DOI: https://doi.org/10.54393/pbmj.v5i1.214

PAKISTAN BIOMEDICAL JOURNAL

https://www.pakistanbmj.com/journal/index.php/pbmj/index

Volume 5, Issue 1 (January 2022)

Orignal Article

Mean Level of Protein C, Protein S and Antithrombin III in Pediatric Nephrotic Syndrome

Rumana Imtiaz[1*], Muhammad Asif Naveed[2], Javaria Fatima[1], Shazia Yaseen[1], Saima Irum[1], Sarah

[1]Haematology Department, Children hospital, Lahore, Pakistan
[2]Haematology Department, King Edward Medical University, Lahore, Pakistan

ARTICLE INFO

Key Words:

Protein C, Protein S, Anthitrombin III, Nephrotic syndrome

How to Cite:

Imtiaz, R. ., Naveed , M. A. ., Fatima , J. ., Irum, S. ., Yaseen, S., & Rafi, S. (2022). Mean Level of Protein C, Protein S And Antithrombin III In Pediatric Nephrotic Syndrome. Pakistan BioMedical Journal, 5(1), 221–224.
https://doi.org/10.54393/pbmj.v5i1.214

***Corresponding Author:**

Rumana Imtiaz
Haematology Department, Children hospital, Lahore, Pakistan
romanaimtiaz2808@gmail.com

ABSTRACT

Thromboembolic consequences are more common in people who have nephrotic syndrome. This study tends to shed light if there is increase or decrease in level of protein C, S or antithrombin III in nephrotic syndrome. **Objective:** is to determine the mean level of protein C, protein S and AT III in children with nephrotic syndrome.The research was conducted at Department of Haematology at Children Hospital Lahore. It was a Cross-sectional study. And the study was completed in six months from 25-08-2017 to 29-02-2018.**Methods:** Patients fulfilling the inclusion criteria were taken for Protein C, Protein S and Antithrombin III assays Collect blood 3ml (9 vol) in 0.109M (3.2%) anticoagulant (1 Vol) and Centrifuge. All centrifuge specimens were run in DIAGNOSTIC STAGO. **Results:** A total of 100 children with nephrotic syndrome were enrolled after fulfilling inclusion criteria. The mean age of the children was 6.26±2.72 month. 69(69%) were male children. Protein C level was 95.31±16.02, Protein S level 84.05±13.31 and antithrombin III level was 86.50±16.36. **Conclusions:** Protein C, S and Antithrombin III level were within normal range. Further studies are needed to delineate the exact pathogenesis behind thromboembolic phenomenon in nephrotic syndrome children.

INTRODUCTION

Nephrotic syndrome consists of proteinuria, hypoalbuminemia and oedema. Multiple problems in hemostasis and coagulation in NS patients are caused by a variety of processes. One of these is the preferential urine loss of proteins implicated in systemic hemostasis inhibition, such as protein C, S, and antithrombin III. The loss of these anticoagulants causes an imbalance in the body's procoagulant and natural anticoagulant systems. This imbalance predisposes the patient to hypercoagulability, which involves impaired blood flow (stasis), vascular damage, and change in coagulation factors, according to the Virchow triad [3]. The major enzymic agent in the coagulation system is thrombin. Naturally occurring anticoagulants, primarily antithrombin III, that regulate thrombin activity[4]. The frequency of thromboembolic complications varies from 3% -13% in different studies[3].This percentage may be under estimated in childhood because of the high number of asymptomatic or sub-clinic events, so there may a need of regular monitoring of the levels of protein C,S and ATIII to prevent these conditions[4]. During relapse of the disease in children with nephrotic syndrome, an international study conducted in Iran found that the mean ATIII level was 81.7 % ±18 %, while the control group had an ATIII level of 104.4% ±15%. (5) Another old study from Saudi Arabia found that during relapse, the average AT III level was 46.6% ±(range 7—84%)[6]. The data is quite variable in different studies so exploration is required to know the exact situation. Moreover there was no local study in Pakistan of mean values of protein C ,S and ATIII in children suffering of nephrotic syndrome so we conducted this study to measure protein C, S and AT-III in nephrotic syndrome.

