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ETIOLOGIC DIAGNOSIS OF ANEMIA IN CHILDREN ADMITTED WITH NEPHROTIC SYNDROME IN A TERTIARY CARE HOSPITAL OF ODISHA, INDIA

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ABSTRACT:

Background: Nephrotic syndrome is the most common chronic glomerular disease in children. Mechanism of anemia in patients with nephrotic syndrome is complex and incompletely understood. Mild anemia is seen sometimes in patients with nephrotic syndrome. Anemia is generally microcytic and hypochromic, typical of iron deficiency, but is resistant to therapy with iron because of large loss of serum transferrin in urine.Data on prevalence of anemia in nephrotic syndrome is limited. Basing on this background this study is undertaken.

Materials and methods: It is a cross sectional, hospital based,Prospective observational study done in Department of paediatrics, MKCGMCH, Berhampur from October 2019 to September 2021 taking 113 cases. All statistical analysis was done using statistical software SPSS (version 21.0).

Results:Sex predilection was observed more in male children. The most common age group was 2-6 years. The most common type of nephrotic syndrome is steroid responsive NS (n=67) which is 59.3% followed by infrequent relapse and steroid resistant NS. The prevalence of anemia in nephrotic syndrome is 27.9%(n=31). Among anemia in nephrotic syndrome microcytic hypochromic anemia (63.3%) is common morphologic variant.Most patients with anemia were steroid resistant(76.9%). Nephrotic syndrome with anemia had low serum ferritin among 38.6%(n=12).

Conclusion: The present study revealed steroid responsive is most common type of nephrotic syndrome. Infection is the most common complication in nephrotic syndrome. There was an association of anemia in nephrotic syndrome more commonly microcytic hypochromic..

Keywords: anemia, nephrotic syndrome, ferritin

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INTRODUCTION

Nephrotic syndrome is the most common chronic glomerular disease in children.[1] The clinical and biochemical profile of nephrotic syndrome is due to heavy proteinuria(>40mg/m^2/hr.), hypoalbuminemia, lowered plasma oncotic pressure and edema which follow sustained loss of large amounts of protein in urine.[1]Mechanism of anemia in patientswith nephrotic syndrome is complex and incompletely understood. Much of the morbidity of nephrotic syndrome is due to significant loss of plasma proteins of various molecular weights in urine, including albumin, coagulation factors, immunoglobulin, transferrin, erythropoietin, hormone binding proteins.[2-3]

Mild anemia is seen sometimes in patients with nephrotic syndrome. Anemia is generally microcytic and hypochromic, typical of iron deficiency, but is resistant to therapy with iron because of large loss of serum transferrin in urine.[4]Data on prevalence of anemia in nephrotic syndrome is limited. Available information suggest anemia may be frequent complication in nephrotic syndrome. Feinstein and his group showed prevalence of 59% in their study group, with most of the patients with anemia having steroid resistant nephrotic syndrome.[5] Franca Diego and his group showed about 28% of their population has developed anemia during the course of disease.[6] A common denominator in these anemic patients is persistence or therapy resistant nature of nephrotic syndrome.[7-8] Although the mechanism of action of anemia in chronic kidney disease is known, anemia in nephrotic syndrome with normal kidney function are complex.[7-8]

Though nephrotic syndrome is very common disease for which children get admission in our hospital, there is no data on its prevalence and overall outcome of patients. This is an observational study undertaken to know the prevalence of disease in our hospital, its demographic profile, recurrence rate, biochemical profile, complication in special reference to anemia.

MATERIALS AND METHODS:

This Cross -sectional study, hospital based Prospective observational study wasdone in Department of pediatrics, MKCG Medical College, Berhampur from October 2019-September 2021.Institutional ethical clearance was taken for the study.The data collection was done as per the designed proforma.Considering incidence of nephrotic syndrome in india6% & a confidence interval of 95%, the sample size taken was 113 in number.

INCLUSION CRITERIA:

Children with age group of 1 to 14 years who are diagnosed to be nephrotic syndrome according to ISKDC(International study of kidney disease in children for diagnosis of Nephrotic syndrome) criteria were included in this study.Criterias included for the study wereNephrotic range proteinuria(>3.5gm/day), Hypoalbuminemia(<2.5g/dl),Hyperlipidemia(>200mg/dl) andEdema.

