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HLA Class II Associations with Idiopathic Nephrotic Syndrome in Children

Fadwa M. Alsharif and Zahira M.F. El-Sayed

Department of Medical Laboratory Technology,
Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah, 21589, Saudi Arabia

Abstract: *Background:* Nephrotic syndrome is a constellation of clinical findings that is the result of massive renal losses of protein. The idiopathic nephrotic syndrome (INS) points to a genetic predisposition and associations with certain HLA class II antigens support this hypothesis. Objective: The aim of this study is to declare the correlations between HLA class II and INS children, which includes steroid resistant nephrotic syndrome (SSNS) and steroid sensitive nephrotic syndrome (SSNS) children; also, relative risk (RR) values for associated alleles were expressed. Material and Methods: HLA class II allele frequencies in 30 children with INS were investigated, 15 steroid resistant (SR) and 15 steroids sensitive (SS), also 20 controls were included. The blood samples were taken then isolated lymphocytes were used for HLA(class II)typing using 72 well tray with redropped ant-HLA DR/DQ sera and cell death was detected by using a Zeeisis fluorescent microscope. Results: The results revealed an increased frequencies of HLADR3 and DR7 and DQ2 (RR=2.25, 2 and 2) respectively, among INS patients, they had the highest statistically significant frequencies in comparison with controls (P<0.001). On the other hand DR6 and DR2 and DQ1 revealed significant negative association (protective genes), (P<0.001. Among steroid sensitive children DR3, DR7 & DQ 2 ((RR= 3.86, 3.22 and 2) respectively were the most positive associated alleles, while DR6, DR2 and DQ1 showed negative associations with the same group. DR3 showed positive correlation among steroid resistant children (RR=3.22), while DR6 & DR2 (P<0.001) revealed negative association with them.in Conclusion: INS is common observed syndrome which leads collection of manifestation in children. Familial tendency of the syndrome attributed to genetic correlation with HLA class II. DR7 andDQ2 were the most positively associated alleles among investigated children, while DR2 and DR6 were the most negatively correlated alleles, protective alleles.

Key words: Nephritic Syndrome · Steroid Sensitive · Steroid Resistant · HLA Typing Class II

INTRODUCTION

Nephrotic Syndrome is a collection of signs and symptoms that occur when glomeruli are damaged. Most often, Nephrotic Syndrome is defined by its primary diseases that attack the kidney's filtering system while "idiopathic," means that they have arisen without a known cause. These primary diseases include Minimal Change Disease (MCD), Focal Segmental Glomerulosclerosis (FSGS) and Membranous Nephropathy (MN) and are identified by kidney biopsy [1]. There are many other "secondary" causes of NS, including diabetes, cancer, amyloidosis, lupus, vasculitic disorders, viral infections, drugs and allergies, among others. MCD is the most common cause of Nephrotic Syndrome in children - almost 85% of children with Nephrotic Syndrome symptoms have MCD [2, 3].

Nephrotic syndrome may affect adults and children, of both sexes and of any race. In total, 26 million Americans suffer from Chronic Kidney Disease, with Nephrotic Syndrome as one of the most common forms [4]. "Idiopathic" Nephrotic syndrome (NS), or Nephrotic Syndrome that arises seemingly spontaneously, is a rare disease syndrome and yet responsible for approximately 12% of all causes of end-stage kidney disease (ESRD) and up to 20% of ESRD in children. Approximately 5 out of every 100,000 children are diagnosed with Nephrotic Syndrome every year (incidence) and 15 out of every 100,000 children are living with it today [5].

Corresponding Author: Fadwa M. Alsharif, Department of Medical Laboratory Technology,
Faculty of Applied Medical Sciences, King Abdulaziz University,
P.O. Box 80324, Jeddah, 21589, Saudi Arabia.

