Nephrotic Syndrome

Definition:

This is a clinico – laboratory condition characterized by:

1- Heavy proteinuria (mainly albuminuria) (> 1 g/m^2/24 hr).
2- Hypo albuminemia (serum albumin < 2.5 g/dL).
3- Generalized edema.
4- Hypercholesterolemia (> 250 mg/dL).

Classification:

1- **Idiopathic nephrotic syndrome:** no definite cause is known (90%).
There are three histopathologic subtypes:
(a) Minimal change (85%)
(b) Focal sclerosis (10%).
(c) Mesangial proliferation (5%).

2- **Secondary nephrotic syndrome** (10% of cases):
- Systemic lupus erythematosus.
- Henoch schönlein purpura.
- Amyloidosis, diabetes mellitus.
- Infections as falciparum malaria and post streptococcal G.N.
- Drugs as penicillamine and aminoglycosides.
- Heavy metals as gold and mercury.
- Vascular as renal vein thrombosis.

3- Congenital nephrotic syndrome (Finnish type):

It is due to defect in nephrin protein of GBM, It occurs usually at birth or in the first 3months after birth; It has a poor prognosis that ends in chronic renal failure.

Prognosis: *Death* occurs by the age of 3-5 years.

Treatment: no effective medical treatment in this type and the only treatment is renal transplantation.

Pathophysiology of the manifestations of N.S:

1- Proteinuria:
- It is usually defined as protein excretion in the urine to more than 40mg/m^2/hr or more than 1gm/m^2/day.
- It results from an increase in glomerular capillary wall permeability.
- The mechanism is unknown but it may be related to loss of the negative charged glycoproteins within the capillary wall.
- In nephrotic syndrome, the degree of proteinuria may be massive reaching more than 10 gm/day.
- In minimal change nephrotic syndrome, the proteinuria is usually selective (mainly albuminuria).

2- Hypoproteinemia:
- It is mainly hypoalbuminemia. It results from loss of proteins in urine.
- Total serum protein level is usually less than 5 gm% and serum albumin level is usually less than 2.5 gm%.

3- Generalized edema:

The mechanism of edema formation is as follow:

Hypoalbuminemia leads to decreased oncotic pressure → the fluids is shifted from the intravascular compartments to the interstitial space → edema

4- Hyperlipidemia: Almost all serum lipids (cholesterol, triglycerides and lipoproteins) are elevated. ***The causes are:***

a- The hypoproteinemia stimulates generalized protein formation in the liver including lipoproteins.

b- Lipid catabolism is diminished due to loss of the enzyme lipoprotein lipase in the urine.

Idiopathic Nephrotic Syndrome

Etiology: unknown

Pathologic classification:

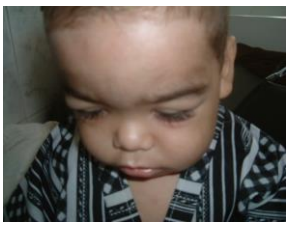
1- **Minimal change** nephrotic syndrome (MCNS). It forms 85% of cases. By light microscope nothing abnormal and by electron microscope we find fusion and retraction of epithelial cell foot processes.

2- **Focal sclerosis** (10% of cases)
By light microscope: some glomeruli appear normal and others appear sclerosed & fibrosed.

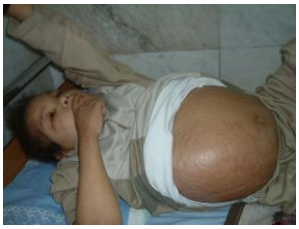
3- **The mesangial proliferation type** (5%)
By light microscope: mesangial cells and matrix proliferation.

Clinical manifestations:

Periorbital edema of NS



Ascites of NS



Age incidence: 2-8 years.

1- Generalized edema**:** Initially around the eyes and in lower limbs then it becomes generalized with or without ascites, pleural or pericardial effusion.

2- The blood pressure is rarely raised.

3- Relapses: patients may present with relapse and it is common in MCNS. It can be defined as recurrence of oedema and proteinuria in patient who was in remission.

Complications

1- Increased tendency to arterial and venous thrombosis due to increase certain coagulation factors and hypovolemia.

2- Increased susceptibility to bacterial infection because the patient is immunocompromised due to loss of the immunoglobulins in proteinuria. The infection may occur as cellulitis, pneumonia, septicemia and peritonitis which are the most serious infection.

3- Renal impairment.

