Nephrotic Syndrome

Objectives:

● Define the term nephrotic syndrome .

● Discuss classification, etiology, and pathophysiology of nephrotic syndrome.

● Know clinical presentation and laboratory evaluation of a child with nephrotic syndrome.

● Discuss the treatment of nephrotic syndrome.

Nephrotic Syndrome it Is a common paediatric disorder characterized by :

Heavy proteinuria >3.5g/day, or a urine protein:creatinine ratio > 2

Hypoalbuminemia (<2.5g/dl)

Edema

Hyperlipidemia with S.cholestrol >200 mg/dl.

Etiology:

Idiopathic N.S [90%] of cases.

Causes of idiopathic N.S include:

1. Minimal change (85%) .

2. Mesangial proliferation (5%).

3. Focal segmental (10%).

Secondary N.S (10%):

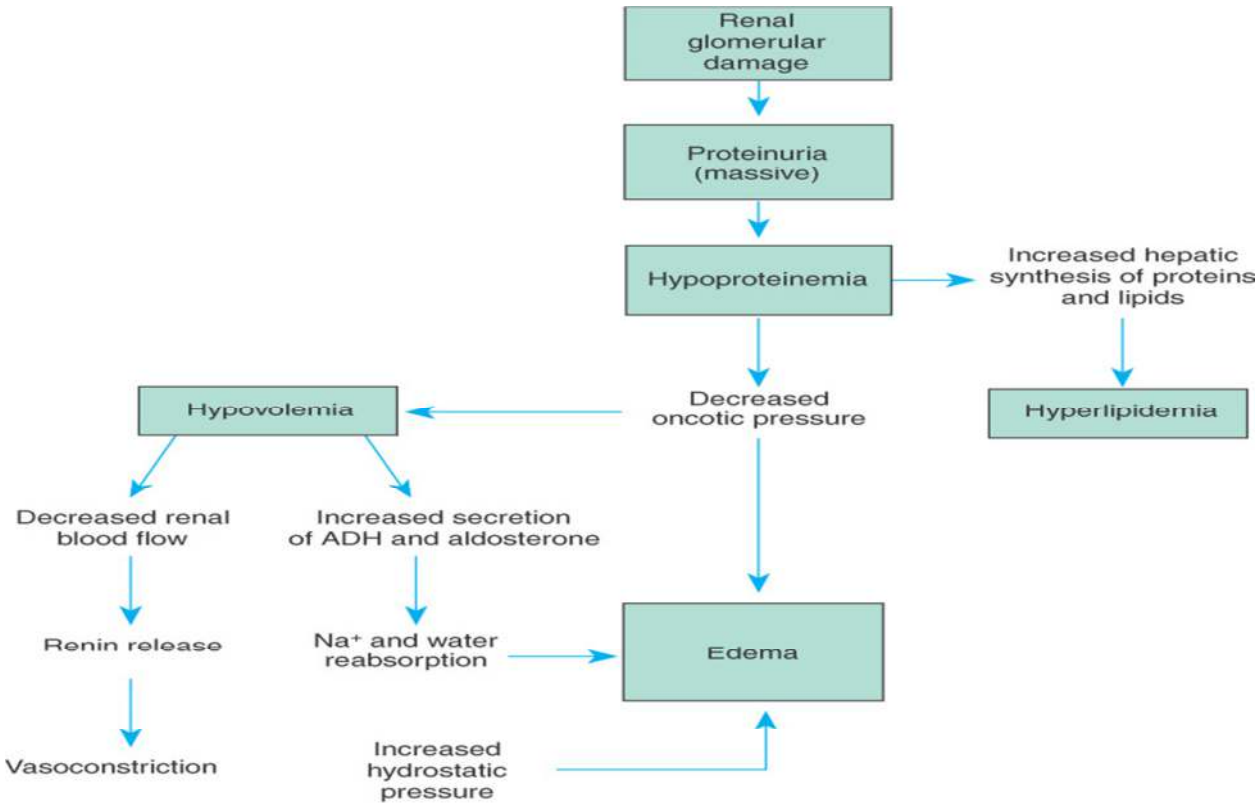
► related to glomerular disease such as

membranous or membranoproliferative G.N , lupus nephritis, and Henoch-Schonlein purpura nephritis

► infectious agents associated with nephrotic syndrome include hepatitis B virus, hepatitis C virus, leprosy, and HIV.

►Tumers like lymphoma.

Pathophysiology:



Clinical Manifestations:

♂>♀ **2:1**

Most common age 2-6year

Edema initially noted around the eyes

(periorbital) & in the lower extremities

(Pitting edema).

With time may become generalized with development of ascites, pleural effusion, &genital edema.

Anorexia.

Abdominal pain.

Diarhoea.

Haematuria &HT uncommon.

Diagnosis

•Urinalysis:

proteinuria usually detected by dipstick test ,which reported as:

– ve

Trace {10-20mg/dl}.

1+ ≈ {30mg/dl}.

2+ ≈ {100mg/dl}.

3+ ≈ {300mg/dl}.

4+ ≈ {2000mg/dl}.

• A spot urine protein : creatinine ratio should be > 2.0

•24 hour urine collection for albumin usually >3.5g/day.

•Renal function test: usually normal.

•Serum albumin <2.5g/dl

↓Total S.protein (normal level 6-8g⁄dl).

•Elevated serum cholesterol >200mg/dl.

•Normal level C3 &C4.