Pediatric nephrotic syndrome, also known as nephrosis, is defined by the presence of nephrotic-range proteinuria, edema, hyperlipidemia and hypoalbuminemia [6]. Nephrotic-range proteinuria in adults is characterized by protein excretion of 3.5 g or more per day. However, because of the great range of body sizes in children, the pediatric definition of nephrotic-range proteinuria is more cumbersome [7].

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 [8]. 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 [9].

The diseases associated with idiopathic nephrotic syndrome share several immunological alterations such as the presence of circulating factors which promote proteinuria and increased serum levels of autoreactive IgA antibodies and interleukins [10]. Gene. In family studies, the presence of multiplex cases of idiopathic nephrotic syndrome sharing HLA antigens has suggested the influence of immunogenetic markers [11,12].Immunogenetic studies of unrelated patients conducted on distinct populations have shown associations with HLA class I (HLA-B8, -B12) and class II (HLADR7) antigens for idiopathic nephrotic syndrome patients irrespective of the variant FSGC [13-15]. Immunogenetic studies of unrelated patients conducted on distinct populations have shown associations with HLA class I (HLA-B8, -B12) and class II (HLADR7) antigens for idiopathic nephrotic syndrome [16-18].

The study aims to declare the correlations between HLA class II and INS children, (steroid resistant and steroid sensitive children); also, RR values for associated alleles were expressed.

MATERIALS AND METHODS

Subjects: Thirty patients were diagnosed as having INS and were attending the outpatient clinic of Pediatric Department, King Abdulaziz University Hospital; also twenty normal subjects with the same age group were examined as a control group. The patients were 10 females and 20 males and their mean age was 4.21±.5 years. Idiopathic nephritic syndrome children were classified into two groups:

Group (A): Included fifty steroid resistant children who didn't response to steroid therapy or have many relapse

Group (B): Included fifty steroid sensitive children who responded to steroid therapy with edema and proteinuria.

All patients and controls were subjected to the following:

- History taking: personal history, family history, history proteinuria, edema and hematuria.
- Complete clinical examination, abdominal examination and blood pressure.
- Ultrasound of abdomen to investigate the clinical condition of kidney, liver and spleen.
- Laboratory examination includes renal function, cholesterol which increases above 300mg/dL (N=120-220mg/dL).
- Microscopic examination of urine to detect hematuria.
- Study of different human leukocyte antigen (HLA): The blood samples were collected into acid dextrose, then the blood centrifuged at 100/g and two third of the cell free was then removed and then the sample was completed at final volume with cooled phosphate buffered solution (PBS). The B-lymphocyte HLA class II was then resuspendes by gently stirring of the bead suspension into blood samples. The B lymphocytes were then isolated by applying the magnet Biotest (MSD) to the outer wall of the sample container. The isolated lymphocytes were washed twice and the lymphocytes were resuspeded into (PBS). The lymphocytes were then adjusted to certain concentration with lymphocytes solution (Biotest). The isolated lymphocytes were then used for HLA (class II) typing using 72 well tray with redropped ant-HLA DR/DQ sera.
- HLA-DR and DQ typing with lymphocyte HLA class II. 1ml of lymphocytes was added to each well HLA DR typing trays (Gentrak, Incorporated (USA). Ethurdin bromide in HBSS with 5% ethylene diamintetraacetic acid (EDTA) was added to each well to detect cell death using a Zeeisis fluorescent microscope [19].

Statistical Analysis: The results obtained were analyzed to detect the relative risk (RR) using fisher exact test and Odd's ratio (Armitage) [20].

RESULTS

Table (1) revealed the general character of investigated INS children, they included 20 males and 10 females, their mean age was 4.2± 1.5 and they divided into 15 SSNS and 15 SRNS patients. While, table (2) detected that.DQ2 was positively associated with idiopathic nephrotic syndrome children while DQ1 revealed significant negative association. However, table (3) showed that, DR7 and DR3 were the most common alleles among steroid sensitive children; also negative association was recorded between steroid sensitive children and DR6 & DR2.Also, table (4) shows that, significant positive correlation was detected between DQ2 and steroid sensitive patients, while negative association was recorded between DQ1 and detected group.

