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Update Management of nephrotic Syndrome in Pediatrics

Essay

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Hanan ghazaly yousef

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LIST OF ABBREVIASIONS

- **ACE :** Angiotensin converting enzyme inhibitors.
- **ACTN4 :** _-actinin-4 gene.
- **ADH :** Antidiuretic hormone.
- **AFP :** Alpha-fetoprotein.
- **AIN :** Acute interstitial nephritis
- **ANP :** Atrial Natriuretic Peptide**.**
- **ARBs :** Angiotensin receptor blockers**.**
- **ARF :** Acute renal failure.
- **ATN :** Acute tubular necrosis.
- **C3 :** Complement 3.
- **C4 :** Complement 4.
- **CBC :** Complete blood count.
- **Chl :** Chlorambucil.
- **CNF :** Congenital nephrotic syndrome.
- **CsA :** Cyclosporine A.
- **CYP :** Cyclophosphamide.
- **DDS :** Denys-Drash syndrome.
- **DMP :** Diffuse mesangial proliferation.
- **DMS :** Diffuse mesangial sclerosis.
- **DVT :** Deep venous thrombosis.
- **EM :** Electron microscopy.
- **EMU :** Early morning urine.
- **ESRD :** End-stage renal disease.
- **ESRF :** End-stage renal faliure.
- **FRNS :** Frequent relapses nephrotic syndrome.
- **FS :** Frasier syndrome.
- **FSGS :** Focal segmental glomerulosclerosis.
- **GBM :** Glomerular basement memberane.
- **GFR :** Glomerular filtration rate.
- **HDL :** High-density lipoprotein.
- **HIV :** Human immunodeficiency virus.
- **HMG :** Hydroxymethylglutaryl.
- **IDL :** Intermediate-density lipoprotein.
- **IF :** Immunofluorescent.
- **IMPDH :** Inosine monophosphate dehydrogenase.
- **INS :** Idiopathic nephrotic syndrome.
- **ISKDC :** International Study of Kidney Diseases in Childhood.

- **K :** Potassium.
- **KDOQI :** Kidney Disease Outcome Quality Initiative.
- **LAMB2 :** laminin _2 gene.
- **LDL :** Low-density lipoprotein.
- **LM :** Light microscopy**.**
- **MCD :** Minimal-change disease.
- **MCNS :** Minimal-change nephrotic syndrome.
- **MMF :** Mycophenolate Mofetil.
- **MN :** Membranous nephropathy.
- **MPGN :** Membranoproliferative glomerulonephritis.
- **MZB :** Mizoribine.
- **Na :** Sodium**.**
- **NFP :** Net filtration pressure.
- **NPHS1 :** The nephrin gene.
- **NPHS2 :** The podocin gene.
- **NS :** Nephrotic syndrome.
- **PLCE1 :** Phospholipase C epsilon gene.
- **PNS :** Primary nephrotic syndrome.
- **RVT :** Renal vein thrombosis.
- **SBEM :** Spontaneous bacterial empyema.
- **SDNS :** Steroid-dependent nephrotic syndrome.
- **SLE :** Systemic lupus erythematosus.
- **SRNS :** Steroid-resistant nephrotic syndrome.
- **SSNS :** Steroid sensitive nephrotic syndrome.
- **TAC :** Tacrolimus.
- **TE :** Thromboembolism.
- **TG :** Triglycerides.

INTRODUCTION :

Pediatric nephrotic syndrome, also known as nephrosis, is defined by the presence of nephrotic-range proteinuria, edema, hyperlipidemia, and hypoalbuminemia,nephrotic-range proteinuria in children is protein excretion of more than 40 mg/m^2/h **, (Jerome .,2011) .**

The glomerular diseases that cause nephrotic syndrome generally can be divided into primary and secondary etiologies. Primary nephrotic syndrome (PNS), also known as idiopathic nephrotic syndrome (INS), is associated with glomerular diseases intrinsic to the kidney and not related to systemic causes. A wide variety of glomerular lesions can be seen in INS. These include MCNS, focal segmental glomerulosclerosis (FSGS), membranous nephropathy (MN), membranoproliferative glomerulonephritis (MPGN), diffuse mesangial proliferation and others. Nephrotic syndrome may also be caused by genetic abnormalities. Infantile NS (presenting before age 3 mo) and congenital NS (presenting at age 4-12 mo) have been associated with defects in the nephrin gene (NPHS1), phospholipase C epsilon 1 gene (PLCE1), and the Wilms tumor suppressor gene (WT1) , **(Hogg .,2011)** .

INS is divided into steroid-sensitive (SSNS) and steroid-resistant nephrotic syndrome (SRNS) because response to steroids has a high correlation with histological subtype and prognosis. The landmark study of nephrotic syndrome in children, the International Study of Kidney Disease in Children (ISKDC), found that the vast majority of preadolescent children with INS had MCNS on kidney biopsy. Whereas 90% of children with MCNS responded to corticosteroid

treatment with remission of their nephrotic syndrome, only 20% of children with FSGS responded to steroids ,

(van den Berlg.,2011).

On the other hand, resistance to corticosteroids has been shown to be the single most reliable predictor of progression to end-stage renal disease (ESRD). Thus, in both steroid-dependent nephrotic syndrome (SDNS) and steroid-resistant nephrotic syndrome (SRNS), the need for an alternative immunosuppressive treatment is evident,

(van den Berg .,2011) .

Alkylating agents (eg, cyclophosphamide [CYP], chlorambucil, nitrogen mustard) offer the benefit of possible sustained remission after a defined course of treatment, although with the possible risk of infertility and other side effects , **(Eddy .,2011)** .

