

## Evaluation of Serum (immunoglobulin G, M) in children with nephrotic syndrome relapse

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### Summary:

**Background:** Nephrotic syndrome is an immune mediated disorder of the kidney associated with T cell dysfunction and secondary disturbance of B cell with changes in levels of immunoglobulin.

**Objectives:** The objectives of this study were to compare immunoglobulin levels in children with nephrotic syndrome in relapse and healthy children, and to assess relationship between the degree of albuminuria and the mean concentrations of immunoglobulin.

**Methods:** We studied 60 children with nephrotic syndrome during January 2008 to January 2011 in the Pediatric Nephrology consultation clinic, Children Welfare Teaching Hospital –Baghdad Medical Complex –Iraq. Urine protein and blood samples were collected from the 60 patients, and serum levels of IgG, IgM were measured. Another 20 healthy children attending the clinic were enrolled as controls.

**Results:** In the 60 relapse cases of steroid sensitive nephrotic syndrome, compared with healthy children, the IgG level was low, IgM level was high and a highly significant relationship was found between the degree of albuminuria and the mean concentration of immunoglobulin in sera of patients ( $p < 0.01$ )

**Conclusion:** immunoglobulin abnormalities support growing evidence that functional glomerular changes in nephrotic syndrome may result from T-cell disturbance and B-cell involvement.

**Key words:** children, nephrotic syndrome relapse, immunoglobulin level

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### Introduction:

Childhood nephrotic syndrome is an immune mediated kidney disease associated with T cell dysfunction and secondary disturbance of B cell that leads to changes in levels of immunoglobulins(1,2)

Nephrotic syndrome (NS), 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<sup>2</sup>/h or urinalysis reveals 2+ or more proteinuria(3)

The glomerular diseases that cause nephrotic syndrome generally can be divided into primary and secondary etiologies. Primary also known as idiopathic nephrotic syndrome (INS) which is divided into steroid-sensitive (SSNS) and steroid-resistant nephrotic syndrome (SRNS). The majority of children with steroid-responsive nephrotic syndrome have repeated relapses.(4,5)

Infection is the major complication of nephrotic syndrome. Children in relapse have increased susceptibility to bacterial infections because of urinary losses of immunoglobulins and properdin factor B, defective cell-mediated immunity, immunosuppressive therapy, malnutrition, and edema/ascites acting as a potential "culture medium.(6)

The objectives of this study were to compare immunoglobulin levels in children with nephrotic syndrome in relapse and healthy children, and to assess relationship between the degree of albuminuria and the mean concentrations of immunoglobulin

### Patients and Methods:

A randomized case control study was carried out in the Children Welfare Teaching Hospital –Baghdad medical complex –Iraq, from January 2008 to January 2011.

A total of 129 steroid responsive idiopathic nephrotic syndrome (INS) patients presenting with new relapse, attending nephrology consultation clinic during the study period, Five milliliter (5 ml) venous blood samples and urine specimens were collected randomly from 60 cases (35 male and 25 females), their ages ranged between 1-15 and they were not taking cytotoxic therapy. Together with blood and urine sample from 20 healthy, normal children (10 males and 10 females) with the same age range served as a control group after taking their parents agreement..

The dipstick measure for urine protein and the blood samples were centrifuged to obtain sera which were used for measuring immunoglobulins (IgG, IgM) ..All samples were investigated and measured in teaching laboratories of medical city.

The concentration of immunoglobulins (IgG, IgM) in sera samples was estimated by quantitative SRID (Mancini method) according to the manufactures instructions. (Reference normal values of immunoglobulins were IgG (610-1400 mg/dl) and IgM (30-142mg/dl) respectively.

### Study definition

SSNS was defined as responding to steroid therapy within 4 weeks after initiation of the therapy.[3,6] relapse was defined a proteinuria (urine albumin 2+ or more) after initial responsive episode.[3,6]

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Statistical analysis: Statistical analyses were performed using computer-based software, Statistical Package for Social Science (SPSS). P value <0.01 was considered statistically significant.

### Results

Of the 60 patients enrolled in the study, 35(58.3%) were male and 25(41.6) female ,with a male to female ratio 1.4:1.

Comparisons of IgG, IgM showed that the IgG level was lower while the IgM level was higher in the patient groups than in healthy controls (P<0.01) (table 1).