METHODS

The research was carried out at Children Hospital Lahore. It was a cross-sectional study. The study was completed in six months after the approval from ethical board. Starting from 25-08-2017 to 29-02-2018.It was estimated as 100

DOI: https://doi.org/10.54393/pbmj.v5i1.214

cases using 95% confidence level, d=004 with an expected mean level of antithrombin III as 81.7±18.37 % in children presenting with nephrotic syndrome [5]. Non-probability consecutive sampling was used. Patients diagnosed with Nephrotic syndrome as mentioned(at least 6 months age0) Children of 1.5 years to 15 years of age And Children of both genders. Children suffering from congenital deficiency of protein C and antithrombin (on previous medical record) Children on anti-coagulants/anti-platelets drugs. Patients who met the inclusion criteria were recruited for the study from the nephrology departments of the Children's Hospital and the Institute of Child Health in Lahore City. An informed consent was taken from the parents of all patients. All the necessary details were recorded on prescribed proforma.

RESULTS

A total of 100 children with nephrotic syndrome were enrolled after fulfilling inclusion criteria. The mean age of the children was 6.26±2.72 month. Out of 100 patients, 69(69%) were males while 31(31%) were females. Mean duration of disease was 10.27±2.62 months. Incidence of malnutrition was 38(38%) and 62(62%) were having normal nutritional status. Protein C level was 95.31%±16.02 whereas Protein S level was 84.05%±13.31 and antithrombin-III level was 86.50%±16.36. Antithrombin III levels in normal nourished was higher than malnourished children and this difference in antithrombin III levels was significant as described in Table 3.

	Mean protein C level			
	Variables	Mean	SD	P-value
Age group	1.5 to 7 years ➢ 7 years	95.44 95.05	15.26 17.56	0.908
Gender	Male Female	95.49 94.90	16.17 15.96	0.866
Duration of	6 to 10 months	94.51	17.51	0.595
Disease	➢ 10 months	96.23	14.91	
Malnutrition	Yes No	97.28 94.09	15.36 16.41	0.336

Table 1: Stratification of data for the Protein C

	Mean protein C level			
	Variables	Mean	SD	P-value
Age group	1.5 to 7 years ➢ 7 years	84.38 83.42	12.11 15.47	0.73
Gender	Male Female	82.79 86.83	13.53 12.57	0.161
Duration of	6 to 10 months	83.70	13.54	0.780
Disease	➢ 10 months	84.45	13.17	
Malnutrition	Yes No	84.76 83.61	15.90 11.56	0.667

Table 2: Stratification of data for the Protein S

	Mean protein C level			
	Variables	Mean	SD	P-value
Age group	1.5 to 7 years ➢ 7 years	87.26 85.08	15.79 17.51	0.531
Gender	Male Female	85.73 88.19	16.47 16.25	0.928
Duration of	6 to 10 months	84.50	16.46	0.829
Disease	➢ 10 months	88.84	16.10	
Malnutrition	Yes No	87.86 78.66	12.48 18.39	0.035