An increased risk of seizures is noted with chlorambucil , Additionally, a higher incidence of infections and leukopenia may be seen with chlorambucil compared with CYP. Because of these risks, and the need to give nitrogen mustard intravenously, CYP has generally been the preferred alkylating agent , **(Latta .,2011)** .

Estimation of blood levels of CsA is required in patients with suspected non compliance, unsatisfactory response or recommended for patients who continue to show steroid dependence or frequent relapses despite treatment with the above medications, **(Cattran ., 2007**). induced sustained remission by IVCYP in children with MCNS who were steroid resistant; the results indicated a better outcome than prolonged management with oral cyclophosph. Later, (Rennert et al., (1999) reported 70% remission rate in patients with FSGS by using the same protocol.

Although most children with idiopathic nephrotic syndrome (INS) respond to corticosteroid therapy, 40%-90% of respondents have subsequent relapses. One of the major problems in the management of children who have frequent relapses is the serious side effects resulting from continuous steroid therapy. Cytotoxic agents sustain remission when there is steroid-dependency, but are less efficacious when there is steroid resistance, and also have serious side effects**,**

Therefore, cytotoxic agents do not seem to benefit patients with steroid-resistant focal segmental glomerulosclerosis (FSGS), as emphasized by the controlled study of the International Study of Kidney Disease in Children (**ISKDC), (van den Berg .,2011)** .

A diagnosis of primary steroid resistance was made if the proteinuria persisted after 4 weeks of daily prednisone therapy in a dose of 60 mg/m2/day in the absence of any evidence of underlying infection, **(Habashy ., 2003).** Secondary steroid resistance was defined as no response to 4 weeks of daily prednisone therapy at a dose of 60 mg/m2/day in a child previously known to have a steroid sensitive course. practice of performing kidney biopsy at presentation in all children was abandoned and over the years the role of kidney biopsy has become more and more restricted, **(Gulati ., 2002).**

Children with nephrotic syndrome are at risk for venous and, rarely, arterial thrombosis , All children with nephrotic syndrome should receive immunization against pneumococcal infections, **(Avner ., 2007**).

Adequate treatment of the initial episode, both in terms of dose and duration of corticosteroids, is important. Evidence from multiple studies suggests that appropriate therapy at the first episode of

nephrotic syndrome is an important determinant of the long-term course of the disease, **(Hodson ., 2007).**

Aim of the study:

1- Clarify what is the etiology and pathophysiology of the nephrotic syndrome during childhood.

2- Recognize what is the update diagnosis , differential diagnosis and complications of the nephrotic syndrome during childhood.

3- Recognize the update in the prevention and recent treatment of the nephrotic syndrome during childhood.

4- Review the update in the prognosis of the nephrotic syndrome during childhood.

Anatomy of the kidney

- ## Gross anatomy of the kidney:

The urinary organs comprise the kidneys, which secrete the urine, the ureters, or ducts, which convey urine to the urinary bladder, where it is for a time retained; and the urethra, through which it is discharged from the body.

- **The Kidneys (Renes):**

The **kidneys** are paired bean-shaped organs situated in the posterior part of the abdomen, one on either side of the vertebral column, behind the peritoneum, and surrounded by a mass of fat and loose areolar tissue, **(Steven , 2001**).Their upper extremities are on a level with the upper border of the twelfth thoracic vertebra, their lower extremities on a level with the third lumbar. The right kidney is usually slightly lower than the left, Each kidney range in length and weight respectively from approximately 6cm and 24g in a full-term newborn to 12cm or more and 150g in adult, ***(Ira and Ellis, 2008).*** The lateral border of each kidney is convex.on the concave medial margin of each kidney is the renal hilum where branches of the renal artery, vein, nerves, lymphatics and the expanded pelvis of the ureter pass.The hilum communicates with a flattened space within the kidney called the renal sinus, within this space the renal pelvis branches into major and minor calyces, *(Steven ., 2001).* The kidney has an outer layer, the cortex, that contains the glomeruli, proximal and distal convoluted tubules and collecting ducts and an inner layer, the medulla, that contains the straight portions of the tubules, the loops of Henle, the vasa recta and the terminal collecting ducts, ***(Fogo, 2004).***

Within the medulla are the renal pyramids their bases adjacent to the cortex**.** The apex of each medullary pyramid called the papilla extends into the renal sinus and is capped by a funnel shaped minor calyx.The minor calyces receive the urine that is released from the kidney into the external collecting system**,** ***(Steven ., 2001).***

Each human kidney contains approximately one million functional units called nephrons**.** Each nephron is made up of a renal corpuscle and a complex tubular portion**,** ***(Steven ., 2001).*** In humans, formation of nephrons is complete at birth, but functional maturation with tubular growth and elongation continues during the first decade of life**,** ***(Kon, 2004).*** The most mature nephrons are located near the medulla, juxta medullary nephrons and the younger immature nephrons are found in the outer cortex**,** ***(Brenner and Rector, 2008).***

- **The renal blood vessels:**

The renal arteries arise from the lateral region of the abdominal aorta at the level of the first and second lumbar vertebrae**,** ***(Steven ., 2001).*** Multiple renal arteries may occur.The main artery divides into segmental branches within the medulla and these into interlobar arteries that pass through the medulla to the junction of the cortex and medulla, ***(Ira and Ellis, 2008)***, at this point, the interlobar arteries branch to form the arcuate arteries which run parallel to the surface of the kidney. Interlobular arteries originate from the arcuate arteries and give rise to the afferent arterioles of the glomerui. The afferent arteriole divides into the glomerular capillary network, which then merges into the efferent arteriole, efferent arterioles of glomeruli next to the medulla (juxtamedullary glomeruli) are larger than those in the outer cortex and provide the supply (vasa recta) to the tubules and medulla,