

Serum IgE level in relapsing idiopathic nephrotic syndrome in children

Abstract

Background: Nephrotic syndrome patient have altered serum IgE level during acute attack and remission.. An increase in the serum IgE may be a reflection of body immuno regulatory imbalance that play direct pathogenic role in the occurrence of NS and proteinuria.

Methods: The aim of this cross sectional comparative study was to assess the level of serum IgE level in relapse of nephrotic syndrome and to see the difference of serum IgE level between infrequent relapse and frequent relapse carried out in the Department of Pediatric Nephrology, Comilla Medical College Hospital during the time from July 2015 to December 2015. A total of 60 subjects were recruited, consisting of 30 of relapse NS was enrolled as a cases and 30 of initial attack NS same age group was enrolled as controls. Serum IgE level was estimated by IMMULITE2000 Reader before starting therapy with prednisolone. The mean serum IgE level of cases and of controls was estimated respectively. Statistical difference between serum IgE level of cases and control was seen by unpaired t test.

Results: The mean serum IgE level of relapse nephrotic syndrome in children was (537.98±52.56IU/ml) which was higher than control(p<0.05).The mean serum IgE level of infrequent relapse and frequent relapse were 860.00±50.00 IU/mL and 1441.00±95.00 IU/mL respectively (p<0.05).

Conclusion: With this study we reaffirm that serum IgE is high in relapse nephrotic syndrome and it is persistently and significantly higher in frequent relapsing group.

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Introduction

Nephrotic syndrome is a pathological entity characterized by massive proteinuria and hypoalbuminemia. Nephrotic range proteinuria is defined as proteinuria exceeding 1000mg/m²/day or spot urinary protein to creatinine ratio exceeding 2. The proteinuria in childhood nephrotic syndrome is relatively selective, constitute primarily by albumin.¹ Estimate on the annual incidence of nephritic syndrome range from 2-7 per 100000 children and prevalence² from 12-16 per 100000. There is epidemiological evidence of a higher incidence of nephritic syndrome in children from Asia.³ The condition is primary in 95 percent cases. An underlying disorder that might be identified in less than 5 percent cases, includes systemic lupus erythematosus, Henoch Schonlein Purpura, amyloidosis and infection with HIV, parvovirus B19 and hepatitis B and C.^{4,5} More than 80 percent patients with nephrotic syndrome show minimal change disease (MCD) characterized by normal histology on light microscopy. The remaining is contributed by focal segmental glomerulosclerosis (FSGS) and mesangioproliferative glomerulonephritis (MesPGN). MCD and FSGS are often considered to represent the same pathophysiological process. Membranous nephropathy and membranoproliferative conditions are uncommon in children.⁶⁻⁸ About 90% children with MCNS responds promptly to corticosteroid therapy with complete clinical and biochemical remission and have excellent long term prognosis. Among who responds to prednisolone, 20-40% have infrequent relapse and 40% have frequent relapse and reminder are steroid dependence.⁹ Relapse can be defined as the reappearance of massive proteinuria for 3 consecutive days after having gone into remission on previous occasion.⁹ Relapse can be of two types i.e. infrequent and frequent. Infrequent relapse can be defined as 3 or <3 relapses in any consecutive months,⁶ and frequent relapse can be defined as 4 or >4 relapses in any 12 months.¹⁰ Altered levels of

different serum immuno globulins (Ig) during active NS and during remission have been documented by a number of studies.¹¹⁻¹⁴ Blood contains three types of globulins; alpha, beta and gamma, based on their electrophoretic migration rates. Antibodies are gamma globulins. There are five classes of antibodies namely IgG, IgM, IgA, IgD and IgE. Among them IgG are reduced in NS. On the other hand serum IgM and IgE are raised while serum IgA are within normal limits when the patients are in active disease.¹⁵ IgE is medically important for two reasons; it mediates immediate (anaphylactic) hypersensitivity reactions and it participates in host defenses against certain parasites. Persons with allergic reactivity have greatly increased amount and IgE may appear in external secretion. The cause of MCNS remains unclear, although several immunologic mechanisms have postulated. Relapses of disease have been reported in association with seasonal allergies^{16,17} or atopic diseases¹⁸ and others have noted elevated serum IgE concentration in children with MCNS.^{15,19,20} In a study conducted in China have shown that during the acute nephrotic syndrome, the serum IgE level in MCNS were significantly elevated, these high serum IgE levels decreased in remission of NS and elevated again during relapse. An increase in the serum IgE may be a reflection of body immunoregulatory imbalance that play direct pathogenic role in the occurrence of NS and proteinuria.²¹ Nephrotic syndrome encompasses morbidity as well as mortality of children. Relapse NS carries a higher mortality and morbidity due to frequent association with severe complications. This morbidity due to complications of relapse of NS should be prevented and this deserves a scientific study to find out different issues related to relapse of NS. Serum IgE level may have association with relapsing NS. The goal of this study was to identify the relationship between serum IgE level and relapse of NS to be used as a diagnostic, prognostic and predictor indicator of relapsing NS.