ISSN: 0975-3583, 0976-2833 VOL13, ISSUE04, 2022

EXCLUSION CRITERIA:

- Nephrotic syndrome with congenital hemolytic anemia
- Chronic kidney disease
- Secondary nephrotic syndrome
- Bone marrow failure syndrome

STATISTICAL ANALYSIS:

To find the correlation between hemoglobin, red cellindices & iron profile, Pearson's correlation coefficient was used.All the statistical analysis had been done by using statisticalsoftware SPSS (version 21.0). $p < 0.05$ is considered as significant.

RESULTS

Among the nephrotic syndrome patients admitted to our hospital showed that 71(62.8%) were male & 42(37.2%) were females. The overall male: female ratio is 1.68:1. Our study showed a predominance of male.

TABLE NO 1- AGE WISE DISTRIBUTION OF CASES :

AGE GROUP	NUMBER	PERCENTAGE	MEAN±SD
0-1 YEARS	0	0%	5.02±2.83
1-3 years	49	43.3%	
4-6 years	31	27.4%	
7-9 years	24	21.2%	
10-14 years	9	7.9%	

In this study mean age of presentation is 5.02±2.83 years among all nephrotic syndrome patients. Among 113 patients 49(43.3%) patients are between age group of 1-3 years & 31(27.4%) are between age group of 4-6 years

TABLE-2:TYPES OF ANEMIA IN NEPHROTIC SYNDROME:

Anemia	Number of patients (n=113)	Percentage
No anemia	82	72.8%
Mild	8	7.07%
Moderate	20	17.6%
Severe	3	2.6%

ISSN: 0975-3583, 0976-2833 VOL13, ISSUE04, 2022

Among 113 nephrotic syndrome patients,n=31(27.4%) patients have pallor with anemia. Among the anemic patients, 8(25.8%) patients have mild anemia, 20(64.5%) patients have moderate anemia& 3(9.6%) patients have severe anemia.

In this study, 27.4% of nephrotic syndrome have anemia. Peripheral smear comment, shwedthat 19(63.3%) patients have microcytic hypochromic anemia(MHA), 2(10%) patients have normocytic hypochromic anemia(NHA), 10(26.7%) patients have normocytic normochromic anemia(NNA).Macrocytic anemia case is not observed in our case.

TABLE-3:MORPHOLOGICAL TYPES OF ANEMIA IN DIFFERENT TYPES OF NEPHROTIC SYNDROME:

Types of NS	Steroid responsive (n=67)		Infrequent relapse (n=16)		Frequent relapse (n=10)		Steroid dependent (n=9)		Steroid resistant (n=13)	
Types of anemia	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%
MHA (n=19)	3	4.4%	2	12.5%	1	10	5	55.5%	10	76.9%
NHA (n=2)	1	1.4%	1	6.2%	0	0	1	11.1%	0	0%
NNA (n=10)	1	1.4%	0	0%	4	40	3	33.3%	3	23%
Total (n=31)	5	7.2%	4	18.7%	5	50%	9	100%	13	100%
pvalue	0.301		0.522		0.078		0.004		0.001	

Table-3 shows that, 5(7.4%) out of 67 steroid responsive NS patients have anemia, 3(18%) out of 16 infrequent relapse NS, 5(50%) out of 20 frequent relapse NS have anemia. All 13 steroid resistant NS & all 9 patients of steroid dependent NS have anemia with p-value <0.005.

TABLE-4:SERUM FERRITIN LEVEL IN NEPHROTIC SYNDROME:

Types of anemia	Number of cases with low sr. ferritin	Percentage	Mean±SD	

ISSN: 0975-3583, 0976-2833 VOL13, ISSUE04, 2022

MHA(n=19)	9	29%	68.83±30.2	CHI SQUARE-80.18 P VALUE-0.002
NHA(n=2)	1	3.2%		
NNA(n=10)	2	6.4%		
Total(n=31)	12	38.6%		

In our study, the mean serum ferritin level is 68.83±30.2. Out of 31 anemic patients, 38.6%(12) patients had low serum ferritin level. MHA, NHA, NNA contributed 29%(9), 3.2%(1)& 6.4%(2) respectively. P value is significant(0.002). Thus, low ferritin level is significant in anemia in nephrotic syndrome.

TABLE-5: COMPARISON DIFFERENT TYPES OF ANEMIA IN NEPHROTIC SYNDROME

Types of anemia	MHA		NHA		NNA		Significance
Parameters	Mean	SD	Mean	SD	Mean	SD	p value
Hb	9.2	1.06	9.4	1.27	9.6	0.92	0.0008
PCV	29.24	4.20	30.35	2.19	31.21	3.11	0.0001
MCV	70.81	9.07	71.7	2.19	82.63	5.66	0.002
MCH	25.44	2.75	26.25	0.28	28.92	1.90	0.001
s. ferritin	25.63	19.28	26	5.6	56.8	29.2	0.321

One way ANOVA test was used to compare the differences in mean of various indices among the children with MHA,NHA,NNA in nephrotic syndrome. The mean difference between groups with respect to hemoglobin, PCV, MCV, MCH, RDW was statistically significant.

