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RISK FACTORS FOR MICROALBUMINURIA IN CHILDREN WITH SICKLE CELL DISEASE IN TERTIARY CARE HOSPITAL IN CENTRAL INDIA - A CROSS SECTIONAL STUDY

Pediatrics

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ABSTRACT

BACKGROUND: Sickle cell disease is common in central part of India. It is associated with a large spectrum of renal abnormalities, of which microalbuminuria , is a known predictor of end-stage renal disease.

METHODS: Prospective, cross sectional, observational study among known 64 sickle cell disease (homozygous) children with stable steady state. Demographic and clinical findings were recorded. Presence of microalbuminuria was checked.

RESULTS: Out of the 224 subjects evaluated with microalbuminuria 36/118 (30.50%) were males while 28/106 (26.41%) were females. Dependent variables of microalbuminuria among subjects with microalbuminuria, comparison of the various social classes (P = 0.170, Pearson Correlation 0.087.), Blood transfusions (P = 0.517, Pearson Correlation 0.137), blood pressure and diastolic BP (P = 0.243, Pearson Correlation 0.042), hospitalizations (P = 0.263, Pearson Correlation 0.072), serum creatinine (P = 0.180, Pearson Correlation 0.022), glomerular filtration rate (GFR) (P = 0.310, Pearson Correlation 0.061) are Statistical no significant, but haemoglobin level (P = 0.003, Pearson Correlation 0.219) was Statistical significant . This increase with age was also noted in other studies and may possibly be as a result of higher number of crisis in these children and disease progression over time.

CONCLUSIONS: Renal involvement is common in sickle cell disease. Increasing age and homozygous state were risk factors. Microalbuminuria is a good screening test for early detection of renal involvement.

KEYWORDS

Sickle Cell Disease, Kidney Functions, Microalbuminuria

INTRODUCTION

Sickle cell disease or sickle cell disease, inherited disorder of the blood in which the oxygen-carrying hemoglobin pigments in erythrocytes (red blood cells) is abnormal. This hemoglobin-S crystallizes in small capillaries, where the concentration of oxygen in the blood is low (but sufficient for normal hemoglobin), causing the red blood cells to assume distorted, sickle like shapes.

The sickled red blood cells tend to clog small blood vessels, depriving the tissues they serve of blood and oxygen. Painful crises result, with symptoms depending on the site affected (e.g., joint and abdominal pain or kidney damage). Strokes or seizures can occur if the brain is affected. Lung infections resulting from the patient's disinclination to take painful deep breaths are a frequent complication. In addition, the sickled erythrocytes are fragile and subject to rupture and destruction, leading to haemolytic anaemia (reduction of oxygen-carrying haemoglobin caused by premature destruction of red blood cells) and such symptoms as fatigue, jaundice, and headaches.

THIS CATEGORY INCLUDES:

I. Heterozygous condition (Hb AS): in this form, both normal adult hemoglobin (Hb A) and sickle hemoglobin (Hb S) are present in the red cells. Medically, therefore, they rarely convey less medically significance, they are said to have the Sickle cell trait[13].
II. Homozygous state (Hb SS): In this type, the red cells are totally lacking normal adult hemoglobin and occupied mainly by sickle hemoglobin(HbS). They phenotypically express severe hemolytic anemia along with other manifestations. They are known as Sickle cell disease (SCA)[13].
III. Doubly heterozygous state: Inheritance of both abnormal genes where the red blood cells contain other alpha or beta chain structural variants or thalassemia in addition to HbS[13].

Repeated ischemia-reperfusion injury to vital organs further amplifies inflammatory & oxidative stress and activation of the innate immune response. It further causes infarction of multiple organs such as the spleen, kidneys, liver, muscle, brain, lung and bone[1,2,3]. Infarction of the bone marrow results in severe bone pain, which is characteristic of the vaso-occlusive painful crisis and is most common complication of sickle cell disease[4].

Lowest level of albuminuria (20–200 mg/L) known as microalbumi nuria it's a preclinical marker of glomerular damage predicting progressive renal failure in conditions like diabetes mellitus also associated with hyperfiltration, and hyperperfusion [5]. Microalbu minuria has been defined as an abnormally or supernormal urinary excretion of albumin in the absence of clinical proteinuria. Others researcher defined microalbuminuria in terms of timed overnight urine collection as an albumin excretion rate greater than 20 μg per minute.[6]

Among children however, prevalence rates of between 15.5 to 47.1% have been reported in different populations using different methods of microalbuminuria quantifications [7,8,9]. The incidence and prevalence rates of the homozygous state (HbSS) in the country are 1:300 and 2 to 3.1% respectively [10,11].There are several manife stations of SCN but one of the earliest features is microalbuminuria, a pre-clinical marker of kidney damage. In the adult population with SCA, microalbuminuria has been reported in up to 68% [12].