Materials and methods

The aim of this cross sectional comparative study was to assess the level of serum IgE level in relapse of nephrotic syndrome and to see the difference of serum IgE level between infrequent relapse and frequent relapse carried out in the Department of Pediatric Nephrology, Comilla Medical College Hospital during the time from July 2015 to December 2015. Study population was all nephrotic syndrome patient aging from 1 year to 10 years irrespective of sex with some inclusion and exclusion criteria. A total of 30 cases and 30 suitably matched controls were enrolled in the study by simple random sampling. Relapses patient was selected as cases and age and sex matched initial attack NS was selected as controls. Before starting therapy with prednisolone serum IgE level of both case and control were measured by highly sensitive analyzer (IMMULITE2000 Elisa Reader). Data was collected by a preformed structured questionnaire. Data was processed, calculated and analyzed using computer software. Un pair *t* test was done to compare the mean difference between serum IgE level in cases and in controls. The statistical analysis was performed using the Statistical Package for Social Service (SPSS) version 16.0 for Windows.

Results

Among 30 cases and 30 controls 53.33% children were male and 46.66% were female. Maximum children were male. Male and female ratio in cases and controls was 1.14:1 (Tables 1-7). Table 2 shows the difference of serum IgE level between case and controls. According to unpaired *t* test, critical value (*p*-value 0.05) of *t* on *t* distribution table is 1.671 which is less than *t* calculated value (7.42). Table-IV shows mean serum IgE was higher in age group 7-10 years than in age group 2-6 years in both cases and controls, *p* value <0.05. Table 6 shows the mean serum IgE level in frequent relapse (144±95 IU/mL) was higher than NS children with infrequent relapse (860±50), *p* value <0.05. Table 7 shows mean serum IgE was higher in age group 7-10 years than in age group 2-6 years in both frequent relapse (cases) and infrequent relapse (controls), *p* value<0.05.

Table 1 Age distribution of cases and controls

Characteristics	Cases (n=30) n (%)	Controls (n=30) n (%)	p value*
Age			
o 2- 6 years	22 (73.0)	22 (73.0)	>0.05
o 7-10 years	08 (27.0)	08(27.0)	

*Chi square test was done to measure the level of significance.

Table 2 Sex distribution of cases and controls

Characteristics	Case (n=30) n (%)	Controls (n=30) n (%)	p value*
Sex			
o Male	16 (53.33)	16(53.33)	>0.05
o Female	14 (46.66)	14(46.66)	

*Chi square test was done to measure the level of significance.

Discussion

The nephrotic syndrome was more common in the age group 2 to 6 years. 73% of initial attack NS, infrequent relapse NS and frequent relapse NS patients were present within this age group which is consistent with other previous report.²²⁻²⁵ Mean age in the age group 2-6 years of cases and controls was 4.7±1.5 and 4.5±1.5 respectively