However, table (5) showed that, DR3 was the most common alleles among steroid resistant children (RR=3.22, 9.66), also negative association was recorded between steroid resistant children and DR6 & DR2 ($P<0.001$).Finally, table (6) shows that, there was no significant positive correlation detected between DQ2 and steroid resistant patients, while negative association was recorded between DQ1 and detected group.

DISCUSSION

In family studies, the presence of multiplex cases of idiopathic nephrotic syndrome sharing HLA antigens has suggested the influence of immunogenetic markers. Immunogenetic studies of unrelated patients conducted on distinct populations have shown associations with HLA class I (HLA-B8, -B12) and class II (HLADR7) antigens for idiopathic nephrotic syndrome patients irrespective of the variant FSGC [21].

Table 1: Different data of children with nephritic syndrome.

No. of examined patients	Age years	Sex	Proteinuria	Proteinuria Above 2gm /24h	Serum cholesterol Mg/dL	Response to steroid	Generalized edema
1	4	M	++	+	420	S.resistant	+ve
2	5	M	+	-	510	Sensitive	+ve
3	5	M	+++	+	320	Sensitive	+ve
4	6	M	++	+	400	S.resistant	+ve
5	4	M	++	+	320	S.resistant	+ve
6	3	F	+	-	460	Sensitive	+ve
7	2	F	+	-	350	S.resistant	+ve
8	5	M	++	+	480	Sensitive	+ve
9	5	M	+	+	400	Sensitive	+ve
10	4	M	+	+	350	S.resistant	+ve
11	2	F	+	+	380	Sensitive	+ve
12	3	M	+	+	370	Sensitive	+ve
13	3	F	+	_	420	S.resistant	+ve
14	6	F	+	+	270	Sensitive	+ve
15	4	M	++	_	200	S.resistant	+ve
16	3	M	++	+	220	S.resistant	+ve
17	5	M	+	+	300	Sensitive	+ve
18	2	M	++	+	250	Sensitive	+ve
19	3	F	++	+	200	S.resistant	+ve
20	4	F	++	+	430	S.resistant	+ve
21	3	M	+	+	320	S.resistant	+ve
22	3	M	+	+	520	Sensitive	+ve
23	5	M	++	-	450	S.resistant	+ve
24	6	F	+	+	320	Sensitive	+ve
25	2	M	+	+	480	S.resistant	+ve
26	4	M	+	-	200	Sensitive	+ve
27	4	M	+	+	220	S.resistant	+ve
28	4	F	+	+	450	Sensitive	+ve
29	3	F	+	+	320	S.resistant	+ve
30	5	M	++	+	250	S.resistant	+ve

Table 2: Distribution of HLA DQ antigen in children with idiopathic nephrotic syndrome and controls

	Patients(30)			Controls(20)				
HLA antigen	No	%	Gene freq.	No	%	Gene freq	RR	X2
DQ1	0	0	0	13	65	0.408	-	26.35**
DQ2	10	33	0.183	0	0	0	2	8.33**
DQ5	12	40	0.225	6	30	0.163	1.19	0.52
DQ6	8	26.7	0.144	5	25	0.134	1.03	0.02
DQ7	8	26	0.1.44	5	25	0.134	1.03	0.02
DQ8	6	20	0.106	2	10	0.051	1.31	0.89

*Sig. P<0.05 **Highly sig. P<0.001

Table 3: Distribution of HLA DR antigen in children with steroid sensitive children.