Laboratory investigations:

- Proteinuria moderate or massive and is selective.
- No hematuria but sometimes microscopic hematuria may be present and it is usually transient.
- No RBCs casts but lipoid casts may be present.

- Plasma protein total level is usually less than 4.5gm/dl. Albumin level is usually less than 2.5gm/dl.
- Serum cholesterol level is usually more than 220mg/dl.
- C_3 level is normal.
- Blood urea and serum creatinine are usually normal.

Treatment of idiopathic nephrotic syndrome:

The essential treatment is corticosteroids and or cytotoxic drugs.

A- Observation: temperature, weight gain, blood pressure, urine volume and fluid intake.

B- Diet: should be:

1- Low in sodium.
2- Low in fat.
3- High in proteins
4- High in calories.
5- Fluids: not restricted except if there is oliguria.
6- Potassium given in sufficient amount if diuretics are used.

C- Drugs:

1- Antibiotics:

a) Prophylactic: Oral penicillin or its derivatives (400.000 IU daily).

b) Therapeutic: Broad spectrum antibiotics that cover gram –ve and gram +ve organisms are given in high doses.

2- Diuretics: Avoid aggressive diuretic therapy as the intravascular compartment is already contracted, but can be used in severe edema.

a) Chlorothiazide 10-20 mg/kg/day in 2 divided doses.

b) Furosemide (lasix): 1-2 mg/kg/dose orally. Monitoring of blood pressure and serum electrolytes is essential.

3- Salt poor human albumin: Used in cases of marked hypoalbuminemia (< 2g/dl) with severe edema. It is given by IV drip method followed by furosemide.

4- Corticosteroid therapy: is the essential treatment:

a) *Induction therapy:*

- Prednisone (after confirming a negative PPD test) is given at a dose of 60 mg/m^2/day (maximum daily dose is 80 mg) divided into 2 -3 doses.
- The corticosteroid should be given for at least 4 - 6 consecutive weeks even if the urine became free of proteins before this period. This is to decrease the relapse frequency.

b) *Alternate therapy:*

After the initial 4-6 wk course, the prednisone dose should be tapered to 40 mg/m^2/day given every other day as a single morning dose. The alternate-day dose is then slowly tapered and discontinued over the next 2-3 mo. **The clinical responses to this regimen are:**

1- About 93% of patients respond to daily steroid therapy within 1month. They are called initial responders or ***steroid sensitive patients***.

2- Children who continue to have proteinuria (2+ or greater), after 8 wk of daily divided steroid therapy are considered ***steroid resistant***, and *a diagnostic renal biopsy* should be performed. Those patients should receive *cyclophosphamide therapy* for 2 mo together with low dose steroid.

3- Patients who do not respond to cyclophosphamide are given *cyclosporine*.

- A subset of patients will **relapse** while on alternate-day steroid therapy or within 28 days of stopping prednisone therapy. Such patients are termed ***steroid dependent***. Relapses should be treated with daily divided-dose prednisone at the doses noted earlier until the child enters ***remission*** (urine trace or negative for protein for 3 consecutive days). The prednisone dose is then changed to alternate-day dosing and tapered over 1-2 mo.

- Patients who respond well to prednisone therapy but relapse four or more times in a 12 mo period are termed ***frequent relapsers***.

5- Vaccination: After complete remission each child should receive polyvalent pneumococcal and haemophilus influenzae vaccines.

6- Low dose aspirin may be given to decrease thrombosis**.**

Indications of renal biopsy in Nephrotic Syndrome:

1- The age less than 2 years or more than 8 years.
2- Cases with persistent hematuria and hypertension.
3- Steroid resistant or dependent cases.
4- Presence of renal impairment.
5- All cases of secondary nephrotic syndrome.

Renal Failure

Acute Renal Failure

Definition: It is a clinical syndrome characterized by sudden drop in renal function associated with fluid and electrolyte disturbance.

Etiology:

a. Prerenal:
Severe dehydration, hemorrhage, burns, sepsis, heart failure.

b. Renal:
- **Infection** Poststreptococcal glomerulonephritis, pyelonephritis.
- **Systemic** disease: SLE.
- **Hematologic**: Acute and severe hemolysis, hemolytic uremic syndrome.
- **Vascular**: Renal vein or renal artery thrombosis.
- **Acute tubular necrosis**.
- **Drugs**: Aminoglycosides, nonsteroidal anti-inflammatory drugs.
- **Toxins** and poisons.
- **Hypoxic ischemic injury**: lead to tubular damage.

c. Postrenal: It occurs as a result of obstruction which may be
- **Congenital**: Posterior urethral valve.
- **Acquired**: Stones or tumors.