which was statistically not significant (*p*>0.05) and is consistent with previous data^{23,24} where study subjects were age matched. In nephrotic syndrome boys are more commonly affected than girls. Out of 60 children, 32 were males and 28 were female patients. Male and female ratio in cases and controls was 1.14: 1 which was consistent with previous data.^{9,23,24,25} Study subjects were found to be more common in males, so cases and controls were also sex matched. Mean blood urea and serum creatinine levels was observed statistically not significant (*p*>0.05) in initial attack and relapsing NS and is similar with prior findings.^{4,13,35} Mean serum total protein, spot urinary protein creatinine ratio and 24 hours urinary total protein was also observed statistically not significant (*p*>0.05) in initial attack and relapsing NS and is in harmony other outcomes.^{4,10,26} Mean serum cholesterol level in relapsing NS was observed to be significantly higher (401±42mg/dl) than that in initial attack (310±42mg/dl), again mean serum cholesterol level in frequent relapse NS was also observed to be significantly higher (462±42mg/dl) than that in infrequent relapse NS (340±42mg/dl), which was statistically significant (*p* value<0.05) and is coherent with other outcomes.^{4,26} Serum IgE is increased with age. Mean serum IgE level in age group 7-10 years both case and control was observed to be significantly (*p*<0.05) higher than that in age group 2 to 6 years (Table-IV and VI) which was statistically significant (*p* value <0.05) and is in harmony with other results.^{15,27-35} Mean serum IgE level (Table 3) in cases was observed to be significantly (*p*<0.001) higher than controls and this is consistent with other studies.^{12,24} Mean serum IgE level (Table-IV) of frequent relapse was significantly (*p*<0.05) higher than that infrequent relapse which was statistically significant and is similar with previous studies.^{17,19} High serum IgE level during the period of relapse and remission can be considered to be a predictor of frequent relapse.

Table 3 Baseline characteristics of cases and controls

Parameters	Groups		
	Cases (n=30) Mean±SD	Controls (n=30) Mean±SD	p value*
Age: 2- 6 years (n=22)	4.70±1.50	4.50±1.50	>0.05
Age: 7-10years (n=08)	7.70±1.80	7.40±1.50	>0.05
Serum total protein(gm/L)	50.30±0.83	48.97±1.11	0.362
Serum albumin in gm/dl (±SD)	1.37±0.59	1.57±0.67	0.0385
Serum cholesterol in mg/dl(±SD)	401.00±42.00	310.00±42.00	0.0405
Spot UPCR	10.43±1.42	8.82±0.96	0.564
24 hours urinary total protein	3.20±0.34	2.93±0.11	0.427
TCE count (0-400/ cmm)	401.00±42.00	350.00±42.00	0.263
Blood urea (mmol/L)	5.24±1.35	4.50±0.45	0.801
Serum creatinine(mmol/L)	76.57±2.73	75.38±2.05	0.946
Urine pus cell (<5/ HPF)	5.00±1.00	4.00±1.00	0.97

*Unpaired *t* test was done to measure the level of significance.

Table 4 Difference of Serum IgE level between cases and controls

Nephrotic syndrome	Mean	± SD	t	df	p value*
Cases (n=30)	1150.7	±74.61	7.42	58	<0.001
Controls (n=30)	537.98	±52.56			

*Unpaired t test was done to measure the level of significance.

Table 5 Comparison of serum IgE level between cases and controls in different age groups

	Age (years) group		p value*
	2- 6 (n=22)	7-10 (n=08)	
	Mean ±SD	Mean ±SD	
Cases (n=30)	1110.50±52.00	1261.32±64.00	<0.05 ^s
Controls (n=30)	510.98±52.00	612.23±52.00	<0.05 ^s

*Unpaired t test was done to measure the level of significance

Table 6 Comparison of serum IgE level between Frequent Relapse and Infrequent Relapse NS

	Groups		p value*
	Frequent Relapse (n=15)	Infrequent Relapse (n=15)	
	Mean±SD	Mean±SD	
#Serum IgE in Relapse (IU/mL)	1441.00±95.00	860.00±50.00	<0.05 ^s

*Unpaired t test was done to measure the level of significance.

Table 7 Comparison of serum IgE level between Frequent Relapse and Infrequent Relapse NS in different age groups

	Age (years) group		p value*
	2- 6 (n=11)	7-10 (n=04)	
	Mean±SD	Mean±SD	
Frequent Relapse (n=15)	1402.00±69.00	1548.00±72.00	<0.05 ^s
Infrequent Relapse (n=15)	840.00±50.00	915.00±50.00	<0.05 ^s

*Unpaired t test was done to measure the level of significance.

Conclusion

With this study we reaffirm that serum IgE is high in relapse nephrotic syndrome and it is persistently and significantly higher in frequent relapsing group.

Recommendation

This finding suggests that IgE may play an important role in the pathogenesis of MCNS and level of the serum IgE can be used as a prognostic and predictor indicator and thus we shall prevent and alert subsequent complications as well as morbidity of relapse nephrotic syndrome. Further studies including large sample size is recommended.

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None.

Conflicts of interest

Authors declare no conflict of interest.

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