	Patients(30)			Controls(20)				
HLA antigen	No	%	Gene freq.	No	%	Gene freq	RR	X2
DQ1	0	0	0	13	65	0.408	-	26.35**
DQ2	10	33	0.183	0	0	0	2	8.33**
DQ5	12	40	0.225	6	30	0.163	1.19	0.52
DQ6	8	26.7	0.144	5	25	0.134	1.03	0.02
DQ7	8	26	0.1.44	5	25	0.134	1.03	0.02
DQ8	6	20	0.106	2	10	0.051	1.31	0.89

Table 4: Distribution of HLA DQ antigen in children with steroid responsive children

	Patients(30)			Controls(20)				
HLA antigen	No	%	Gene freq.	No	%	Gene freq	RR	X2
DQ1	0	0	0	13	65	0.408	-	26.35**
DQ2	10	33	0.183	0	0	0	2	8.33**
DQ5	12	40	0.225	6	30	0.163	1.19	0.52
DQ6	8	26.7	0.144	5	25	0.134	1.03	0.02
DQ7	8	26	0.1.44	5	25	0.134	1.03	0.02
DQ8	6	20	0.106	2	10	0.051	1.31	0.89

Table 5: Distribution of HLA DR antigen in children with steroid resistant children

	Patients(30)			Controls(20)				
HLA antigen	No	%	Gene freq.	No	%	Gene freq	RR	X2
DQ1	0	0	0	13	65	0.408	-	26.35**
DQ2	10	33	0.183	0	0	0	2	8.33**
DQ5	12	40	0.225	6	30	0.163	1.19	0.52
DQ6	8	26.7	0.144	5	25	0.134	1.03	0.02
DQ7	8	26	0.1.44	5	25	0.134	1.03	0.02
DQ8	6	20	0.106	2	10	0.051	1.31	0.89

Table 6: Distribution of HLA DQ antigen in children with steroid responsive children

	Patients(30)			Controls(20)				
HLA antigen	No	%	Gene freq.	No	%	Gene freq	RR	X2
DQ1	0	0	0	13	65	0.408	-	26.35**
DQ2	10	33	0.183	0	0	0	2	8.33**
DQ5	12	40	0.225	6	30	0.163	1.19	0.52
DQ6	8	26.7	0.144	5	25	0.134	1.03	0.02
DQ7	8	26	0.1.44	5	25	0.134	1.03	0.02
DQ8	6	20	0.106	2	10	0.051	1.31	0.89

In order to define the immunogenetic background of NS more precisely, HLA class II alleles frequencies in 30 children with NS were investigated for HLA typing. Our results observed an increased frequency of HLA DR3 and HLA-DR7 (RR =2.25 and 2) and DQ2 (RR= 2) among all investigated INS patients which had the highest statistically significant value than those of the controls (P<0.001). Our results were confirmed by others [22, 23] they declared that, DR7 was the most prevalent alleles among INS patients in their researches.

Our results revealed that, DR6 and DR2 and DQ1 had significant negative association, they were highly prevalent in controls rather than patients (P<0.001), they have a role of protection against INS and considered as protective alleles. These were confirmed by others [24] who found that DQR2 were negatively associated with INS.

INS was divided into steroid-sensitive (SSNS) and steroid-resistant nephrotic syndrome (SRNS) because response to steroids has a high correlation with histological subtype and prognosis [25].

Many studies were performed to declare the association of DR alleles with SSNS patient but few reports were performed for prove this association with SRNS. Our results found that DR3, DR7 and DQ2 (RR= 3.86,3.22,and 2) respectively, were the most common alleles among SSNS children, (P<0.001), mean while DR6,DR2 and DQ1 showed negative associations.

Our results were correlated to that detected by Kari and others [22] who investigated the major histocompatibility complex class I and II loci in three Bengali families with nine children affected with steroid-sensitive nephrotic syndrome (SSNS). Similar to previous reports, there was a high frequency of HLA-DR7.1 (DRB1*0701), DR53 (DR B4*01011-0104) and DQ2 (DQB2*0201-3) antigens in the affected children.

Also, Zaki *et al*. [23] Found that, HLA-DR and HLA-DQ antigens were investigated in Polish children with idiopathic nephrotic syndrome (INS), HLA typing was performed and response to therapy were analyzed according to particular HLA associations. The results were compared with healthy individuals. In INS children, they observed an increased frequency of HLA-DR7, DR3/7, DQ2 and DQ8, whereas HLA-DR13, DR15, DQ5 and DQ6 were decreased. In steroid-dependence and secondary steroid-resistance, an increased frequency of HLA-DR3, DR7, DR3/7 and DQ2 was documented. In contrast, primary steroid-resistant nephrotic syndrome was associated with HLA-DR4 and DQ8.

