensitivity in adults and children and could not be generalized among the children with immunocompromised state.

CONCLUSION

Major infections are one of the biggest risk factors for global burden of morbidity in nephrotic syndrome cases. Identification of the focus of infection early in the management is the cornerstone in treating children with relapse of nephrotic syndrome.

This study was conducted with an objective to outline the type of major infections prevalent in nephrotic syndrome and the risk factors in culture positive cases of infection.

Thus from our study it was concluded that the prevalence of major infections in admitted cases of nephrotic syndrome in our setup was 61%. UTI was the major infection associated in children with nephrotic syndrome in this part of North Karnataka with a prevalence of 27.27% with E.coli being the predominant organism.

With proper clinical suspicion supported by proper microbiological evidence to isolate organism and appropriate medical management we had achieved a clinical improvement in 93.18% of admitted cases.

Most of the infections occurred during the period of relapse and not during first episode suggesting role of impaired immunity in pathogenesis of major infections in these children.

SUMMARY

The prevalence of major infections in children admitted with Nephrotic syndrome was 61% in our study setup.

From our study conducted we have been able to find a higher predisposition of males 72.73% with major infections in Nephrotic syndrome most of whom belonged to the age group above 5 years.

The most prevalent major infection was Urinary tract infection 27.27% and the etiological organism prevalent was E.coli 18.18%.

Out of the total cases 59.09% of the cases with clinical suspicion of infection had culture positive major infection while 40.91% had culture negative status suggesting viral pathology for these infections.

The study showed that 86.36% of the infections occurred during relapse in already diagnosed cases of nephrotic syndrome and 96.15% of the culture positive major infections were during relapse with a significant p value of 0.0405.

The study did not show any positive correlation between culture positive major infections and serum albumin value, steroid status or Hs-CRP value.

The study showed no relation between the status of full immunisation based on the National immunisation schedule where the pneumococcal vaccination was not included.

We have found that streptococcus pneumoniae constituted 6.82% of the organisms isolated in the study and hence pneumococcal vaccination should be administered to all cases of nephrotic syndrome to prevent the incidence of infection with the same.

The use of blood culture was an important parameter in determining the type of infection at our setup. The admission culture sample and the respective growth has aided in the management. Though treatment was started with empirical antibiotics that showed community sensitivity pattern decreased response warranted change of antibiotic based on our cultures and thereby helping better outcome.

We have also emphasised the importance of midstream clean catch urine sample culture in the diagnosis of urinary tract infection which constituted the maximum percentage of infection in our study.

In our study we have also tried to include the importance HS-CRP as a marker of active infection in children with nephrotic syndrome as the urinary excretion of the same was not significant in previous studies.

79.55% had Hs-CRP values that were predictive of high risk of infection. 13.64% had moderate risk of infection and 6.82% had low risk of infection.

BIBLIOGRAPHY

1. Pal A, Kaskel F. History of nephrotic syndrome and evolution of its treatment. Vol. 4, Front Pediatr. 2016 May 30. 4:56.

2. Moorani KN, Raj M. Spectrum of Infections in Children with Newly Diagnosed Primary Nephrotic Syndrome. Vol. 51, Pakistan Journal of Medical Research. 2012. Vol. 51 Issue 1,p 10-14.

3. Bagga A SR 6th edition. Pediatric nephrology,6th Edition. 2016. 191–229.

4. Sinha A, Puraswani M, Kalaivani M, Goyal P, Hari P, Bagga A. Efficacy and safety of mycophenolate mofetil versus levamisole in frequently relapsing nephrotic syndrome: an open-label randomized controlled trial. Kidney International. 2019 Jan 1;95(1):210–8.

5. Ajayan P, Krishnamurthy S, Biswal N, Mandal J. Clinical spectrum and predictive risk factors of major infections in hospitalized children with nephrotic syndrome. Indian Pediatrics. 2013;50(8).

6. Narla D. Therapeutic Response to Corticosteroids Remains a Valid Approach to Initial Management of Children With Idiopathic Nephrotic Syndrome. Frontiers in Pediatrics. 2020 Sep 2;8.

7. Kumar M, Ghunawat J, Saikia D, Manchanda V. Incidence and risk factors for major infections in hospitalized children with nephrotic syndrome. Jornal brasileiro de nefrologia : 'orgao oficial de Sociedades Brasileira e Latino-Americana de Nefrologia. 2019 Oct 1;41(4):526–33.