•Renal biopsy:

Renal biopsy is not indicated in most of children with N.S, it is indicate in case of:

1. Age <1year>12 year.

2. Gross haematuria.

3. Hypocomplementemia

4. Impaired renal function.

5. Sustained HT.

Complications:

1.Infections:

Is the major complication of N.S, types of infections are:

♦Spontaneous bacterial peritonitis(SBP):

Presented with abdominal pain, tenderness, vomiting &Fever.

Most common organisms causing such infection are:

Strepticoccal pneumonea*e& *E .coli.

Dx: Peritoneal leukocyte counts > 250 cells/µL are highly suggestive of spontaneous bacterial peritonitis

Treatment of SBP:

Cefotaxime or ampicillin with aminoglycoside for 10-14 days.

Other types of infections are:

♦sepsis **♦ UTI**

♦pneumonia **♦ cellulitis**

Causes of increase susceptibility to infection are:

♦ Urinary loss of IgG.

♦ Edema.

♦ Defective cell mediated immunity.

♦ Immunosupressive therapy.

♦defects in the complement cascade from urinary loss of complement factors (predominantly C3 and C5), as well as alternative pathway factors B and D, lead to impaired opsonization of microorganisms.

2.Arterial & venous thrombosis: *including*

Renal vein thrombosis.

Pulmonary embolus.

Sagital sinus thrombosis.

This is due to:

♦vascular stasis from hemoconcentration and intravascular volume depletion, increased platelet number and aggregability, and changes in coagulation factor levels.

♦There is an increase in hepatic production of fibrinogen along with urinary losses of antithrombotic factors such as antithrombin III and protein S.

3. Obesity and Growth

4.H.T

5.Renal failure

Treatment of Nephrotic syndrome:

Non specific treatment

These include:

• Treatment of infections.

• Appropriate diet.

• Diuretic drugs.

• Observation chart.

Diet :

Balanced diet consisting of 1.5-2g/kg/day of proteins and adequate calories is recommended.

Fats should constitute no more than 30%of total calories.

Sodium restriction (<1500 mg daily).

Observation chart of child with N.S :

This chart should include:

Vital signs, especially BP

Body WT.

Urine albumin.

Urine output.

Diuretic Drugs

Oral diuretics (chlorthiazide or spironolactone) for *mild-moderate edema*.

***for severe edema*: i.v chlorothiazde 10mg/kg/day bid or furosemide**

(1-2mg/kg/dose bid).

I.V 25% albumin (0.5-1.0 g albumin/kg) as a slow infusion followed by furosemide (1-2 mg/kg/dose IV) is sometimes necessary.

Specific Treatment:

Prednisolone 60 mg/m2/day or 2 mg/kg/day, maximum of 60 mg daily as a single daily dose for 4-6wk. median time of response is 10 days (urine trace or –ve for protein for 3

consecutive days).

After the initial 4-6 wk course, the steroid (prednisolone) dose tapered to 40 mg/m2/day or 1.5 mg/kg/day on alternative day & slowly tapered for a period ranging from 8 wk to 5 mo.

Relapse:

Relapse of nephrotic syndrome is defined as a first morning urine protein : creatinine ratio of >2

or ≥ 3+protein on urine dipstick testing for 3 consecutive days with presence of oedema.

Frequent relapse is 4 or more relapse/ year

Steroid Resistant

Steroid resistance is the inability to induce remission within 8 wk of daily steroid therapy.

Steroid Dependant

Steroid dependent is a relapse during steroid tapering or a relapse within 2 wk of the discontinuation of therapy.

Alternative agents:

These are drugs other than steroid used in treatment of N.S

Indications:

1. Frequent relapse.

2. Steroid resistant.

3. Steroid dependant.

4. Severe steroid toxicity:

♥Cushioned appearance

♥ HT ♥ Cataract

♥ Growth failure

These agents include:

▲Cyclophosphamide:

2mg/kg/day in single dose for 8-12wk with alternative day prednisolone .

During the course of cyclophosphamide therapy WBC count must monitored

weekly, withheld if the count <5000/mm3.

Side effect:

♦ Neutropenia.

♦ Hemorrhagic cystitis.

♦ Alopecia.

♦ Sterility.

♦ Increase risk of future malignancy.

▲Calcineurin inhibitors (cyclosporine or tacrolimus) are recommended as initial therapy for children with steroid-resistant nephrotic syndrome.

▲Mycophenolate can maintain remission in children with steroid-dependent or frequently relapsing nephrotic syndrome.

Levamisole, an antihelmintic agent with immunomodulating effects that has been shown to reduce the risk of relapse in comparison to prednisone.

▲rituximab, monoclonal antibody against CD20, may be hulpful in children with steroid-dependent and/or steroid-resistant nephrotic syndrome.

Family counseling

The following points should explain to the family:

> The condition is not infectious or hereditary, pt. is unlikely to develop chronic Renal disease especially steroid responsive.

>High percentage will achieve complete remission especially steroid responsive.

>The pt. may have some relapses that decrease in the frequency with increasing age.

>The pt. should bring to medical attention if develops abdominal pain, fever or look ill.

>Diet.

>Vaccinations: Patients with N.S receiving a dose of equivalent to 2 mg/kg/day of prednisolone or more for more than 2weeks considered *immuno-compromised*.

Live vaccines should only be administered once the child is off steroid for 6 weeks.

Routine, non live viral vaccines should be administered according to their recommended schedules.

Prognosis:

The majority of children with steroid responsive nephrotic syndrome have repeated relapses, which decrease in frequency as the child grows older. The steroid responsive N.S will not develop chronic renal failure. Steroid resistant focal segmental G.N carry poor prognosis.