Our results were corresponding to that detected by Nélio *et al.* [26] who found that, HLA-DR1/DR7 antigens were significantly increased in the total group of patients with SSNS compared to controls patients. The HLA-B7/DR7 haplotype was significantly increased in both SSNS and FSGC patients. The authors [26] evaluated the presence of HLA-DR7 in patients and controls; they concluded that these susceptibility markers were independent. There are several reports showing increased frequency of HLA-DR7 antigen in children with SSNS of distinct ethnic background, i.e., Australian [27], French [28], Spanish [29], German [30] English [31] North American [32],Chinese children [33], whereas HLA-DR8 antigen is observed only in adult Japanese patients [34].

In addition, HLA-DQ2 antigen and the combination of HLA-DR3/DR7 antigens have also been positively associated with SSNS, whereas HLA-DR2, -DR6 and -DQ1 have been negatively associated with SSNS in children of French and German ancestry [28].

Our study revealed that, DR3 showed positive correlation among steroid resistant children (RR=3.22), while DR6 & DR2 revealed negative association with them (P<0.001). The results were agreement with Konrad *et al.* [21] who reported that, the occasional familial occurrence of idiopathic nephrotic syndrome (NS) points to a genetic predisposition. Reports on associations with certain HLA class II antigens support this hypothesis. In order to define the immunogenetic background of NS more precisely, HLA class. HLA alleles were defined in patients with steroid-sensitive (SS) and steroid-resistant (SR) NS and in controls, typing revealed that the previously reported association between SSNS and HLA-DR7 is confined to (DRB1*07) with a combined relative risk (RR = 6.2). HLA-DQB typing showed an increased frequency of the allele (DQB1*0201) (RR = 7.8). HLA-DQA typing showed an association of SSNS with DQA3 (DQA1*0201, 0301, 0302) (RR = 4.1). The highest RR (16.5) for SSNS was found in German patients who carried the two DRB1 specificities (DRB1*0301) and (DRB1*07). All associations were stronger in SS patients, while SR patients exhibited no significant associations with HLA class II alleles.

The results were not agreement with that detected by Cheung *et al.* [35], their study was to detect the immunogenetic background of Singaporean Chinese patients with childhood SRNS. The frequency of HLA- A*11 allele was significantly higher in the SRNS patients compared to controls (78.1% vs 54.2%, respectively; relative risk, RR=3.01, Pc=0.011). However,

there was no significant difference in the allele frequencies of HLA- B*, HLA- DRB1* and HLA- DQB1* between the SRNS patients and controls, unlike that in previous studies. They suggest that the immunogenetic background of Singaporean Chinese with childhood SRNS was different from that in other populations.

In most children with steroid-resistant nephrotic syndrome (SRNS), the underlying cause is not known [8,36] However, advances in molecular genetics of glomerular diseases have shown single gene defects that affect glomerular podocyte differentiation and function are responsible for a quarter to a third of all pediatric cases of SRNS in many parts of the world.

In conclusion NS has genetic background, HLA typing proved this association. The results found positive association among steroid sensitive children with DR3, DR7&DQ 2 ((RR= 3.86, 3.22 and 2) respectively, they were the most prevalent alleles, while DR6, DR2 and DQ1 showed negative associations with the same group. DR3 showed positive correlation among steroid resistant children (RR=3.22), while DR6 & DR2 ($P<0.001$) revealed negative association with them.