SUBJECTS AND METHODS

The study was a cross-sectional descriptive study conducted at NKP Salve Institute of Medical Sciences, Lata Mangeshkar Hospital and Research Centre, Digdoh Hills, Hingna Road, Nagpur Maharashtra from August 2017 to October 2019. Study subjects consisted of 224 sickle cell disease children in steady state, that is apparently well (subjectively and objectively) without any evidence of recent infections, crises or other problems and had been well for at least one month after the last crisis.

A total of 224 children who met the study inclusion criteria were selected as controls, Children Diagnosed as Sickle cell disease by Hemoglobin Electrophoresis(HPLC) having SS Pattern and stable patients aged 5-18yrs. Exclusion Criteria- Children of Sickle Cell trait, Children of Sickle cell disease (Hb-SC, Hb-beta $^{+}$,Hb-beta ^{0}), Unstable patients, Excluded were children with sickle cell crises symptoms (fever, bone pain crisis, other) in the preceding one or two weeks, children with prior known overt proteinuria or gross haematuria, including currently menstruating adolescent females, and children with comorbid conditions like hypertension, urinary tract infections, diabetes mellitus, retroviral infection, and children with any history of kidney disease.

STUDY POPULATION

Patients were seen in the outpatient department of pediatrics in stable state. After signing an informed consent form, these patients were screened with following inclusion and exclusion criteria for recruiting into the study. Sample size was calculated using the formula (n= 4 P*Q/L2) (% of micro albuminuria) by using this value 20.3%, sample size is 64 by keeping power 80%, alfa error=0.05. All relevant demographic details like age, gender, residence were noted. Detailed clinical history of each patient was noted. History of hospital

admissions, number of hospitalization, and number of blood transfusion was noted, and Physical Examination and Anthropometry-

1-Weight (Kgs)- Weight was measured to the nearest 0.1 kg using an electronic weighing machine with minimal clothing and no shoes.

2-Height (cm)- Height was measured using the same stadiometer, and children with barefoot with minimal clothing and ensure that the back of the head, shoulder blades, buttocks, calves, and heels are touching the vertical board/wall having their heels together, arms to the side, legs straight, shoulders relaxed, and the head in the horizontal plane.

SAMPLING PROCEDURES:
All stable patients with sickle cell disease who visited the sickle cell clinic (SCC) / routine OPD during the study period were recruited into the study. For every child, a detailed history was taken including patient's age, gender and relevant medical history of recurrent admissions, blood transfusions. A thorough physical examination was carried out on each child. The standing height was measured using a stadiometer. All enrolled subjects were given bottles for the collection of urine. Subjects were instructed

ETHICS APPROVAL-
The institutional ethics committee approved protocol of the study before patient recruitment.

DATA ANALYSIS
Data was analyzed using the SPSS version 25.0. Data were analyzed quantitatively and presented in the form of frequency tables and proportions. The statistical significance of mean values. Further statistical analysis using Pearson Correlation analysis and multivariate regression model were also carried out. A P-value less than 0.05 were considered as significant.

RESULTS
Out of the 224 subjects evaluated with microalbuminuria 36/118 (30.50%) were males while 28/106 (26.41%) were females. The without microalbuminuria 82 (69.49%) males and 78 (73.58%) females. The maximum number of children from 5 years to 10 years with microalbuminuria 39 (32.23%) and without microalbuminuria 82 (67.76%), 11 years to 14 years with microalbuminuria 14 (26.92%) and without microalbuminuria 38 (73.07%), and 15 years to 18 years with microalbuminuria 11 (21.56%) and without microalbuminuria 40 (78.43%).

