Prediction of Steroid Responsiveness In Primary Nephrotic Syndrome In Children Using Urinary Retinol-binding Protein, Beta-2-Microglobulin And Alpha-1-Microglobulin

Thesis

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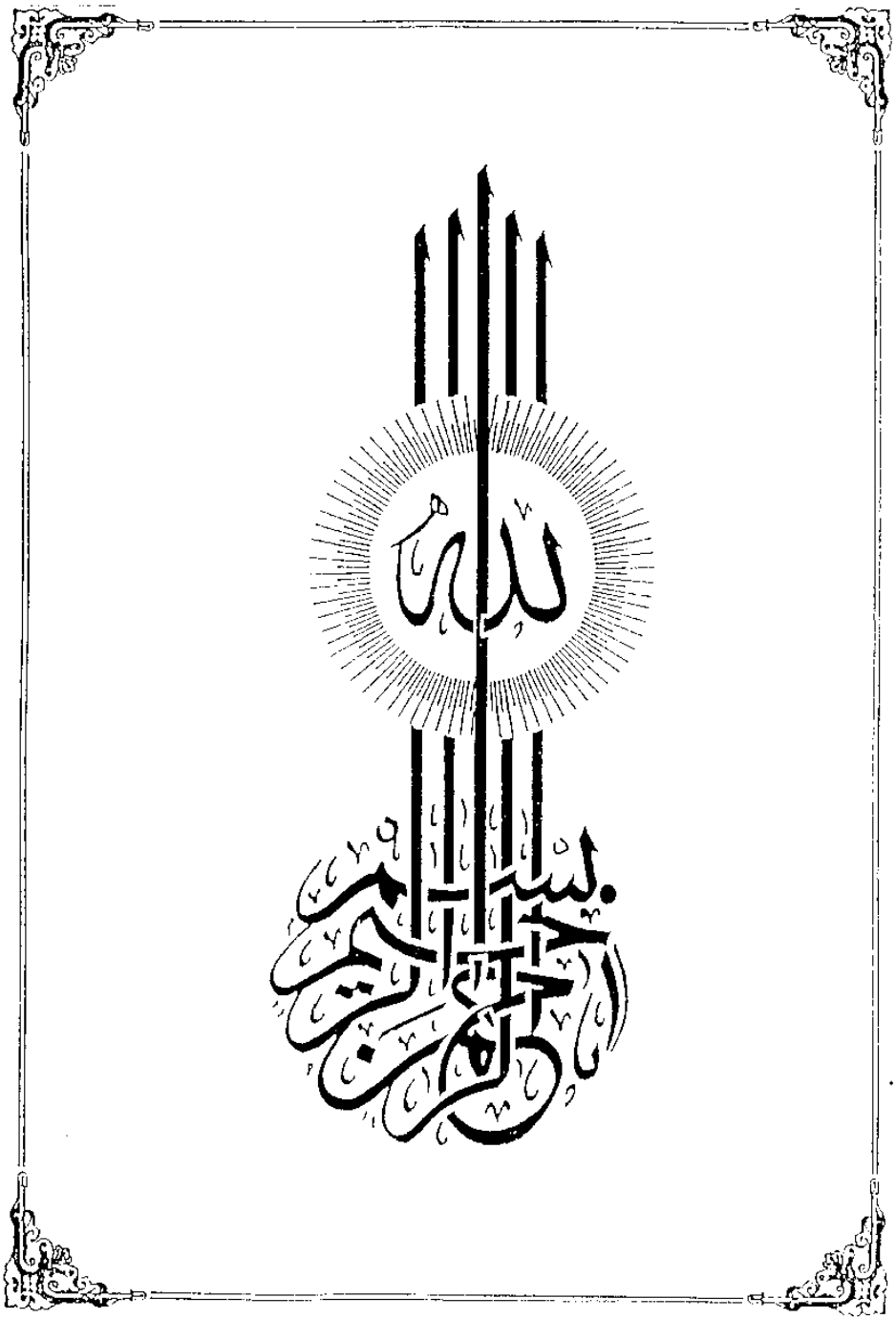

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List of abbreviations

$\propto_1$-M = Alpha-1-Microglobulin.

B_2-M = Beta-2-Microglobulin.

CMV = Cytomegalo Virus.

CSF = Cerebrospinal Fluid.

FGS = Focal global Sclerosis.

FSGS = Focal Segmental Glomerulosclerosis.

GFR = Glomerular Filtration Rate.

HLA = Human Leukocytic Antigen.

HMW = High Molecular Weight.

Ig = Immunoglobulin.

IVU = Intra Venous Urography.

LDL = Low Density Lipoprotein.

LMW = Low Molecular Weight.

MCNS= Minimal Change Nephrotic Syndrome.

MGN = Membranous Glomerulonephritis.

MPGN=Membranoproliferative Glomerulonephritis.

RBCs = Red Blood Cells.

RBP = Retinol-Binding Protein.

SLE = Systemic Lupus Erythematosus.

VLDL = Very Low Density Lipoprotein.

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INTRODUCTION AND AIM OF THE WORK

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Nephrotic syndrome is a wide spread disease between children and steroids play an important role in its treatment.