8. Ajayan P, Krishnamurthy S, Biswal And N, Mandal J. Clinical Spectrum and Predictive Risk Factors of Major Infections in Hospitalized Children with Nephrotic Syndrome. Indian Pediatr.2013 Aug:50(8):779-81.

9. Gulati S, Kher V, Gupta A, Arora P, Rai PK, Sharma RK. Spectrum of infections in Indian children with nephrotic syndrome. Pediatric Nephrology. 1995;9(4).

10. Bard JD, TeKippe EME. Diagnosis of bloodstream infections in children. Vol. 54, Journal of Clinical Microbiology. American Society for Microbiology; 2016. p. 1418–24.

11. Kaneko K, Tsuji S, Kimata T, Kitao T, Yamanouchi S, Kato S. Pathogenesis of childhood idiopathic nephrotic syndrome: a paradigm shift from T-cells to podocytes. Vol. 11, World Journal of Pediatrics. Institute of Pediatrics of Zhejiang University; 2015. p. 21–8.

12. Chapter 3: Steroid-sensitive nephrotic syndrome in children. Kidney International Supplements. 2012 Jun 1;2(2):163–71.

13. Srivastava RN. 50 Years of Nephrotic Syndrome in Children, and Hereafter. Indian Pediatr 2013;50 107-110 .

14. Vallepu N, Velpula S, Kumar Dasari B, Kumar Thimmaraju M, Babu Gummadi S, Yelugam N, et al. Causes and Pathophysiology of Nephrotic Syndrome in Childhood. Renal Diseases 2019 November.2020.

15. Ha TS. Genetics of hereditary nephrotic syndrome: A clinical review. Vol. 60, Korean Journal of Pediatrics. Korean Pediatric Society; 2017. p. 55–63.

16. Mohammed DY, Ali Selim MS, Abo Zeid AM, Neemat-Allah MAA. Rate and Type of Infections in Children with Nephrotic Syndrome. Archives of Clinical and Medical Case Reports. 2018;02(02):31–9.

17. Veissi S, Smeets B, van den Heuvel LP, Schreuder MF, Jansen J. Nephrotic syndrome in a dish: recent developments in modeling in vitro. Vol. 35, Pediatric Nephrology. Springer; 2020. p. 1363–72.

18. Prince Andolino T, Reid-Adam J. Nephrotic Syndrome. Pediatr Rev.2015 Mar;36(3):117-25.

19. Manta M, Singh S. Infection associated relapses in children with nephrotic syndrome: A short-term outcome study. Saudi journal of kidney diseases and transplantation : an official publication of the Saudi Center for Organ Transplantation, Saudi Arabia. 2019;30(6).

20. Jin Park S, il Shin J. Complications of nephrotic syndrome. Vol. 54, Korean Journal of Pediatrics. Korean Pediatric Society; 2011. p. 322–8.

21. Sinha A, Bagga A, Banerjee S, Mishra K, Mehta A, Agarwal I, et al. Steroid Sensitive Nephrotic Syndrome: Revised Guidelines.Indian Pediatr 2021;58:461-481.

22. Hingorani SR, Weiss NS, Watkins SL. Predictors of peritonitis in children with nephrotic syndrome. Pediatric Nephrology. 2002;17(8):678–82.

23. Uncu N, Bülbül M, Yıldız N, Noyan A, Koşan C, Kavukçu S, et al. Primary peritonitis in children with nephrotic syndrome: Results of a 5-year multicenter study. European Journal of Pediatrics. 2010;169(1):73–6.

24. Simoes EAF,Cherian T et al.Acute respiratory infections in children.Disease control priorities in developing countries.2006.Chapter 25.135-42

25. Shah SA, Carter HP. New-Onset Nephrotic Syndrome in a Child Associated With COVID-19 Infection. Frontiers in Pediatrics. 2020;8.

26. Sarkar M. Child India. IAP Newsletter 2021 June,(1)5-10

27. Narain U, Gupta A. Urinary tract infection in children with nephrotic syndrome. Pediatric Infectious Disease Journal. 2018 Feb 1;37(2):144–6.

28. Bunde S, Sharif M, Saxena A, Resident J.Bacterial meningitis in a known case of steroid-resistant nephrotic syndrome. Indian Journal of child health,2021.8(9)338-339.

