



A COMPARATIVE STUDY OF PLATELET INDICES IN STEROID RESPONSIVE AND NON-RESPONSIVE NEPHROTIC SYNDROME IN PAEDIATRIC AGE GROUP IN NORTH INDIA

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ABSTRACT

Aim: The importance of changes in the platelet indices have been emphasized in most chronic diseases in recent years. These indices can also be used as a prognostic biochemical marker in Nephrotic Syndrome (NS). **Methodology-** 35 NS patients of pediatric age group along with 20 controls were included in this Comparative cross-sectional study. **Result-** The platelet count before and after steroid therapy was found to be significantly higher in the test group as compared to the control group (P-value<.001) and the mean platelet count was also significantly higher in the non-responders group as compared to the responder group. **Conclusion-** Our result suggests that values of platelet indices can be used as a biochemical marker to classify the type of NS and to predict its response to steroid treatment.

KEYWORDS : Platelet Indices, Steroid, Nephrotic Syndrome, Comparative Study, North India

INTRODUCTION

Nephrotic syndrome in the simplest words can be described as a combination of proteinuria, hypoalbuminemia, hyperlipidemia, and edema. [1]

Nephrotic syndrome is a renal glomerular disorder characterized by massive proteinuria ($\geq 3.5\text{g/day}$), hypoalbuminemia (albumin $\leq 3.0\text{g/dl}$), hypercholesterolemia, ($>200\text{mg/dl}$) and generalized edema. It is classified into two types - 1. Primary NS and 2. Secondary NS. [2]

Type of primary nephrotic syndrome - minimal change disease, mesangial proliferative glomerulonephritis, membranoproliferative glomerulonephritis, focal segmental glomerulosclerosis, membranous nephropathy, and others. [3]

The prevalence of nephrotic syndrome worldwide is approximately 16 cases per 100,000 children with an incidence of 2 to 7 per 100,000 children. Males appear to be more affected than females at a ratio of 2:1 in children, but this predominance fails to persist in adolescence. [4] The pattern of kidney diseases varies in different places due to differences in genetic status, socioeconomic status, access to health care, and the presence of background infection. [5] MCD occurs up to 6 times more commonly in some Asian (India, Pakistan, Bangladesh) children than in Caucasian counterparts in Europe. [6] In developed countries, its incidence is reported to be 20 to 40 per million population, whereas in the Indian subcontinent, it is estimated at 90 to 100 per million population. [5] As there is no study has been done to evaluate Platelet indices in children of responsive and non-responsive type of nephrotic syndrome treated with steroids. The present study helps to find out if there is any difference in platelet indices in steroid responsive and steroid non-responsive nephrotic syndrome in pediatric age group.

METHODS

This study was carried out in Children of paediatric age group presenting to a tertiary care Govt. hospital OPD & IPD in

Northern India with diagnosis of NS (1st attack or one relapse within 6 months of initial response or one to three relapses in any 12-month period) consider as case and healthy children (as control) were enrolled in the study.

Children with other associated acute or chronic illness, any known disorder affecting platelet size/number/function like thrombocytopenia, Acute Ischemic Cerebrovascular Events, severe sepsis, any history of drug intake affecting platelet parameters like Aspirin, etc, Frequent relapses, steroid dependent and resistant, Secondary Nephrotic syndrome, were excluded. A total of 50 patients were included in the study in which 20 responders, 20 control and 10 non-responders. The data collection was carried out from 1st November 2018 to 31st March 2020.

Informed written consent was taken from all the patients/parents/guardians/attendants before the enrolment

Data Analysis:

Data were analyzed using a trial version of Statistical Package of Social Science (SPSS) software version 25.0. Categorical variables are presented in number and percentage (%) and continuous variables presented as mean \pm SD and median. Normality of data tested by Kolmogorov-Smirnov test. If the normality is rejected then non-parametric test used. Quantitative variables were compared using The unpaired t-test/Mann-Whitney Test. Chi-Square test /Fisher's exact test were used for the comparison of Qualitative variables. The P-value less than 0.05 were considered statistically significant.

Ethical Considerations:

This study was approved by the Institutional Ethics Committee of institute.

RESULTS

Table 1: Comparison of demographic parameters between test and control group.