The response to steroids carries a greater prognostic weight than the histological features seen on initial biopsy. Thus, it would appear to be advisable to distinguish the two types of idiopathic nephrotic syndrome according to the response to steroids : as steroid-responsive and steroid-resistant.

(*Niaudet et al., 1988*).

The majority of children (about 90%) are steroid resposive, but more than half of them relapse on withdrawal of steroid therapy or when the dosage is decreased.

(*Wiliams et al., 1989*).

In 10% of cases, the nephrotic syndrome is resistant to steroid therapy. The severity of these cases lies essentially in the risk of developing end - stage renal failure, which occurs in up to 50% of cases.

(*Tejani et al., 1983*).

Proximal tubular dysfunction has been reported in some nephrotic patients with massive proteinuria particulary those with prominent histologic features of tubular atrophy and interstitial fibrosis.

(*Bouissou F et al., 1980*).

Considering that renal biopsy is not routinely indicated in many patients with the primary nephrotic syndrome and because there is not an excellent correlation between histologic features and steroid responsiveness. We suggest that urinary tubuler markers (Retinol - binding protein, Beta-2- Microglobulin and Alpha -1-Microglobulin) level may be helpful in identifying patients with the nephrotic syndrome who are more likely to be responsive to steroids.

(*Ricardo sesso et al., 1992*)

Aim of the work

Study of the possible value of Retinol - binding protein,Beta-2-Microglobulin and Alpha -1-Microglobulin as indicators to responsiveness to steroid therapy in primary N.S.

REVIEW OF LITERATURE

Review of Literature

Nephrotic Syndrome

Definition:

Nephrotic syndrome, one of the commonest renal diseases in childhood, is characterized by proteinuria, hypoalbuminemia, hypercholesterolemia & edema.
An increased glomerular permeability resulting in proteinuria is the primary renal abnormality in nephrotic syndrome, while hypoalbouminemia, edema & hypercholesterolemia are believed to be secondary pathophysiologic events.

(Kher, et al., 1988).

Hematuaria, hypertension & reduced glomerular filtration rate may occur at any time in the course of many different primary & secondary glomerular disease.

(Habib and Kleinknecht 1971) &(Rubin, 1981).

Classification of Nephrotic Syndrome:

Nephrotic syndrome can result from a variety of

morphologically distinct renal diseases that can give rise to significant proteinuria.
Minimal change or nil disease accounts for 80 - 85% of cases, various types of chronic glomerulonephritis and inherited disease account for the remaining 15 - 20% of cases.

(ISKDC, 1971)&(White RHR, 1970).

To a large extent, clinical course & response of nephrotic patients to therapy is determined by the underlying glomerular pathology & the etiology of nephrotic syndrome. Therefore any classification must take into account the renal histopathology & its etiology.

(Kher KK, 1988).

Traditionally, nephrotic syndrome is classified into primary & secondary subtypes; primary nephrotic syndrome refers to patients in whom the etiology is not known, while secondary type is seen in the course of systemic disease.

The following table list the classification of nephrotic syndrome:

Primary nephrotic syndrome:

Chronic glomerulonephritis.
Focal glomerulosclerosis.
Membranous glomerulonephritis.
Membranoproliferatve glomerulonephritis.
Mesangial proliferative glomerulonephritis; with lgM deposition.

with IgA-IgG deposition (Berger's disease)
Congenital nephrotic syndrome (Finnish type)

Nephrotic syndrome secondary to renal involvement in systemic disorders:

Henoch-Schonlein Purpura.
systemic lupus erythematosus.
systemic infection:
- Hepatitis B.
- Congenital&secondary syphilis.
- Subacute bacterial endocarditis.
- Ventriculoarterial shunt infections.
- Malaria.
- Varicella.
- AIDS.

Sickle cell disease.
Diabetes mellitus.
Drugs:
- Gold.
- D-penicillamine.
- Mercury.
- Captopril.
- Heroin.
- Nonsteroidal anti-inflammatory drugs.

Neoplasm: Hodgkin disease & other lymphomas.
Chronic inflammatory diseases:
- Familial Mediterranean fever.
- Amyloidosis.

Hereditary disorders as Alport's syndrome.

(*Kher KK, et al., 1988*).

Incidence of nephrotic syndrome:

The incidence among children less than 10 years of age is approximately 1.8 - 5 cases per 1,000,000 per year.

(Glassock RJ,1986).

For reasons that are poorly understood, minimal change disease is more common in Asian & Arab population.

(Sharples P,1985).

Minimal change disease is found in over 85% of cases of nephrotic syndrome due to primary glomerular disease in children between the age of 2 & 6 years.

(Cameron J, and Glassock RJ, 1988).

The reported variation in prevalence of this lesion is probably accentuated by differences in selection, referral bias, geography & history interpretation, male predominance is about 2 - 2.5 in children, whereas the sex variation is closer to unity in adults.

(Cameron J, and Glassock RJ, 1988).

The lesion has been reported to occur in siblings.

(Bader PI,1974).

Etiology of primary nephrotic syndrome:

The cause of the syndrome is not definitely known. Several immunologic phenomenae were reported suggesting that immune mechanisms may contribute.

Among these immunologic phenomenae are that;