There was a Significant decrease in mean concentration of IgG in sera of patients (242 mg/dl) when Compared with the mean IgG concentration (869 mg/dl) of control group (p< 0.01) table(2)

A highly significant increase in the mean concentration of IgM in sera of patients group(184 mg/dl) when compared with the mean IgM concentration(77 mg/dl) of control group (p< 0.01) table(2)

Table 3 showed the presence of a highly significant relationship (p< 0.01) between the degree of albuminuria and the mean concentration of immunoglobulin (Ig G&IgM)in sera of patients with nephrotic syndrome.

An increase in albuminuria is accompanied by a reduction in mean concentration of serum IgG level. While , an increase in albuminuria is associated with direct proportional elevation in the mean concentration of serum IgM level .

**Table 1. IgG and IgM levels in the patients and controls**

Parameters	Patients	Controls	95% CI	P(T-test)
	n (%)	n (%)		
IgG (mg/dl)				
<610 (low)	59(98.33)	0 (0.0)	(1.94, 60.0)	0.000 HS*
610-1320 (normal)	1 (1.67)	20(100.0)		
IgM (mg/dl)				
20-134 (normal)	14 (23.33)	18 (95.0)	(0.80, 25.1)	0.000 HS*
>134 (high)	46(76.67)	1 (5.0)		

\*HS highly significant

**Table2: Comparison of mean concentrations of immunoglobulins in serum of studied groups**

Parameters	Mean	Median (±SD)	p-value
IgG (mg/dl)			
Patients	242	262 (186)	< 0.01
Control	869	852 (182)	
IgM (mg/dl)			
Patients	184	177 (77)	< 0.01
control	77	74 (31)	

**Table3: relationship between the degree of albuminuria and the mean concentration of immunoglobulin (Ig G&IgM)**

Studied group	Urine albumin	No.	Mean±Sd conc.ofserum IgG(mg/dl)	p-value	Mean±Sd conc.ofserum IgM(mg/dl)	p-value
patients	++	26	383.7±260.8	< 0.01	255.8±85	< 0.01
	+++	15	385.2±270.4	< 0.01	252.6±91.4	< 0.01
	++++	19	413.5±254.0	< 0.01	194.4±69	< 0.01
control	nil	20	869± 182		77±31	

### Discussion:

Patients with nephrotic syndrome had unusual susceptibility to encapsulated bacterial infection; studies showed that there are changes in the serum immunoglobulin levels associated with proteinuria in nephrotic patients. (6,7)

In this study we found a significantly low IgG level and elevated IgM level in the patient group compared with the healthy controls .these findings were similar to studies done by Rashid H, et al and Mishra OP et al.[8,9]

According to studies, changes in the serum immunoglobulin levels can be attributed to either T cell dysfunction and /or increased urinary excretion of albumin.

In the study done by Giangiacomo et al [10] and Lin Cj. Later (11), they concluded that T cell dysfunction

is responsible for failure to convert surface IgM-bearing B lymphocyte (plasma cell) into subsequent IgG and IgA secreting plasma cell apart from urinary loss of immunoglobulin which was suggested previously by Peterson et al.[12]. Subsequent works supporting similar view of T cell defect were made by Warsaw and Check,[13] and Rashid et al.[14] Chen et al[15] reported that enhanced suppressor T cell activity resulted in increased IgM and decreased IgG production in children with nephrotic syndrome. On the other hand Kaysen et al, stated that in nephrotic syndrome there is an increased urinary excretion of albumin and other serum proteins accompanied by a decrease in their serum concentration .like albumin, IgG is also lost in urine, the fractional rate of its catabolism increased and its serum concentration altered (16)

While the high molecular weight immunoglobulin (IgM) may be increased to defend serum protein concentration and oncotic pressure. marked proteinuria associated with nephrotic syndrome is thus likely to affect the serum immunoglobulin levels (17)

In our study we found, an increase in albuminuria accompanied by a reduction in IgG level. While , a direct proportional relationship was found between the degree of albuminuria and the mean concentration of serum (IgM )when there is an increase in albuminuria it is associated with elevation of IgM level).

Conclusion, immunoglobulin abnormalities in patients with nephrotic syndrome compared with healthy children , support growing evidence that functional glomerular changes in nephrotic syndrome may result from T-cell disturbance and B-cell involvement.

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