Demographic Parameters	Test group (n=35)	Control group (n=20)	Total	P-value	Test performed
Age (years)					
<=5	17 (48.57%)	9 (45%)	26 (47.27%)	0.656	Fisher Exact test
5.1-10	13 (37.14%)	6 (30%)	19 (34.55%)	0.909	Mann Whitney test;343.5
>10	5 (14.29%)	5 (25%)	10 (18.18%)		
Mean ± Stdev	6.4 ± 3.81	6.72 ± 5.05	6.52 ± 4.26		
Gender					
Female	10 (28.57%)	8 (40%)	18 (32.73%)	0.385	Chi-square test, 0.755
Male	25 (71.43%)	12 (60%)	37 (67.27%)		
Total	35 (100%)	20 (100%)	55 (100%)		

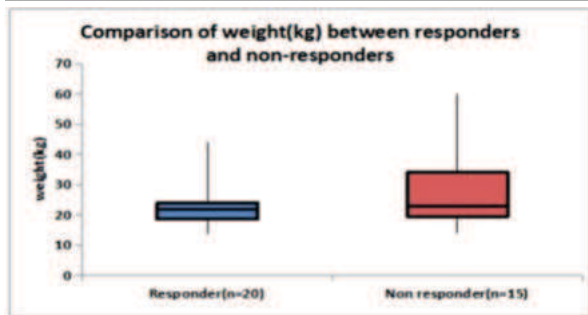


Figure 1. Comparison of weight (kg) between responders and non-responders

In the study no significant difference was seen in the distribution of age(years) and gender, rural-urban background between responders and non-responders.(P-value > 0.05)

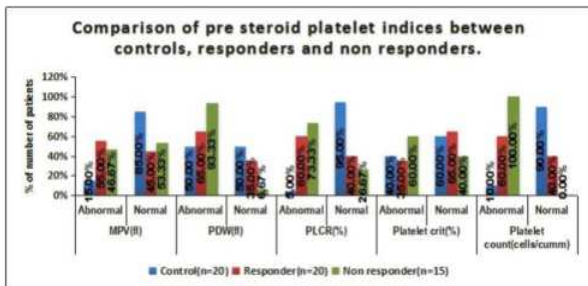


Figure 2: Comparison of pre-steroid platelet indices between controls, responders & non-responders.

No significant difference was seen in the distribution of pre steroid MPV between non responder as compared to responder and control. (P-value >0.05). Significant difference was seen in the distribution of pre steroid MPV between responder as compared to control. (P-value <0.05)

Proportion of patients with PDW: abnormal and normal in responder was 65% and 35% respectively which was comparable with control (50% and 50% respectively) and non-responder (93.33% and 6.67% respectively) with no significant difference in distribution between them. Significant difference was seen in the distribution of pre steroid PDW between control as compared to non-responder (P-value<.05) Proportion of patients in control with pre steroid PDW abnormal was 50% of patients which was significantly lower as compared to non-responder (93.33% of patients).

Significant difference was seen in PDW between controls, responders and non-responders. (P-value <.05) Mean ± stdev of PDW in control was 12.3 ± 1.62 which was significantly lower as compared to responder (16.48 ± 6.14) and non-responder (18.51 ± 1.66). Significant difference was seen in the distribution of pre steroid PLCR between control as compared to responder and non-responder. (P-value<.05) Proportion of patients in control with pre steroid PLCR(%): normal was 95% of patients which was significantly higher as compared to responder (40% of patients) and non-responder (26.67% of patients).

Significant difference was seen in PLCR(%) between controls, responders and non-responders. (P-value <.05) Median (IQR) of PLCR(%) in control was 29.65(20.4-30.9) which was significantly higher as compared to responder (12.9(10.425-15.25)) and non-responder (11.5(9.15-15.25)). The variable platelet crit(%) was not normally distributed. Thus non-parametric test was used for the comparison. No significant difference was seen in platelet crit(%) between controls, responders and non-responders. (P-value >.05) Median (IQR) of platelet crit(%) in responder was 0.29(0.24-0.33), control was 0.29(0.288-0.545) and non-responder was 0.37(0.265-0.39) with no significant difference between them.

Significant difference was seen in the distribution of pre steroid platelet count between Responder and Non responder(P-value<.05) Platelet count was abnormal in 60% of patients in responder and 100% of patients in non-responder which was significantly higher as compared to 10% of patients in control. Platelet count was normal in 90% of patients in control which was significantly higher as compared to 40% of patients in responder and 0% of patients in non-responder. Significant difference was seen in platelet count between controls, responders and non-responders. (P-value <.05) Median (IQR) of platelet count in non-responder was 620(570-726) which was significantly higher as compared to responder (422(280.5-340.75)) and control (288.5(216.25-340.75)).