29. Mantan M, Singh S. Infection Associated Relapses in Children with Nephrotic Syndrome: A Short-term Outcome study.Saudi J Kidney Dis Transpl. 2019 Nov-Dec;30(6):1245-1253.

30. Spectrum of Infections in Children with Primary Nephrotic Syndrome: Cross Sectional Study: Journal of pediatric nephrology. 2021;9(1).

31. Senguttuvan P, Ravanan K, Prabhu N, Tamilarasi V. Infections encountered in childhood nephrotics in a pediatric renal unit.Indian J Nephrol. 2004 Jan.14:85-88.

32. Enya T, Sugimoto K. SARS-CoV-2 infection associated with the recurrence of nephrotic syndrome in a Japanese boy. Pediatr Nephrol 36,209. 2021.

33. Tain YL,Lin G,Cher TW.Microbiological spectrum of septicemia and peritonitis in nephrotic children.Pediatr Nephrol.1999 Nov;13(9):835-37.

34. Lebel A, Kropach N, Ashkenazi-Hoffnung L, Huber-Yaron A, Davidovits M. Infections in Children With Nephrotic Syndrome: Twenty Years of Experience. Clinical Pediatrics. 2020;59(7).

35. E. S, I. K, A. D, A. B-D, M. K, M. D. Is serum CRP level a reliable inflammatory marker in pediatric nephrotic syndrome? Pediatric Nephrology. 2016;31(8).

36. Wasilewska A, Zoch-Zwierz W, Tobolczyk J, Tenderenda E. High-sensitivity C-reactive protein (hs-CRP) level in children with nephrotic syndrome. Pediatric Nephrology. 2007 Mar;22(3):403–8.

37. Wang HW, Wu Y, Chen Y, Sui SF.Polymorphism of structural forms of C-reactiveprotein. Int J Mol Med 2002;9(6):665-671.

38. Peisajovich A, Marnell L, Mold C and DuClosTW. C-reactive protein at the interface betweeninnate immunity and inflammation. Expert RevClinImmunol 2008;4(3):379-390.

39. Lebel A, Kropach N, Ashkenazi-Hoffnung L, Huber-Yaron A, Davidovits M. Infections in Children With Nephrotic Syndrome: Twenty Years of Experience. Clinical Pediatrics. 2020 Jun 1;59(7):692–8.

40. Krishnan C,Rajesh T V et al. Major infections in children with nephrotic syndrome. International Journal of Contemporary Pediatrics. 2017 Feb 22;4(2):346.

41. Albar H, Bilondatu F, Daud D. Risk factors for relapse in pediatric nephrotic syndrome. Paediatrica Indonesiana. 2018;58(5).

42. Jamro B, Lal S, Shaikh AH, Jamro S. Types of infection in primary nephrotic syndrome. Pakistan Paediatric Journal. 2012;36(2).

43. Kumar K, Sharma S, Gupta N, Student PG. Prevalence of Different Clinical Variants of Nephrotic Syndrome in Children 1-18 Years of Age in Tertiary Care Hospital of North India . Vol. 121, International Journal of Scientific Study. 2020.

44. Kaur J, Pal A, Batra S. Body composition analysis in nephrotic syndrome patients-A case control study in a tertiary care hospital of Haryana. 2019;8(7)1-2

45. Wei CC, Yu IW, Lin HW, Tsai AC. Occurrence of infection among children with nephrotic syndrome during hospitalizations. Nephrology. 2012;17(8).

46. Urinary Tract Infection in Nephrotic Syndrome: A Hospital Based Cross sectional study.2016 july;15(2)41-44

47. Altuntas N, Alan B. Midstream Clean-Catch Urine Culture Obtained by Stimulation Technique versus Catheter Specimen Urine Culture for Urinary Tract Infections in Newborns: A Paired Comparison of Urine Collection Methods. Medical principles and practice : international journal of the Kuwait University, Health Science Centre. 2020;29(4):326–31.

48. Shostak E, Krause I, Dagan A, Ben-Dor A, Keidar M, Davidovits M. Is serum CRP level a reliable inflammatory marker in pediatric nephrotic syndrome? Pediatric Nephrology. 2016 Aug 1;31(8):1287–93.

