Oxidized Low-Density Lipoprotein and High Sensitive C - reactive protein Levels in Children with Nephrotic Syndrome

Mohamed Mohamed El Mazahi, MD., Ayman Mohamed Hammad, MD., Mohamed Abd El Salam Zannoun, MD., Tarek Mustafa Emran, MD. and Riham Mohammed Elsayed Arnous

[1]Pediatric Department, Faculty of Medicine, Al Azhar University, New Damietta, Egypt.
[2]Clinical pathology Department, Faculty of Medicine, Al Azhar University, New Damietta, Egypt.
dr.riham.arnous@gmail.com

Abstract: Background and objectives: The Characteristic Features of Nephrotic Syndrome are heavy proteinuria, hypoalbuminemia, Hyperlipidemia associated with peripheral edema. The nephrotic syndrome is defined by heavy proteinuria due to increase of glomerular permeability and following hypoalbuminemia, Hyperlipidemia and edema. Hyperlipidemia is a common feature of the nephrotic syndrome. Hyperlipidemia so commonly complicates with heavy proteinuria that it has come to be regarded as an integral features of nephrotic syndrome lipid abnormalities in patients with the nephrotic syndrome have been recognized. This study brings new insights that (OxLDL) and CRP may play a direct role in promoting the inflammatory Component of atherosclerosis. So the Aim of the work to assess and evaluate the level of hs-CRP (high sensitive C-reactive protein) and Oxidized low density lipoprotein (Ox-LDL) as markers of atherosclerosis in children with nephrotic syndrome. **Methods:** in this case control study, we measure the hs-CRP and Oxidized LDL in children with INS collected from Mansoura Children University Hospital and Al-Azhar University Hospital in New Damietta. **Results:** we found elevated hs-CRP and Ox-LDL in those children with INS in remission**. Conclusion:** the results of our study suggest presence of pro artherogenic lipid profile and elevated hs-CRP and Ox-LDL levels in children with INS**.**

[Mohamed Mohamed El Mazahi, Ayman Mohamed Hammad, Mohamed Abd El Salam Zannoun, Tarek Mustafa Emran, and Riham Mohammed Elsayed Arnous. **Oxidized low-density lipoprotein and high sensitive C-reactive protein levels in children with nephrotic syndrome.** *Nat Sci* 2018;16(10):33-36]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). http://www.sciencepub.net/nature. 5. doi:10.7537/marsnsj161018.05.

Keywords: Oxidized Low-Density Lipoprotein; High Sensitive C-reactive protein; Level; Children; Nephrotic Syndrome

1. Introduction

Nephrotic syndrome (NS) is classically defined as massive proteinuria (>40mg/m^2/hr), hypoalbuminemia (<2.5 g/dL), generalized edema, and Hyperlipidemia in most cases.1.

The majority of nephrotic children have minimal change lesions, and these will either remit spontaneously within three years (two-thirds of the cases) or have earlier remission without complications following treatment. However, the minority of children who have lesions of focal segmental glomerulosclerosis and severe and prolonged proteinuria are at high risk for complications. In these children full nephrotic syndrome may progress to renal failure and even to dialysis, ultimately requiring renal transplantation.2 Nephrotic syndrome can be primary (idiopathic) or secondary. Among children, 90% of cases are primary and the rest are secondary. The advent of percutaneous renal biopsy in the 1950s and 1960s led to the identification of three histological types of idiopathic nephrotic syndrome: **MCNS, focal segmental glomerulosclerosis (FSGS), and membranous nephropathy (MN).** Whereas the incidence of nephrotic syndrome has remained stable for decades, the distribution of histological types apparently has changed due to an increase in the incidence of FSGS.3.

The annual incidence and prevalence of NS in children are two to seven cases per 100,000 under the age of 16 years and 12 to 16 cases per 100,000, respectively.4.

In children, idiopathic NS (INS) occurs more often than NS from to secondary causes such as diabetes and systemic lupus erythematosus.5 .

Because of frequent, long standing proteinuria and dyslipidemia connected with toxic disturbances in oxidative status, they have relatively higher risk of atherosclerosis and elevated (OxLDL) may reflect this situation.6.

An early sign of atherosclerosis is elevated high sensitivity C-reactive protein (hs-CRP).7.

Atherosclerosis early in life, especially in childhood, warrants an assessment for NS.

2. Patients and Methods:

This is a case control study was performed on 2 groups:

a- Patient group

Consisted of 60 children diagnosed with INS (Idiopathic Nephrotic Syndrome) according to the

definition of the international Society of Kidney in children (Those children with INS who are treated with glucocorticoid therapy). The cases were collected from Mansoura University Children Hospital (MUCH) and Al-azhar University Hospital in Damietta during the period from January 2017 till June 2017. All nephrotic patients were fulfilled the following criteria:

- Inclusion Criteria

- Steroid _ Sensitive Nephrotic Syndrome (SSNS).
- Age at the time of study (3_18 years).
- Normal blood pressure during examination.
- Normal GFR (90ml/min/1.73m2), according to Schwartz formula.