Table 3: Stratification of data for Antithrombin-III

DISCUSSION

Thrombosis complications are well-known nephrotic syndrome outcomes, which arise in hypercoaguability as a result of the loss of intermediate-sized antithrombotic proteins in the urine. As a result, nephrotic syndrome may be linked to decrease in the levels of protein S, protein C and antithrombin III [8]. The vast majority of linked spontaneous thrombotic disorders are venous, with arterial thrombosis being rare. Acute thrombosis of arterial bypass grafts caused by acquired nephrotic syndrome's hypercoagulability has not been fully recognized [9]. In addition to inactivating the activated forms of factors V and VIII, activated protein C also has the ability to facilitate in vivo fibrinolysis, making it an important anticoagulant in the body [10]. In our study, mean protein C level was 95.31%±16.02 whereas Protein S level was 84.05%±13.31 and antithrombin-III level was 86.50%±16.36. In a study conducted by Soff GA, Protein C was evaluated in the plasma of 11 nephrotic syndrome patients (24-hour protein 8.4 +/- 1.6 g, SEM; serum creatinine 4.2 +/-.74 mg/dl, SEM)[11]. As controls, ten azotemic non-nephrotic patients (serum creatinine 6.0 +/- 1.25 mg/dl, SEM) were used. Despite the presence of protein C antigen in all nephrotic urine samples analyzed, no significant reduction in protein C levels was seen in nephrotic patients (mean 108 percent, range 65-200 percent) when compared to controls (mean 127 percent, range 100-200 percent) [12]. Although some publications have focused on lower protein C levels in NS [13,14]. there are also conflicting reports on alterations in protein C functional activity. Protein C levels were considerably higher in the outset of NS compared to the control group, according to Anand et al, and levels returned to normal with the disease's remission [15]. Citak and colleagues discovered that protein C levels in nephrotic children were significantly greater than in the control group, and that this difference persisted even after corticosteroid medication [16]. In nephrotic children, Yermiahu et al found that plasma levels of protein C and protein S were within acceptable limits. In terms of changes in the research parameters, age, gender, and

DOI: https://doi.org/10.54393/pbmj.v5i1.214

disease duration had no significant impact. Another old study from Saudi Arabia found that during relapse, the average AT III level was reduced and was 46.6% ±(range 7–84%)[6,17,18].Our study showed that protein C, S and Antithrombin III levels are within normal range. Hence, other factors causing thromboembolism shall also be explored[19,20].

CONCLUSION

It is concluded that although nephrotic syndrome is hypercoagulable state but protein C, S and antithrombin III levels are in normal range which shows that there is need of more extensive study to solve the multifactorial puzzle of hypercoagulability.

REFERENCES

[1] Singh R, Bhalla K, Nanda S, Gupta A, Mehra S. Correlation of spot urinary protein: Creatinine ratio and quantitative proteinuria in pediatric patients with nephrotic syndrome. J Family Med Prim Care. 2019 Jul;8(7):23432346.doi:10.4103/jfmpc.jfmpc_403_19.

[2] Pasini A, Benetti E, Conti G, Ghio L, Lepore M, Massella L, et al.,The Italian Society for Pediatric Nephrology (SINePe) consensus document on the management of nephrotic syndrome in children: Part I - Diagnosis and treatment of the first episode and the first relapse. Ital J Pediatr. 2017 Apr 21;43(1):41. doi: 10.1186/s13052-017-0356-x.

[3] Lin R, McDonald G, Jolly T, Batten A, Chacko B. A Systematic Review of Prophylactic Anticoagulation in Nephrotic Syndrome. Kidney International Reports. 2020 Apr 1;5(4):435–47. doi: 10.1016/j.ekir.2019.12.001.

[4] Sharp W, Olivero JJ. Venous Thrombosis in Nephrotic Syndrome. Methodist DeBakey Cardiovascular Journal [Internet]. 2018 Jul 1 [cited 2022 Jan 2];14(3):237. doi: 10.14797/mdcj-14-3-237.

[5] Mortazavi F, Majidi J. Evaluation of hemostatic factors in children with nephrotic syndrome. Pak J Med Sci 2008;24(3):356-9

[6] Elidrissy AT, Gader AM. Antithrombin III (AT III) and fibrinogen levels in nephrotic syndrome in children. Haemostasis. 1985;15(6):384-8. doi: 10.1159/000215177.