49. Black S, Kushner I, Samols D. C - reactiveprotein. J BiolChem 2004; 279:48487- 90.

ANNEXURE I – CONSENT FORM

CONSENT FOR PARTICIPATION IN RESEARCH

"MAJOR INFECTIONS AND THEIR RISK FACTORS IN CHILDREN ADMITTED WITH NEPHROTIC SYNDROME IN A TERTIARY CARE CENTRE- ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"

Principal investigator : _____

Guide : _____

You are hereby requested to involve yourself/your child in the above said research to be conducted at KLE'S Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi from January 2020 to December 2020 by me_____, post graduate student in the department of Pediatrics, Jawaharlal Nehru Medical College, Belagavi.

PROCEDURE INVOLVED

The study aims to investigate the prevalence of infections in a group of nephrotic syndrome patients admitted in hospital, the etiological organisms associated with and the risk factors that can lead to the infections. The focus of infection will be identified and the responsible etiological agent identified whereby appropriately sensitive antibiotic therapy will be instituted and the outcome would be studied.

VOLUNTARY PARTICIPATION

Your and your child's participation in this study is your voluntary decision. Whether to participate or not to participate will not affect your current or future

relationship with the KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi.You are free to discontinue the participation in the study at any time for any reasons and you will not be paid any reimbursement for participation in the research.

Risk and benefits

There are no major risks involved, other than discomfort and pain caused during collection of biological sample.

Privacy and Confidentiality

The only people who will know that you are a research participant are member of the research team. No information about you or provided by you, during research will be disclosed to others without your written consent. When the results of the research are published or discussed in the conferences, no information will be disclosed that would reveal your identity. Any information obtained in connections with this study and that can beidentified with you remain confidential and will be disclosed only with your permission.

Queries

If you have any questions about your rights or research participation you may contact Dr. Roopa M Bellad,Md,Dch Professor, Department Of Pediatrics. KAHER Jawaharlal Nehru Medical College, Belgaum -590010.

You will be given a copy of this form for your information and to keep for your records.

STATEMENT OF CONSENT

I hereby voluntarily agree for my and my baby participation in this study. I understand that even if I choose to allow my baby to take part in this study I have the liberty to withdraw at any time. My signature below indicates that I have read or have been told about this entire consent form including the risks and benefits and have had all my questions answered. I will be given a copy of this consent form.

Signature of the authorized representative/ parent: _____

Date: _____

Name: _____

Relation to the Subject: _____

Signature of the witness: _____

Date: _____

Name: _____

Signature of investigator: _____

Date: _____

Name: _____

ANNEXURE II - ETHICAL CLEARANCE LETTER

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to – be University)

Accredited "A" Grade by NAAC (2nd Cycle) Placed in Category "A" by MHRD (GoI)

JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)

Website: [illegible] Phone: (+91-(0)831 Office: [illegible]
E-Mail: [illegible] Principal: [illegible]
Fax No. +91 (0)831 – [illegible]

Ref: MDC/DOME/123 Date: [illegible]/2019

To,

(REG NO.BM0119004)
PG student in Pediatrics,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled "MAJOR INFECTIONS AND THEIR RISK FACTORS IN CHILDREN ADMITTED WITH NEPHROTIC SYNDROME IN A TERTIARY CARE CENTRE- ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY ", is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. [illegible])
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. [illegible])
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

ANNEXURE III - PROFORMA

" MAJOR INFECTIONS AND THEIR RISK FACTORS IN CHILDREN ADMITTED WITH NEPHROTIC SYNDROME IN A TERTIARY CARE CENTRE."- ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY.

Principal Investigator:

Serial No: **IP No:**

Name :

Age :

Sex :

Address: **Contact No:**

DOA:

Socioeconomic status:

Chief Complaints:

History In Brief:

Past history:

H/O Diabetes

H/O Hypertension

H/O Hypothyroidism

H/O Siblings with similar complaints

H/O Drug intake

H/O Consanguinity

Natal history (Birth history):

Gestational Age at Birth-

Birth weight-

Type of Delivery-LSCS/NORMAL

If LSCS Indication-

Place of Delivery-

Cried at-

APGAR Score-

Admission to NICU (with reason)-

Post natal history:

HIE-

Jaundice-

Feeding difficulty-

RDS-

Infections-

Developmental history:

Gross motor **Fine motor** **Social & Adaptive** **Language**

IMMUNISATION HISTORY:

ANTHROPOMETRY:

Parameter	Child's measurment	Expected	Percentile
Weight			
Height/Length			
HC			
CC			
MAC			

GPE:

Vitals:

HR:

RR:

TEMP:

BP:

PALLOR: **BLEEDING:**

CLUBBING: **DEHYDRATION:**

CYANOSIS: **JVP:**

LYMPHADENOPATHY: **CFT:**

OEDEMA: **RASHES:**

ICTERUS: **GRUNTING:**

RETRACTIONS: **SHOCK:**

CONGENITAL MARKERS: **ACIDOSIS:**

SYSTEMIC EXAMINATION:

CVS:

RESPIRATORY:

PER ABDOMEN/RENAL SYSTEM:

CNS:

GENITALS:

Probable Diagnosis:

INVESTIGATIONS:

CBC:

HB	TC	Neutrophil	Lymphocyte	Eosinophil	RBC	PLT COUNT	ESR	RETIC COUNT

Calcium	Phosphate	Magnesium	Albumin	Alk phosphtase	HS-CRP	Procalcitonin

ELECTROLYTES:

SODIUM	POTASSIUM	CHLORIDES	BICARBONATE

Blood culture and sensitivity

Urine Examination (Routine & Microscopy):

Color:	**Nitrite:**
Appearance:	**Bilirubin:**
PH:	**Urobilinogen:**
Specific Gravity:	**RBC:**
Protein:	**WBC:**
Glucose:	**Epithelial cells:**
Ketone bodies:	**Casts:**
Bacteria:	

Urine Protiene/Creatinine Ratio

Urine Culture & sensitivity:

SPECIAL INVESTIGATIONS (according to etiology)

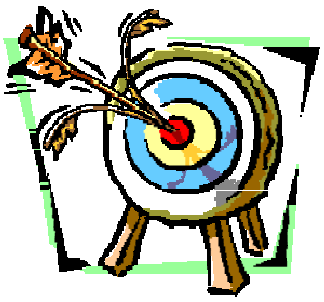
FINAL DIAGNOSIS:

ANNEXURES IV - MASTER CHART

SL no	NAME	AGE	GENDER	WT (Kg)	HT (cm)	1st EPISODE	ON STEROIDS	CULTURE	SAMPLE	ORGANISM	DIAGNOSIS	S.ALB(<1.5)	CHOLESTEROL	HsCRP	IMMUNISATION	RESULTS	TYPE OF NS	MEDICINE
1	NARAYAN	2Y	M	15.2	90	N	Y	POSITIVE	URINE	E.coli	UTI	NEG	250	204	F	IMPROVED	SDNS	LEVAMISOLE
2	SONAM	2Y	F	13.6	96	N	N	POSITIVE	URINE	K.pnuemoniae	UTI	NEG	430	2	F	IMPROVED	1ST EPISODE	
3	MAHANTESH NAIK	6Y	M	14.2	106	N	Y	POSITIVE	URINE	ECOLI	UTI	POS	361	20	N	IMPROVED	SDNS	LEVAMISOLE
4	PRAMOD	14Y	M	37.8	141	N	Y	POSITIVE	PUS	ECOLI	CELLULITIS	POS	422	10.8	F	IMPROVED	SRNS	CYCLOSPORINE
5	SHRUSHTI	5Y	F	14.6	98	N	Y	POSITIVE	BLOOD	P. aueroginosa	SEPTICEMIA	NEG	289	38	F	IMPROVED	SRNS	TACROLIMUS
6	PRAJWAL	15Y	M	26	130	N	Y	POSITIVE	STOOL	Non Enteric Pathogen	ACUTE GE	NEG	156	100	N	IMPROVED	SRNS	TACROLIMUS
7	SAMARTH	3Y	M	13.2	90	N	Y	NEGATIVE	BLOOD		LRTI	NEG	346	2.7	N	IMPROVED	SDNS	LEVAMISOLE
8	MANTHAN	5Y	M	18	110	N	Y	NEGATIVE	ASCITIC FLUID	S.pnuemoniae	PERITONITIS	NEG	430	304	F	IMPROVED	SDNS	LEVAMISOLE
9	SHASHANK	15Y	M	37.8	156.5	N	Y	NEGATIVE	ASCITIC FLUID		PERITONITIS	NEG	442	15.8	N	IMPROVED	SRNS	CYCLOSPORINE
10	HAREL LUCAS	3Y	M	13.4	89	N	Y	POSITIVE	PUS	P. aueroginosa	FOURNIERS GANGRENE	NEG	270	617	F	IMPROVED	SDNS	MMF
11	SADIQ	1y 6m	M	8.5	72	Y	N	NEGATIVE	ASCITIC FLUID		PERITONITIS	NEG	284	77.8	F	IMPROVED	SRNS	CYCLOSPORINE
12	PRITHVI	8Y	M	28	124	N	Y	POSITIVE	BLOOD	S.pnuemoniae	SEPTICEMIA	POS	281	252.3	N	IMPROVED	SDNS	LEVAMISOLE
13	PRAMOD	14y	M	37.8	141	N	Y	POSITIVE	STOOL	K.pnuemoniae	ACUTE GE	POS	533	12.8	F	IMPROVED	SRNS	CYCLOSPORINE
14	SOUMYA	5y	F	16	100	N	Y	POSITIVE	ASCITIC FLUID	K.pnuemoniae	PERITONITIS	NEG	560	0.6	F	IMPROVED	SDNS	LEVAMISOLE
15	SHUBHA	14y	F	78	125	N	Y	POSITIVE	BLOOD	Candida albicans	SEPTICEMIA	NEG	345	338.6	F	DEATH	SRNS	CYCLOSPORINE
16	SUKALP	2Y	M	11.9	86	Y	N	NEGATIVE	BLOOD		TUBERCULOSIS	POS	280	86	F	IMPROVED	1ST EPISODE	
17	ADARSH GIRIYAPPA	2Y	M	7	77	N	Y	NEGATIVE	URINE		UTI	POS	428	110	F	IMPROVED	SRNS	CYCLOSPORINE
18	MOHAMMAD ZAIN	4Y	M	15	90	N	Y	POSITIVE	BLOOD	CONS	SEPTICEMIA	POS	423	13.4	F	IMPROVED	SDNS	
19	ADITYA AKASH KOLI	6Y	M	20	113	N	Y	NEGATIVE	ASCITIC FLUID		PERITONITIS	POS	336	172	F	IMPROVED	SDNS	LEVAMISOLE
20	NAYANAVATHI	4Y	F	12.9	83	N	Y	POSITIVE	ASCITIC FLUID	ECOLI	PERITONITIS	POS	234	264.2	F	AMA	SRNS	CYCLOSPORINE
21	AKSHATHA	9Y	F	24	123	N	Y	POSITIVE	URINE	ECOLI	UTI	POS	267	15	F	IMPROVED	1ST EPISODE	
22	PRAMOD	15Y	M	38	141	N	Y	NEGATIVE	URINE		UTI	POS	568	12	F	DEATH	SRNS	CYCLOSPORINE
23	BASAVARAJ	16Y	M	46	144	N	Y	POSITIVE	URINE	ECOLI	UTI	POS	510	88	F	IMPROVED	SDNS	TACROLIMUS
24	MAHANTESH NAIK	6Y	M	15	106	N	Y	POSITIVE	BLOOD	CONS	SEPTICEMIA	POS	453	211	F	IMPROVED	SDNS	LEVAMISOLE
25	SHIVAM VEERABHADRA JARALI	2Y 3M	M	14.3	85	N	Y	NEGATIVE	URINE		UTI	POS	627	0.2	F	IMPROVED	SDNS	MMF
26	MANJUNATH	15Y	M			N	Y	POSITIVE	SPUTUM	S.pnuemoniae	LRTI	NEG	365	14.3	F	IMPROVED	SRNS	CYCLOSPORINE
27	PRAJWAL	16Y 11M	M	29.3	131	N	Y	POSITIVE	STOOL	E.coli	ACUTE GE	POS	510	45.9	F	IMPROVED	SRNS	TACROLIMUS