Clinical manifestations:

Prerenal: There are signs of dehydration, low cardiac output (hypotension) and **oliguria**.

Renal causes:
- There is often a history of the offending agent as drugs or infection.
- The patient has hypertension and hypervolemia and may present with hypertensive encephalopathy or congestive heart failure.
- Edema and oliguria may be present.
- Palpable renal mass as in case of renal vein thrombosis or obstruction of urinary tract.

Postrenal: The same manifestation as in renal causes plus evidence of obstruction.

Investigations:

1- Increased serum creatinine (N 0.5 – 1.5 mg %).
2- Increased blood urea (N 20 – 40 mg %).
3- Increased serum K^+ (N 3 – 5 mEq/L).
4- Increased serum phosphate (N. 3.5 – 5.5 mg %).
5- Decreased serum Ca^{++} (N 9 – 11 mg %).
6- Decreased serum Na^+ (N 130 – 145 mEq/L).
7- Metabolic Acidosis: ($NaHCO_3$ < 16 mEq/L).

8- Renal ultrasound to diagnose obstruction.

Treatment:

(A) Medical treatment:

I. Treatment of the cause:

- Correction of hypovolemia by isotonic saline or blood according to the fluid lost. After that you can give furosemide to stimulate diuresis.
- Treatment of infection.
- Stoppage of nephrotoxic drugs or exposure to toxins.
- If no diuresis after furosemide give the daily fluids as follow:
  400 ml of fluids/m^2 + urine output / 24hr

II. Nutrition:

- Give sufficient calories to prevent catabolism.
- The diet should be rich in carbohydrate, low in potassium and phosphorus.
- Proteins: give the daily requirements only.

III. Hyperkalemia: can be treated by

- *Calcium gluconate 10 % 1 ml / kg (IV over 3- 5 min).*
- $NaHCO_3$ 1-2 mEq / kg / dose (IV over 5 – 10 min).
- Glucose and insulin (0.1 unit insulin + 0.5 gm glucose / kg IV over 1 hr).

IV. Hyperphosphatemia: Treated by oral calcium carbonate.

V. Hypocalcemia: Give calcium gluconate IV.

VI. Hyponatremia**:** Fluid restriction.

VII. Acidosis**:** $NaHCO_3$ 2-3 mEq / kg IV and can be repeated if needed.

VIII. Hypertension**:** By antihypertensive drugs.

(B) Dialysis: is indicated if the medical treatment fails to correct the abnormalities of acute renal failure. Dialysis may be peritoneal or hemodialysis.

(C) Surgical treatment: In case of obstruction, the patient must be immediately operated upon to remove the cause of obstruction.

Complications:

1- Chronic renal failure.

2- Death.

Chronic Renal Failure

Chronic renal failure (CRF) is defined as an irreversible reduction in GFR. Although the terminology used to describe the degrees of renal dysfunction varies, many clinicians use the following definitions:

- Mild chronic renal insufficiency: GFR 50 -75 mL/min/l.73 m^2
- Moderate chronic renal insufficiency: GFR 25-50 mL/min/l.73 m^2
- Chronic renal failure (CRF): GFR 10-25 mL/min/l.73 m^2
- End stage renal disease (ESRD): GFR < 10 mL/min/l.73 m^2

Causes**:** Like the renal and postrenal causes of acute renal failure but the effect is gradual.

Clinical picture**:**

- Non specific symptoms e.g. Headache, fatigue, lethargy, anorexia, and vomiting.
- Hypertension, oliguria, edema, pallor and growth retardation.

Investigations**:** Like acute renal failure.

Treatment:

I- Supportive (conservative): like acute renal failure.
II- Dialysis (peritoneal or hemodialysis).
III- Renal transplantation: It is the treatment of choice.

Polyuria

Definition:
Urine volume > 5 L/day or 400 ml/m^2/day.

In neonate: the normal urine output is1-3 ml/kg/hour.

In infants and early childhood: the normal urine output is 3 - 6 ml/kg/hour.