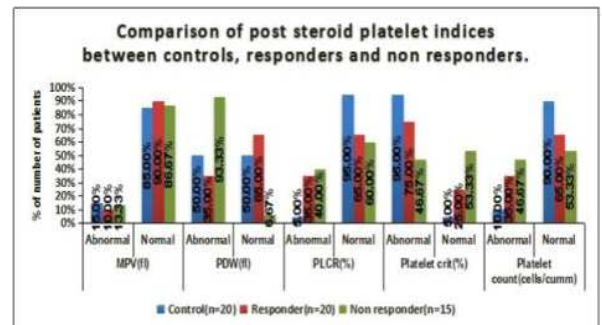


Figure 3: Comparison of post steroid platelet indices between controls, responders and non-responders.

Table2:- Comparison of platelet indices between before and after steroids in responders.

Platelet indices	Before steroid (n=20)	After steroid (n=20)	Total	value P	performed Test
MPV (fl)					
Abnormal	11 (55%)	2 (10%)	13 (32.50%)	0.006	Fisher Exact test
Normal	9 (45%)	18 (90%)	27 (67.50%)		
Mean ± Stdev	8.32 ± 2.33	9.82 ± 1.36	9.07 ± 2.03	0.002	Wilcoxon Signed Ranks Test; z value = 3.175
PDW (fl)					

Abnormal	13 (65%)	7 (35%)	20 (50%)	0.058	Chi square test,3.6
Normal	7 (35%)	13 (65%)	20 (50%)		
Mean ± Stdev	16.48 ± 6.14	16.53 ± 4.19	16.5 ± 5.19	0.972	Paired t test; t value = 0.035
PLCR(%)					
Abnormal	12 (60%)	7 (35%)	19 (47.50%)	0.113	Chi square test,2.506
Normal	8 (40%)	13 (65%)	21 (52.50%)		
Mean ± Stdev	17.99 ± 14.12	25.64 ± 10.42	21.82 ± 12.85	0.002	Wilcoxon Signed Ranks Test; z value = 3.173
Platelet crit(%)					
Abnormal	7 (35%)	15 (75%)	22 (55%)	0.011	Chi square test,6.465
Normal	13 (65%)	5 (25%)	18 (45%)		
Mean ± Stdev	0.3 ± 0.1	0.4 ± 0.08	0.35 ± 0.11	0.0002	Wilcoxon Signed Ranks Test; z value = 3.758
Platelet count					
Abnormal	12 (60%)	7 (35%)	19 (47.50%)	0.113	Chi square test,2.506
Normal	8 (40%)	13 (65%)	21 (52.50%)		
Mean ± Stdev	409.35 ± 219.34	378.8 ± 104.97	394.08 ± 170.43	0.510	Paired t test; t value = 0.672

Table 3:-Comparison of platelet indices between before and after steroids in nonresponders.

Platelet indices	Before (n=15) steroid	After steroid (n=15)	Total	P-value	performed Test
MPV(fl)					
Abnormal	7 (46.67%)	2 (13.33%)	9 (30%)	0.109	Fisher Exact test
Normal	8 (53.33%)	13 (86.67%)	21 (70%)		
Mean ± Stdev	7.67 ± 1.47	9.13 ± 1.55	8.4 ± 1.66	0.001	Wilcoxon Signed Ranks Test; z value= 3.358
PDW(fl)					
Abnormal	14 (93.33%)	14 (93.33%)	28 (93.33%)	1.000	Fisher Exact test
Normal	1 (6.67%)	1 (6.67%)	2 (6.67%)		
Mean ± Stdev	18.51 ± 1.66	19.61 ± 1.7	19.06 ± 1.74	0.003	Paired t test; t value = 3.651
PLCR(%)					
Abnormal	11 (73.33%)	6 (40%)	17 (56.67%)	0.139	Fisher Exact test
Normal	4 (26.67%)	9 (60%)	13 (43.33%)		
Mean ± Stdev	14.17 ± 8.76	21.51 ± 9.64	17.84 ± 9.79	0.005	Wilcoxon Signed Ranks Test; z value= 2.783

Platelet crit(%)					
Abnormal	9 (60%)	7 (46.67%)	16 (53.33%)	0.464	Chi square test,0.536
Normal	6 (40%)	8 (53.33%)	14 (46.67%)		
Platelet count(cells/cumm)					
Abnormal	15 (100%)	7 (46.67%)	22 (73.33%)	0.002	Fisher Exact test
Normal	0 (0%)	8 (53.33%)	14 (46.67%)		
Mean ± Stdev	646.4 ± 119.66	450.07 ± 97.34	548.23 ± 146.47	<.0001	Paired t test; t value= 6.792

DISCUSSION

In this study 55 children of paediatric age group were selected from the children attending at Department of Paediatrics. 35 (63.6%) were with nephrotic syndrome with 1st attack or One relapse within 6 months of initial response or one to three relapses in any 12-month period type of Nephrotic syndrome (Cases) and rest 20(36.4%) of the children were with other disease than nephrotic syndrome (as control). All the 35 cases were treated with steroid out of which 20(57.1%) were responder to steroid and rest 15(49.2%) of the cases were non-responder to steroid. The NS and its treatment results in various biochemical, pathological, clinical alterations and many a times lead to complications.