DISCUSSION

In our study among the 113 nephrotic syndrome patients admitted to our hospital showed that 71(62.8%) were male & 42(37.2%) were females showing a malepredominancewhich corroborates

ISSN: 0975-3583, 0976-2833 VOL13, ISSUE04, 2022

with study done by Nanjundaswamy[9] et al(2002) &Beth A vogt et al(2004)[10]. In our study among 113 patients, 49(43.3%) patients were between the age group of 1-3 years & 31(27.4%) were between age group of 4-6 years &mean age of presentation is 5 years. Shah et al(1969)[11] showed that 61.7% of nephrotic syndrome was presented between 2-6 years of age.In our study, most common type of nephrotic syndrome is steroid responsive nephrotic syndrome with incidence of 59.3%(67), which is similar to Kumar et al (2020)[12]which reported 50.8% were steroid sensitive NS.

In our study, among 113 nephrotic syndrome patients 31(27.9%) patients hadanemia. Among the anemic patients, 8(25.8%) patients had mild anemia, 20(64.5%) patients had moderate anemia& 3(9.6%) patients had severe anemia which is similar to Franca & Diego et al (2016)[13] which showed 28% of study population had anemia during the course of disease. The prevalence of anemia was high in this study may be due to small sample size and different criteria used for defining anemia.Depletion of iron stores as a result of prolonged transferrin and iron losses may be the reason behind development of anemia. EPO deficiency with an inappropriately mild response to anemia seems to be an important factor in either the development of anemia or its persistence if initiated by a different factor.

In our study, out of 31 anemic patients, 19(63.3%) patients had microcytic hypochromic anemia(MHA), 2(10%) patients have normocytic hypochromic anemia(NHA), 10(26.7%) patients have normocytic normochromic anemia(NNA). MHA is most common form of anemia in nephrotic syndrome followed by NNA.Mahr et al (2005)[14]had attained similar findings in anemia with predominant microcytic hypochromic anemia.

In our study, it is observed that 5(7.4%) out of 67 steroid responsive NS patients have anemia, 3(18%). All cases of steroid resistant NS & all 9 patients of steroid dependent NS have anemia with p-value <0.005. Soanemia in steroid resistant NS & steroid dependent NS is highly significant. Feinstein et al (2001)[5] showed similar finding showing most patients with anemia were steroid resistant and steroid dependent. In our study complete blood count reveals the mean Hb is 9.2 in MHA in nephrotic syndrome & children with NHA & NNA in nephrotic syndrome is 9.4 & 9.61 respectively. The mean values of PCV, MCV, MCH, MCHC are less in MHA in nephrotic syndrome as compared to NHA & NNA in nephrotic syndrome suggestive of iron deficiency. This similar observation was made by Duque et al[15] where in MHA low PCV & MCV values were observed suggestive iron deficiency. Several case reports showed massive transferrin losses in NS in association with anemia, which led investigators to suggest that iron deficiency is the main causative factor of anemia.[16]

In our study, mean serum ferritin is 68.83±30.2. Among 31 nephrotic syndrome with anemia patients, 38.6% (12) patients had significantly lower serum ferritin level (p = 0.002). It was also seen that in the study conducted by Maheshwari et al[17], only 35% had low ferritin levels. Feinstein et al (2001)[5] had

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got mean serum ferritin level 25.5±1.25 Serum iron & serum ferritin were lower in anemic group than non anemic patients[5].

CONCLUSION

This present study revealed steroid responsive(59.3%) is most common type of nephrotic syndrome followed by infrequent relapse. There was an association of 27.9% of anemia in nephrotic syndrome which was more commonly microcytic hypochromic anemia (63.3%).Most patients with anemia were steroid resistant and steroid dependent nephrotic syndrome.There is a great association of very low albumin level with steroid resistant nephrotic syndrome.Nephrotic syndrome with anemia is having low serum ferritin in 38% of cases. Nephrotic syndrome with anemia is having association with high serum urea & creatinine level.

LIMITATIONS

This study was performed during covid restriction period. So many patients were not admitted until emergency requirement. So prevalence of nephrotic syndrome couldn't be elicited.

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