REFERENCES

1. Grimbert, P., V. Audard, P. Remy, P. Lang and D.D. Sahali, 2003. Recent approaches to the pathogenesis of minimal-change nephrotic syndrome. Nephrol Dial Transplant, 18: 245-8.
2. Vivarelli, M., E. Moscaritolo and A. Tsalkidis, 2010. Time for Initial Response to Steroids Is a Major Prognostic Factor in Idiopathic Nephrotic Syndrome. J Pediatr, 9: 134-152.
3. Caridi, G., M. Gigante and P. Ravani, 2009. Clinical features and long-term outcome of nephrotic syndrome associated with heterozygous NPHS1 and NPHS2 mutations. Clin J Am Soc Nephron, 4: 1065.
4. Bhimma, R., M. Adhikari, K. Asharam and C. Connolly, 2006. Management of steroid-resistant focal segmental glomerulosclerosis in children using tacrolimus. Am J Nephrol, 26: 544.
5. Maisonneuve, P., L. Agodoa, R. Gellert, J. Stewart, G. Buccianti, A. Lowenfels, R. Wolfe, E. Jones, A. Disney, D. Briggs, M. McCredie and P. Boyle, 2000. Distribution of primary renal diseases leading to end-stage renal failure in the United States, Europe and Australia/New Zealand: results from an international comparative study. Am J Kidney Dis., 35: 157-165.
6. Van den Berg, J. and J. Weening, 2004. Role of the immune system in the pathogenesis of idiopathic nephrotic syndrome. Clin Sci, 107(2): 125-36.
7. Philibert, D., D. Cattran and T. Cook, 2008. Clinico-pathologic correlation in IgA nephropathy. Semin Nephrol, 28: 10-17.
8. Kim, J., C. Bellew and D. Silverstein, 2005. High incidence of initial and late steroid resistance in childhood nephrotic syndrome. Kidney Int, 68: 1275.
9. Büscher, A., B. Kranz and R. Büscher, 2010. Immunosuppression and renal outcome in congenital and pediatric steroid-resistant nephrotic syndrome. Clin J Am Soc Nephrol, 5: 2075.
10. Niaudet, P. and M. Gobbler, 2006. glomerular diseases. Pediatr Nephron, 21: 1653.
11. Bustos, C., E. Gonzalez, J. Muley, J. Alonso and J. Egido, 1994. Increase of tumor necrosis factor alpha synthesis and gene expression in peripheral blood cell of children with idiopathic nephrotic syndrome. Eur J Clin Invest, 24: 799-805.
12. Hildebrandt, F., 2010. Genetic kidney diseases. Lancet; 375: 1287.
13. Benoit, G., E. Machuca and C. Antigenic, 2010. Hereditary nephrotic syndrome: a systematic approach for genetic testing and a review of associated podocyte gene mutations. Pediatr Nephron, 25: 1621.
14. Frishberg, Y., S. Feinstein and C. Rinat, 2006. The heart of children with steroid-resistant nephrotic syndrome: is it all podocin? J Am Soc Nephron, 17: 227.
15. Berdeli, A., S. Mir and O. Yavascan, 2007. NPHS2 (podicin) mutations in Turkish children with idiopathic nephrotic syndrome. Pediatr Nephrol, 22: 2031.
16. Freedman, B., J. Beverly and E. Heise, 1994. HLA associations in IgA nephropathy and focal and segmental glomerulosclerosis. Am J Kidney Dis, 23: 352-357.
17. Niaudet, P., 2006. Genetic forms of nephrotic syndrome. Pediatr Nephrol, 19: 1313.
18. Santín, S., G. Bullich and B. Tazón-Vega, 2011. Clinical utility of genetic testing in children and adults with steroid-resistant nephrotic syndrome. Clin J Am Soc Nephron, 6: 1139.
19. Lagueruela, C., L. Thomas, C. Barbara, M. John and M. Alan, 1990. HLA extended haplotypes in steroid-sensitive nephrotic syndrome of childhood. Kidney International, 38: 145-150.