In our study mean MPV was significantly lower in test group (responders and non-responders) as compared to control group before and after steroid treatment(P-value <.0001) & p=.032). Mean MPV is lower in responder (8.32 ± 2.33) and non-responder (7.67 ± 1.47) as compared to control was (10.61 ± 1.86) before steroid treatment. Mean MPV in non-responder was non-significant lower as compared responder group. After steroid Mean MPV of Non-responder (9.13 ± 1.55) which was significantly lower as compared to control group(10.61 ± 1.86) but c lower as compared to responder group (9.82 ± 1.36) In comparison to responder and non-responder group mean of MPV was non-significant lower in non-responder as compared to responder before and after steroid treatment. The results are in accordance with Golleruglu et al[2] who reported mean MPV value significantly lower in active period of nephrotic syndrome when compared with control group. And also Similar to Gamal et al[7] also shows significant decrease in mean platelet volume during active and remission phases in patient groups than control group (P-value < 0.001, < 0.001 respectively).

The platelet counts before steroid therapy, was significantly higher in test group as compared to control group (P-value<.001) and mean platelet count significant higher in non-responder group(646.4 ± 119.66) as compared to responder group(409.35 ± 219.34). After steroid treatment mean platelet count is significantly higher in test group as compared to control group (P-value 0.001). and mean platelet count significantly higher in non-responder group(450.07 ± 97.34) as compared to responder group(378.8 ± 104.97).

Our results are in accordance with Golleruglu et al [2]mean platelet count in the patient group(403,112± 185,605/mL) was significantly higher than control group (326,896±68,765/mL) (p=0.02). And also in accordance with Gamal et al[7] who in their study found statistically significant increase in platelets count during active and remission phases in patient groups than control group (P-value 0.001, 0.027 respectively). In our study with references to mean PLCR was found to be significantly lower in test group as compare to control group before steroid treatment and after steroid treatment. Lower mean of PLCR was found in non-responder group as compared to responder group before and after steroid

treatment although the difference was not significant. Our result are in accordance with Nickavar at el 2020[8] who found lower mean PLCR value in SRNS group as compared to SSNS although the difference was significant in their study and non-significant in our study. In our study mean PDW was significantly higher in test group as compared to control group before and after steroid treatment and mean PDW in non-responder group (18.51 ± 1.66) was higher than responder group (16.48 ± 6.14) but the difference was not significant before steroid.

But after steroid treatment mean PDW in non-responder group (19.61 ± 1.7) significantly higher as compared to responder group (16.53 ± 4.196). Our result are in accordance to Nickavar at el 2020[8] who found higher PDW value in SRNS as compared to SSNS although difference was not significant statistically. Similar to our study Wasilewska at el 2005[8] found higher PDW value in test group as compared to control. In our study PCT was found to be non-significant lower in test group as compared control group. PCT was found to be non-significantly lower in non-responder group as compared to responder group

CONCLUSION

In our study we concluded that mean platelet count was significantly higher in test group as compared to control group before and after the completion of steroid treatment. We found no significant difference between mean PCT value between test group and control group and between responder and non-responder group before and after steroid treatment. We found mean cholesterol, HDL, LDL, TG significantly higher in test group as compare to control group. We found significant direct correlation of mean MPV with mean PLCR before and after steroid treatment in responder and non-responder groups.

We found inverse correlation of mean MPV with mean platelet count and mean PDW before and after steroid treatment in responder and non-responder groups. Although the difference was not statistically significant. Previous studies which have been done have found significant inverse correlation between mean MPV and mean platelet count. No significant correlation was observed between platelet indices and lipid profile.

Our results suggest that values of platelet indices can be used as a biochemical marker to classify the type of NS and to predict it response to steroid treatment.

Recommendations

A multicentric trial with larger sample size is required to provide more insight regarding the role of platelet indices between steroid responsive and non-responsive nephrotic syndrome in pediatric age group. A study to assess the effect of drug used for treatment in nephrotic syndrome on platelet indices should be performed to further add valuable evidence to the existing literature.

Conflict of Interest

In this study there is no conflict of interest.

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