Table 1: Distribution Of Study Subjects Based On Gender In This Study

	With Microalbuminuria	Without Microalbuminuria	Total
Gender			
Male	36 (30.50%)	82 (69.49%)	118
Female	28 (26.41%)	78 (73.58%)	106
Total	64 (28.57%)	160 (71.42%)	224
Age Group In This Study	MA	WITHOUT MA	Total
5-10 Years	39 (32.23%)	82 (67.76%)	121
11-14 Years	14 (26.92%)	38 (73.07%)	52
15-18 Years	11 (21.56%)	40 (78.43%)	51

Comparison of the various social classes among subjects with microalbuminuria showed statistical not significance in social classes (P = 0.170, Pearson Correlation 0.087.) whereas the comparison of social classes did not reveal any statistical significance as shown in Table 2.

Blood transfusions in the subjects with microalbuminuria (P = 0.517, Pearson Correlation 0.137) .The difference was not statistically significant. The mean haemoglobin level in subjects with microalbuminuria (P = 0.003, Pearson Correlation 0.219), and the difference was statistically significant.

Table No. 2. Pearson Correlation Analysis Of The Dependent Variables Of Microalbuminuria Among Subjects With Microalb uminuria.

Areas (with Microalbuminuria) Subjects	Pearson Correlation	p- Value	Significance
Social class	0.087	0.170	Not Significance
Diastolic blood pressure	0.137	0.517	Not Significance
Systolic blood pressure	0.042	0.243	Not Significance
Previous hospitalization	0.072	0.263	Not Significance
Serum creatinine	0.022	0.180	Not Significance
Hemoglobin level	0.219	0.003	Significance
Glomerular filtration rate	0.061	0.310	Not Significance

There was no significant statistical relationship between the number of blood transfusions in the past, anthropometric characteristics such as weight, height, and BMI. Blood pressure (BP) in the subjects with microalbuminuria was (P = 0.243, Pearson Correlation 0.042). Similarly there was no significant statistical relationship between microalbuminuria and systolic blood pressure and diastolic BP, respectively.

Sixty- four subjects with microalbuminuria had experienced previous hospitalizations following painful crises. The difference was statistically not significant (P = 0.263, Pearson Correlation 0.072) as shown in Table 2. Also subjects with microalbuminuria did not experience any painful crises requiring hospitalization in the preceding two years.

Also there was no significant difference between the mean serum creatinine of the subjects with microalbuminuria and those with negative microalbuminuria (P = 0.180, Pearson Correlation 0.022). Similarly, the difference in glomerular filtration rate (GFR) between with microalbuminuria subjects was not statistically significant (P = 0.310, Pearson Correlation 0.061). In all, the serum creatinine and GFR of the study subjects were within normal limits.

On further statistical analysis using multivariate regression model both haemoglobin levels, and number of previous hospitalizations following painful crises in the study subjects remained statistically significant (P = 0.003, Pearson Correlation 0.219). However, only haemoglobin levels among study subjects showed statistical significance with microalbuminuria .

DISCUSSION
This hospital based observational cross-sectional study was carried out from August 2017 to July 2019 to assess the renal dysfunction (kidney function test, urine dipstick, ultra- sonography, VBG) in children with sickle cell disease. We studied 64 cases that fulfilled the eligibility criteria for this study. All these patients underwent biochemical evaluation with special reference to kidney function test, venous blood gas, urine dipstick and ultra-sonography was done.

Lower haemoglobin levels were significantly associated with microalbuminuria in children with sickle cell disease in this present study, and other researcher also have been reported [14, 15]. Even Ayoola Odeyemi [16] study found significant difference in reticulocyte index, serum albumin and aspartate aminotransferase (AST) values. In contrast to this observation, Mc Burney PG et al. [17] they did not found any factors were significantly related to microalbuminuria: pain, pneumonia, acute chest syndrome, priapism, avascular necrosis, or aplastic episodes.
In conclusion, microalbuminuria occurs in a significant number of children with sickle cell disease. Increasing age, lower haemoglobin concentrations, and higher number of hospitalizations following painful crises were found to correlate positively with microalb uminuria. It is recommended that screening for microalbuminuria should be incorporated into the management of sickle cell disease children with associated risk factors for microalbuminuria. Such measure will assist in early detection and improve case management of a child with sickle cell disease.

LIMITATION -
The results of this study "Risk Factors for Microalbuminuria in Children with Sickle cell disease in Tertiary Care Hospital in Central India - A Cross Sectional Study " Future research is required to further delineate and characterize the prevalence, frequency, and risk factors for microalbuminuria.

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CONFLICT OF INTEREST-
The authors declare that they have no conflict of interest.

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