20. Armitage, A., 1983. Statistical methods in medical research Blackwell Scientific Publication. Oxford, London, 3rd edition.
21. Konrad, M., J. Mytilineos, F. Bouissou, S. Scherer, M. Gulli, I. Meissner, A. Cambon-Thomsen, G. Opelz and K. Schärer, 1994. HLA class II associations with idiopathic nephrotic syndrome in children. Tissue Antigens, 43: 275-280.
22. Kari, J., P. Sinnott, H. Khan, R. Trompeter and G. Snodgrass, 2006. Familial steroid-responsive nephrotic syndrome and HLA antigens in Bengali children. Pediatric Nephrology (Berlin, Germany), 21(12): 1837-1846.
23. Zaki, M., A. Daoud, Q. al Saleh, A. al Najedi and A. White, 1994. HLA antigens in Arab children with steroid-responsive nephrotic syndrome. Pediatric. Nephron, 2(13): 234-237.
24. Kobayashi, T., A. Ogawa, K. Takahashi and M. Uchiyama, 1995. HLA-DQB1 allele associates with idiopathic nephrotic syndrome in Japanese children. Pediatrics International, 37: 293-296.
25. Hodson, E., N. Willis and J. Craig, 2010. Interventions for idiopathic steroid-resistant nephrotic syndrome in children. Cochrane Database Syst Rev: CD003594.
26. Nélio, A., M. Cássia, A. Paula-Santos, B. Paulo, K. Tatsuto, C. Júlio and A. Eduardo, 2000. Immunogenetic features of steroid-sensitive nephrotic syndrome and focal segmental glomerulosclerosis in Brazilian patients of the northeast region of the state of São Paulo. Medicina, Ribeirão Preto, 33: 47-54.
27. Alfiler, C., L. Roy, A. Sheldon and H. Bashr, 1980. HLA-DRw7 and steroid-responsive nephrotic syndrome of childhood. Clin Nephrol, 14: 71-74.
28. Bouissou, F., I. Meissner, M. Konrad, E. Sommer, J. Mytilineos, B. Barthe, G. Opelz, A. Cambon-Thomoson and K. Scharer, 1995. Clinical implications from studies of HLA antigens in idiopathic nephrotic syndrome in children. Clin Nephrol, 44: 279-283.
29. Nunez-Roldan, A., E. Villechenous, C. Fernandezandrade and J. Martin -Govantes J, 1982. Increased HLA-DR7 and decreased HLA-DR2 in steroid-responsive nephrotic syndrome. N Engl J Med, 306: 366-367.
30. Ruder, H., K. Scharerk, V. Lenhard, R. Waldherr, D. Muller-wiefel, A. Wingen and J. Dippell, 1990. Human leukocyte antigens in idiopathic nephrotic syndrome in children. Pediatr Nephrol, 4: 478-481.
31. Clark, A., R. Vaughan, H. Stephens, C. hantler, D. Williams and J. Welshk, 1990. Genes enconding the betachains of HLA-DR7 and HLA-DQw2 define major susceptibility determinants for idiopathic nephrotic syndrome. Clin Sci, 79: 669-670.
32. Lagueruela, C., T. Buettiner, B. Coler, J. Kissane and A. Robson, 1990. HLA extended haplotypes in steroid-sensitive nephrotic syndrome of childhood. Kidney Int, 38: 145-150.
33. Zhou, G., Y. Guo, Y. Ji and G. Zhang, 1994. Major histocompatibility complex class II antigens in steroid-sensitive nephritic syndrome. Pediatr Nephrol, 8: 140-141.
34. Kobayashi, Y., H. Chenxm and K. Fujik, 1985. Association of HLA-DRw8 and DQ3 with minimal change nephritic syndrome in Japanese adults. Kidney Int, 28: 193-197.
35. Cheung, W., E. Ren, S. Chan, W. Gong and H. Yap, 2002. Increased HLA- A*11 in Chinese children with steroid-responsive nephrotic syndrome. Pediatr Nephrol, 17(3): 212-6.
36. Haack, D., K. Schärer, A. Asam-Tauscher and P. Vecsei, 1999. Glucocorticoid receptors in idiopathic nephrotic syndrome. Pediatr Nephrol, 13: 653.