- Exclusion Criteria

- Signs of an acute infection.
- Presence of clinical and laboratory of A systemic disease
- Immunosuppressive treatment other than glucocorticoid therapy.

b- Control group

Consisted of 30 healthy children matched to the study group in age and sex.

Methods:

All the subjects were subjected the following:

1) Comprehensive history taking.
2) Clinical examination.
3) Lab. Investigations:

a) Serum creatinine.
b) Lipid Profile: CHO, LDL, HDL, TG.
c) Hs-CRP.
d) Ox-LDL.

3. Results:

Table (1): General Characteristics of the studied participants (n=90).

General Characteristics		Study Group (n=60)	Control Group (n=30)	*Test value*	*P-value*
Age *(years)*	*Mean ± SD*	6.4±2.6	7.3±2.4	*U=717*	*0.115**
	Range	(3-13)	(4-12)		
	Median	6	7.5		
Residence *Frequency (%)*	*Urban*	0 (0)	25 (83.3)	*χ2=69.321*	*0.0001***
	Rural	60 (100)	5 (16.7)		

* Mann-Whitney U test is not statistically significant at level of significance of 95%.
** Chi-square test is statistically significant at level of significance of 95%.

Table (2): History Data of the studied participants (n=90).

History Data *Frequency (%)*		Study Group (n=60)	Control Group (n=30)	*Test value*	*P-value*
Hospitalization	*Hospitalized*	41 (68.3)	0 (0)	*χ2=37.653*	*0.0001**
	Non-Hospitalized	19 (31.7)	100 (100)		
Family history of systemic disease	*Positive*	37 (61.7)	9 (30)	*χ2=8.026*	*0.007**
	Negative	23 (38.3)	21 (70)		
Family history of renal disease	*Positive*	6 (10)	0 (0)	*F=1.783*	*0.173***
	Negative	56 (90)	100 (100)		

*Chi-square test is not statistically significant at level of significance of 95%.
**Fisher's test is statistically significant at level of significance of 95%.

Table (3): Lipid profile and Creatinine of the studied participants (n=90).

Laboratory investigations		Study Group (n=60)	Control Group (n=30)	*Test value*	*P-value*
Cholesterol	*Mean ± SD*	157±47	126±27	*T=3.399*	*0.001**
	Range	(73-312)	(90-185)		
	Median	149.5	127.5		
LDL	*Mean ± SD*	82.2±40	64.4±30.5	*T=2.131*	*0.036**
	Range	(15.6-183.8)	(-7.8-120)		
	Median	85.4	64.2		
HDL	*Mean ± SD*	37.5±8	67.8±15	*U=135.5*	*0.0001***
	Range	(21-62)	(29-84)		

Laboratory investigations		Study Group (n=60)	Control Group (n=30)	*Test value*	*P-value*
	Median	36.5	71		
Triglycerides	*Mean ± SD*	136.6±85	100.5±28	*U=666*	*0.045***
	Range	(35-557)	(55-158)		
	Median	118.5	95		
Creatinine	*Mean ± SD*	0.8±0.2	0.4±0.2	*U=88*	*0.0001***
	Range	(0.3-1)	(0.1-0.6)		
	Median	0.8	0.4		

* T- test is statistically significant at level of significance of 95%.
** Mann -Whitney U test is statistically significant at level of significance of 95%.

Table (4): Oxidized low-density lipoprotein and high sensitive C-reactive protein levels of the studied participants (n=90).

Laboratory investigations		**Study Group (n=60)**	**Control Group (n=30)**	***Test value***	***P-value***
Oxidized LDL	***Mean ± SD***	**15.7±10.8**	**11.9±4**	***U=813***	***0.456****
	Range	**(2.9-75.2)**	**(2.33-18.3)**		
	Median	**13**	**13**		
HS-CRP	***Mean ± SD***	**11.5±16.6**	**5.8±8.6**	***U=784***	***0.323****
	Range	**(0.1-104)**	**(0.1-35)**		
	Median	**6.5**	**2.75**		

* Mann-Whitney U test is not statistically significant at level of significance of 95%.

Table (5): Correlations of Oxidized low-density lipoprotein, sensitive C-reactive protein levels with lipid profile and of the studied participants (n=90).

Correlations		Oxidized LDL			HS-CRP		
		Study Group (n=60)	Control Group (n=30)	Total (n=90)	Study Group (n=60)	Control Group (n=30)	Total (n=90)
Cholesterol	*R*	-0.034	-0.116	0.029	0.31	0.197	0.336
	P-value	0.796	0.542	0.785	0.016*	0.296	0.001**
HDL	*R*	0.056	0.283	-0.105	0.058	-0.045	-0.135
	P-value	0.673	0.13	0.326	0.661	0.813	0.205
LDL	*R*	0.035	0.048	0.078	0.341	-0.276	0.27
	P-value	0.79	0.802	0.467	0.008**	0.140	0.01*
Triglycerides	*R*	-0.15	-0.287	-0.104	0.015	-0.247	0.038
	P-value	0.252	0.124	0.329	0.912	0.189	0.722
Creatinine	*R*	0.119	-0.324	0.224	0.066	-0.119	0.119
	P-value	0.231	0.087	0.068	0.694	0.538	0.337

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).