Most common Causes of polyuria:

- Weather as in cold temperature.
- Diabetes mellitus.
- Diabetes insipidus.
- Psychogenic polyuria.
- Chronic renal failure
- Acute renal failure (diuretic phase).
- Hypercalcemia.
- Hypokalemia.
- Renal tubular acidosis (RTA).
- Urinary tract infection.
- Use of diuretics.

Urinary Tract Infections (UTIs)

Definition:

Infections affecting the structures participating in the secretion and elimination of urine: the kidneys, ureters, urinary bladder and urethra.

Urinary tract infection (UTI) is one of the most common infections of childhood. It distresses the child, concerns the parents, and may cause permanent kidney damage.

Predisposing factors:

- Female (short urethra)
- Uncircumcised male
- Urinary tract anomalies:
  - Vesicoureteric reflux.
  - Obstructive uropathy.
- Instrumentation (catheters).
- Immunocompromized child.
- Pinworm infestation.
- Tight clothing.

Organism:

Gram –ve:

- Escherichia coli
- Proteus
- Pseudomonas
- Klebsiella

Gram +ve:

- Staph. Aureus
- Strept. Fecalis

Viral:

- Adenovirus

Clinical picture:

Asymptomatic bacteriuria:

Accidental finding of bacteria in urine culture without manifestations of UTI and does not cause renal injury.

Newborn:

Presented as generalized septicemia:

- Poor feeding and refusal of feeding.
- Temperature instability (hyperthermia & hypothermia), but hypothermia is more common.
- Jaundice.

Children:

According to site of infection (localization):

Upper UTI: (pyelonephritis)

- Acute: fever, rigors, and loin pain.
- Chronic: prolonged fever, loss of weight, manifestation of renal failure (e.g. anemia, bleeding tendency, hypertension, neurological manifestation, pericarditis, cardiomyopathy).

Lower UTI: (cystitis, urethritis)

- Dysuria.
- Frequency.
- Drippling.
- Urgency.
- 2^{ry} nocturnal enuresis.
- ± hematuria.

Investigation:

- **Urine analysis:**
  - Pyuria (leukocytes in the urine): pus cells > 5 cells/HPF.
  - Bacteriuria: > 100 cells/HPF.
  - Gram stained films for bacteriuria.
- **Urine culture:**

Urine sample obtained by:

- Suprapubic aspiration: For infants below 1 year and in sick patients: (PT, PTT should be done at first because it is contraindicated in blood diseases as DIC, hemorrhagic blood diseases)
- Urinary catheter sample.
- Urine bag.
- Midstream morning urine: in toilet trained children.
  - In suprapubic aspiration: Any growth is significant.
  - In catheter sample and clean voided urine: We must do colony count.

Colony count:

To differentiate between infected and contaminate specimens:

- More than 100.000 colony/ml of a single organism is +ve culture.
- 10.000-100.000 colony/ml (contaminated) repeat the urine culture.
- Less than 10.000 colony/ml is -ve culture.

- **Blood culture:** may be positive especially in neonate and infancy.
- **Complete blood picture:**
  - Anemia: in prolonged cases (CRF)
  - PMN leukocytosis. ↑ ESR CRP +ve
- **Renal function tests:** BUN Serum creatinine
- **Serum electrolytes:** Na K
- **Radiological examination:** Indications:
  - All boys of any age.
  - All girls less than 5 years.
  - Older girls after 2nd attack of UTI.
  - Persistent symptoms inspite of adequate treatment.

- Palpable mass in loin or suprapubic area.

Renal ultrasound:

- To detect acute pyelonephritis.
- To detect renal or perirenal abscess.
- To rule out obstructive uropathy and hydronephrosis.

Voiding Cystourethrography: To detect vesicoureteric reflux.

Renal DMSA scan:

- Used technetium labeled 2, 3 dimercaptosuccinc acid.
- Used mainly to detect pyelonephrities and renal scars.

Treatment of UTI:

- Adequate hydration.
- Antibiotics: According to culture and sensitivity for 14 days. Until the results of culture and sensitivity become ready, we start with:
  - Urine culture after 1 week to ensure recovery. Repeat urine culture after 3 months to detect recurrence and for 1-2 years even when the child is asymptomatic.

Prevention of UTIs:

- Remove underlying risk factors e.g. stones.
- Adequate hydration.
- Avoid constipation.
- Adequate bladder emptying.
- Prophylactic antibiotics for risk groups:
  - Frequent (recurrent) UTIs.
  - Vesicoureteric reflux.
  - Obstructive uropathy.
  - Neurogenic bladder.