SL no	NAME	AGE	GENDER	WT (Kg)	HT (cm)	1st EPISODE	ON STEROIDS	CULTURE	SAMPLE	ORGANISM	DIAGNOSIS	S.ALB(<1.5)	CHOLESTEROL	HsCRP	IMMUNISATION	RESULTS	TYPE OF NS	MEDICINE
28	MAHANTESH NAIK	7Y	M	15	107	N	Y	POSITIVE	STOOL	Ascaris lumbricoides	ACUTE GE	POS	338	1	F	IMPROVED	SDNS	LEVAMISOLE
29	HAREL LUCAS	3Y	M	13.4	89	N	Y	POSITIVE	BLOOD	Candida albicans	SEPTICEMIA	NEG	325	210	F	IMPROVED	SDNS	MMF
30	SHASHANK	15y	M	37.8	156.5	N	Y	NEGATIVE	BLOOD		LRTI	NEG	323	11.8	N	IMPROVED	SRNS	CYCLOSPORINE
31	PRAJWAL	16Y	M	26	130	N	Y	POSITIVE	PLEURAL FLUID	MRSA	LRTI	NEG	386	18.7	F	IMPROVED	SRNS	TACROLIMUS
32	ABHISHEK SIDAPPA	10Y	M	30	136	N	Y	NEGATIVE	ASCITIC FLUID		PERITONITIS	POS	329	18	N	IMPROVED	1ST EPISODE	
33	AKSHATHA MANJU	9Y	F	24	123	Y	N	NEGATIVE	ASCITIC FLUID		PERITONITIS	POS	499	1.5	F	IMPROVED	SDNS	
34	SHREYAS VITTAL	2Y	M	12.76	84	Y	N	NEGATIVE	STOOL		ACUTE GE	POS	412	20	F	IMPROVED	SDNS	LEVAMISOLE
35	SADIQ	2Y	M	8.9	84	N	Y	POSITIVE	URINE	ECOLI	UTI	NEG	378	45.8	F	IMPROVED	SRNS	CYCLOSPORINE
36	KALMESH	15Y	M	30	136	N	Y	NEGATIVE	ASCITIC FLUID		PERITONITIS	POS	329	51	F	IMPROVED	SRNS	CYCLOSPORINE
37	CHANDANA	11Y	F	23.8	116.5	Y	N	NEGATIVE	ASCITIC FLUID		PERITONITIS	POS	478	1.2	N	IMPROVED	1ST EPISODE	
38	KALPANA	4Y	F	11	81	N	Y	NEGATIVE	BLOOD		LRTI	NEG	258	1.8	N	IMPROVED	SRNS	CYCLOSPORINE
39	MOHAMMAD ZAIN	4Y	M	14.2	95	N	Y	POSITIVE	STOOL	K.Oxytoca	ACUTE GE+SEPSIS	NEG	535	110	F	IMPROVED	SDNS	
40	NAYANAVATHI	5Y	F	12	91	N	Y	NEGATIVE	ASCITIC FLUID		PERITONITIS	POS	502	12.1	F	IMPROVED	SRNS	CYCLOSPORINE
41	KALMESH BHUTALE	15Y	M	30	136	N	Y	POSITIVE	STOOL	Non Enteric Pathogen	ACUTE GE	POS	459	59.1	F	IMPROVED	SRNS	CYCLOSPORINE
42	MAHANTESH NAIK	6Y	M	17.3	110	N	Y	NEGATIVE	URINE		UTI	NEG	460	3.3	F	IMPROVED	SDNS	LEVAMISOLE
43	SAMRUDHI	3Y	F	15.6	91	Y	N	POSITIVE	URINE	K.pnuemoniae	UTI	POS	531	99	F	IMPROVED	1ST EPISODE	
44	YADVIKA	3Y7M	F	19.1	101	N	Y	POSITIVE	URINE	K.pnuemoniae	UTI	POS	268	0.2	F	IMPROVED	SDNS	LEVAMISOLE

Introduction



Objectives

Review of Literature

Methodology

Results

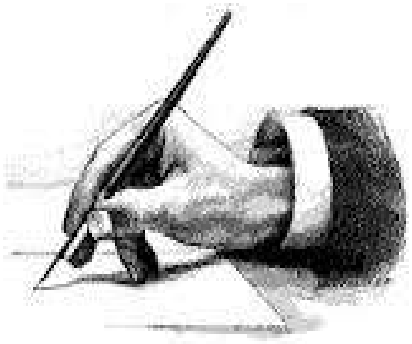
Discussion

Limitations

Conclusion

Summary

Bibliography



Annexure-I

Annexure-II

Annexure-III

Annexure-IV