ORIGINAL RESEARCH

Renal Complications and Their Correlation with Disease Duration in Adult Sickle Cell Disease Patients: A Cross-Sectional Analysis

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ABSTRACT

Background: Sickle cell disease (SCD) is a hereditary hemoglobinopathy marked by the presence of sickle-shaped erythrocytes. While complications related to vaso-occlusion in various organs are well-established, renal manifestations remain poorly understood. Our study aims to determine the prevalence of renal complications in adult SCD patients and assess their correlation with disease duration

.**Methods:** In this cross-sectional study, data from 400 adult SCD patients were extracted from a tertiary care center. Clinical and laboratory parameters, including glomerular filtration rate (GFR), proteinuria, and hematuria, were evaluated. Disease duration was correlated with the presence and severity of renal complications using statistical methods.

Results: The prevalence of renal complications was found to be 57%. The most common abnormalities observed were reduced GFR (38%) and proteinuria (28%). Hematuria was observed in 15% of the patients. A significant correlation was found between disease duration and the severity of renal complications ($r = 0.68$, $p < 0.001$). Patients with disease duration of more than 20 years had a 2.5-fold increased risk of advanced renal complications.

Conclusions: Renal complications are prevalent in adult SCD patients and their severity correlates strongly with disease duration. Regular renal monitoring and early interventions can be pivotal in preventing progressive renal damage in this vulnerable population. Further longitudinal studies are recommended to explore causal relationships and underlying mechanisms.

Keywords: Sickle Cell Disease (SCD), Renal Complications, Disease Duration.

INTRODUCTION

Sickle Cell Disease (SCD) is a group of inherited hemoglobin disorders that lead to the abnormal formation of hemoglobin, causing erythrocytes to assume a distinct sickle shape. These misshapen cells can cause blockages in the blood vessels leading to a plethora of clinical manifestations [1]. One of the organs significantly affected by these pathophysiological changes is the kidney. Renal complications arising from SCD, such as glomerulopathy, hematuria, and proteinuria, are increasingly recognized as crucial determinants of morbidity in these patients [2]. The vaso-occlusive nature of SCD often leads to renal ischemia, a primary factor contributing to the myriad of renal complications seen in these patients [3]. While the general implications of SCD on organs are well-understood, the correlation between disease duration and the severity of renal complications in the adult population warrants in-depth analysis. This understanding can potentially pave the way for timely clinical interventions, decreasing the burden of renal morbidity and mortality among SCD patients [4]. This study endeavors to fill this knowledge gap, offering critical insights into the renal implications of prolonged SCD.

AIM

To comprehensively analyze the renal complications in adult Sickle Cell Disease (SCD) patients and understand the relationship between the duration of the

disease and the onset and severity of these renal manifestations, in order to provide insights for enhanced clinical monitoring and targeted therapeutic strategies.

OBJECTIVES

1. To ascertain the overall prevalence of renal complications, such as reduced GFR, proteinuria, and hematuria, in the adult SCD patient population.
2. To evaluate and establish the relationship between the duration of sickle cell disease and the severity or presence of renal complications, thus understanding the progression and impact over time.
3. To recognize any additional factors contributing to renal complications in SCD patients and suggest early intervention strategies to prevent or minimize renal damage and improve patient outcomes.

MATERIAL AND METHODOLOGY

Study Design and Population: This study employed a cross-sectional design to analyze renal complications in adult SCD patients. We extracted data from a tertiary care center that catered to a large population of SCD patients. All adult patients (>18 years) with a confirmed diagnosis of SCD, based on hemoglobin electrophoresis, who visited the center between January 2022 and December 2022, were considered for inclusion.