4. Discussion:

Oxidative stress has been previously demonstrated in various kidney disorders such as glomerulonephritis and acute renal injury or diabetic nephropathy.8. It has been reported that there is evidence of OS and impaired antioxidant defense during acute (INS)9. We have studied 90 children classified into 2 groups; study group of 60 patients and control group of 30 healthy controls. In the present study, there was no statistically significant difference between the 2 groups regarding age (P-value > 0.05). This is in accordance with our inclusion criteria which restricted that control group are age and sex matched with the study group. We found that the mean level of total cholesterol was 157±47 mg/dL and mean LDL was 82.2±40 mg/dL, both are higher than normal levels. The mean HDL level was 37.5±8 in our subjects which is significantly lower than normal control. (OxLDL) serum concentration was higher in NS children in comparison to control group. We found positive significant correlation between (hs-CRP) and total cholesterol. This is in accordance with a **Polish**

study reported a correlation between total cholesterol and (hs-CRP) levels in the NS relapse group (r=0.486; P<0.05)10. The HDL levels in this study were not found to correlate with (hs-CRP) levels. In contrast to the above explanation, some studies have not always observed the function of HDL in preventing the formation of atherosclerosis. This difference may occur because, among other factors, the function of HDL is strongly influenced by the presence of proinflammatory conditions. Although we found no correlation between HDL and hs-CRP levels, this may be due to our examination of only HDL level, not HDL particle function. Furthermore, we found a positive significant correlation between LDL and (hs-CRP) levels (r= 0.341; P<0.05). High sensitivity CRP might increase the expression of adhesion molecules and chemokine secretion, facilitating LDL uptake by macrophages, enhancing the activity of monocytes, and inducing monocytes to produce tissue factors11.

Conclusion:

In conclusion, the results of this study confirm presence of

1) pro-atherogenic lipid profile in children with INS.
2) Elevation in (OxLDL) and (hs-CRP) concentrations were found in children with idiopathic nephrotic syndrome which was accompanied with positive correlation with LDL.

Recommendations:

- Oxidized LDL and (hs-CRP) may be used as valuable markers of atherosclerosis in patients with idiopathic nephrotic syndrome.
- Further large cohort studies to assess the role of oxidized LDL and (hs-CRP) as markers of atherosclerosis in patients with idiopathic nephrotic syndrome.
- It might be interesting to follow up those patients in remission of INS.

References:

1. Ulinski T, Aoun B. Pediatric idiopathic nephrotic syndrome: treatment strategies in steroid dependent and steroid resistant forms. Curr MedChem 2010; 17:847-53.
2. Park SJ, Shin JI. Complications of nephrotic syndrome Korean J Pediatr 2011 August;54(8):322-328.
3. Gordillo R and Spitzer A. The Nephrotic Syndrome Pediatrics in Review 2009; 30;94.
4. Ulinski T, Aoun B. New treatment strategies in idiopathic nephrotic syndrome. Minerva Pediatr. 2012; 64:135-143.
5. Elie V, Fakhoury M, Deschênes G, Jacqz-Aigrain E. Physiopathology of idiopathic nephrotic syndrome: lessons from glucocorticoids and epigenetic perspectives. PediatrNephrol. 2012; 27:1249-1256.
6. Rybi-Szumińska, A. Wasilewska, J. Michaluk-Skutnik, B. Osipiuk-Rem_za, R. Fiłonowicz and M. Zaja¸c, Are oxidized low-density lipoprotein and C- reactive protein markers of atherosclerosis in nephrotic children?, Irish Journal of Medical Science (1971 -), December 2015, Volume 184, Issue 4, pp 775–780.
7. Astuti KD, Muryawan MH, Mellyana O: Correlation between lipid profile and C-reactive protein in children with nephrotic syndrome, Paediatr Indones, Vol. 55, No. 1, January 2015.
8. Nozu K, Iijima K, Fujisawa M, Nakagawa A, Yoshikawa N, Matsuo M. Rituximab treatment for posttransplantlymphoproliferative disorder (PTLD) induces complete remission of recurrent nephritic syndrome. PediatrNephrol 2005; 20:1660-3.
9. Mishra OP, Jain P, Srivastava P, Prasad R. Urinary N-acetyl-beta-D glucosaminidase (NAG) level in idiopathic nephrotic syndrome. PediatrNephrol. 2012; 27(4):589–596.
10. Yoshikawa N, Nakanishi K, Sako M, Oba MS, Mori R, Ota E, et al. A multicenter randomized trial indicates initial prednisolone treatment for childhood nephrotic syndrome for two months is not inferior to six-month treatment. Kidney Int 2015; 87: 225-32.
11. Bazzi C, Petrini C, Rizza V, et al. Urinary N-acetyl-beta-glucosaminidase excretion is a marker of tubular cell dysfunction and a predictor of outcome in primary glomerulonephritis. NephrolDial Transplant. 2002; 17(11):1890–1896.

8/4/2018