[7] Kaufman DP, Basit H, Knohl SJ. Physiology, Glomerular Filtration Rate. StatPearls [Internet]. 2021 Jul 22 [cited 2022 Jan 3]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK500032/

[8] Artoni A, Passamonti SM, Edefonti A, Gianniello F, Civelli V, Martinelli I. Antithrombotic prophylaxis in a patient with nephrotic syndrome and congenital protein S deficiency. Ital J Pediatr. 2016 Feb 29;42:22. doi: 10.1186/s13052-016-0227-x.

[9] Suri D, Ahluwalia J, Saxena AK, Sodhi KS, Singh P, Mittal BR, et al., Thromboembolic complications in childhood nephrotic syndrome: a clinical profile. Clin Exp Nephrol. 2014 Oct;18(5):803-13. doi: 10.1007/s10157-013-0917-2.

[10] El Ghannam MZ, Ali AAEM, el Samanoudy MI, Kamel AR. Assessment of The Level of Protein C in Children with Nephrotic Syndrome. The Egyptian Journal of Hospital Medicine [Internet]. 2019 Jul 1 [cited 2022 Jan 3];76(3):3828–34. DOI: 10.21608/EJHM.2019.41345

[11] Hoseiny Nejad N, Sharif AS, Otukesh H, Hosseini Shamsabadi R, Hekmat S, Sakhaei M. Determination of the value of albumin, anti-thrombin III, fibrinogen and D-dimer factors in the diagnosis of asymptomatic pulmonary embolism in patients with nephrotic syndrome. Pediatr Nephrol. 2021 Jul;36(7):1803-1808. doi: 10.1007/s00467-020-04904-w.

[12] Soff GA, Sica DA, Marlar RA, Evans HJ, Qureshi GD. Protein C levels in nephrotic syndrome: use of a new enzyme-linked immunoadsorbent assay for protein C antigen. Am J Hematol. 1986 May;22(1):43-9. doi: 10.1002/ajh.2830220107.

[13] Pokrajac D, Kamber AH, Karasalihovic Z. Children with Steroid-Resistant Nephrotic Syndrome: A Single -Center Experience. Materia Socio-Medica [Internet]. 2018 [cited 2022 Jan 3];30(2):84. Available from: /pmc/articles/PMC6029918/

[14] Zaffanello M, Franchini M, Zaffanell0 M. Thromboembolism in childhood nephrotic syndrome: A rare but serious complication informa healthcare Thromboembolism in childhood nephrotic syndrome: A rare but serious complication. 2007 [cited 2022 Jan 3]; Available from: doi.org/10.1080/10245330600940048

[15] Anand N K, Chand G, Talib V H, Chellani H, Pande J. Hemostatic profile in nephrotic syndrome. Indian Pediatrics. 1996;33(12):1005–12.

[16] Citak A, Emre S, Şirin A, Bilge I, Nayir A. Hemostatic problems and thromboembolic complications in nephrotic children. Pediatric Nephrology. 2000;14(2):138–42. doi: 10.1007/s004670050029.

[17] Yermiahu T, Shalev H, Landau D, Dvilansky A. Protein C and protein S in pediatric nephrotic patients - PubMed. Sangre (Barc) [Internet]. 1996 [cited 2022 Jan 4];41(2):155–7.

[18] Xia ZK, He X, Fan ZM, Liu GL, et al., [Nephrotic syndrome complicated with intracranial venous thrombosis treated with urokinase: report of 5 cases]. Zhonghua Er Ke Za Zhi. 2010 May;48(5):338-41.

DOI: https://doi.org/10.54393/pbmj.v5i1.214

[19] Chou KS, Chen JY. [Nephrotic syndrome complicated with cerebral infarction: report of one case]. Zhonghua Min Guo Xiao Er Ke Yi Xue Hui Za Zhi. 1991 Nov-Dec;32(6):396-402.

[20] Elidrissy AT, Abdurrahman MB, Bahakim HM, Jones MD, Gader AM. Haemostatic measurements in childhood nephrotic syndrome. Eur J Pediatr. 1991 Mar;150(5):374-8. doi: 10.1007/BF01955944.