DATA COLLECTION

Patient data was retrospectively gathered from electronic health records (EHRs). The following information was collated:

1. Demographic details (age, gender, race)
2. Clinical history (disease duration, comorbidities, and prior complications)
3. Laboratory results pertaining to renal function (glomerular filtration rate, serum creatinine, urinalysis)

SAMPLE SIZE

Considering a 95% confidence interval, 5% margin of error, and expected renal complications prevalence of 50% (based on preliminary observations), the sample size was determined using the formula for estimating proportions in epidemiological studies. A total of 384 patients was deemed necessary; however, for better accuracy and to account for any missing data, 400 patients were included in the final analysis.

INCLUSIVE AND EXCLUSIVE CRITERIA

INCLUSIVE CRITERIA

1. Patients aged 18 years and above.
2. A confirmed diagnosis of SCD based on hemoglobin electrophoresis.
3. Registered at the center during the stipulated study period.

EXCLUSIVE CRITERIA

1. Patients with coexisting renal diseases unrelated to SCD.
2. Patients on renal replacement therapies like dialysis or those with a kidney transplant.
3. Insufficient data in the EHRs or those with missing key parameters.
4. Patients with other hemoglobinopathies or confounding hematological conditions.

ASSESSMENT OF RENAL COMPLICATIONS

- **Glomerular Filtration Rate (GFR):** Estimated GFR (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formula. Reduced eGFR (<60 mL/min/1.73 m^2) was considered indicative of impaired renal function.
- **Proteinuria:** Determined using a spot urine protein-to-creatinine ratio. A ratio above 0.2 was considered significant for proteinuria.
- **Hematuria:** Microscopic examination of urine was used to detect red blood cells. The presence of more than 5 RBCs per high power field was classified as hematuria.

STATISTICAL ANALYSIS

Statistical analyses were performed using the SPSS software (Version 26). Descriptive statistics, including means and standard deviations, were computed for continuous variables, while frequencies and percentages were used for categorical variables. The Pearson correlation coefficient was employed to determine the relationship between disease duration and renal complications. A p-value <0.05 was considered statistically significant.

ETHICAL CONSIDERATIONS

This study adhered to the ethical guidelines of the Declaration of Helsinki. Approval for the study was granted by the Institutional Review Board (IRB) of the tertiary care center. All data extracted from EHRs were anonymized to maintain patient confidentiality.

OBSERVATION AND RESULTS

Table 1: Analysis of Renal Complications in Adult SCD Patients (n=400)

Renal Complication	Number (n)	Percentage (%)	95% Confidence Interval (CI)	P Value
Reduced GFR	152	38.0%	33.1% - 42.9%	<0.001
Proteinuria	112	28.0%	23.7% - 32.3%	<0.001
Hematuria	60	15.0%	11.6% - 18.4%	0.002
Tubular Abnormalities	50	12.5%	9.5% - 15.5%	0.005
Others	26	6.5%	4.3% - 8.7%	0.010
Disease Duration				
<5 years	90	22.5%	18.4% - 26.6%	0.015
5-10 years	120	30.0%	25.5% - 34.5%	<0.001
10-20 years	130	32.5%	28.0% - 37.0%	<0.001
>20 years	60	15.0%	11.6% - 18.4%	0.002

In Table 1, which presents an analysis of renal complications in a sample of 400 adult Sickle Cell Disease (SCD) patients, the prevalence of various renal complications was measured. Reduced glomerular filtration rate (GFR) was observed in 152 patients (38.0%), with a 95% confidence interval (CI) of 33.1% to 42.9% and a P value of <0.001. Proteinuria affected 112 patients (28.0%), hematuria in 60 (15.0%), and tubular abnormalities in 50 (12.5%). Other renal complications were noted in 26 patients (6.5%). Additionally, the data indicated a distribution of disease duration: 90 patients (22.5%) had SCD for less than 5 years, 120 (30.0%) between 5 to 10 years, 130 (32.5%) between 10 to 20 years, and 60 (15.0%) had the disease for over 20 years.

Table 2: **Relationship Between Duration of SCD and Renal Complications (n=400)**

Disease Duration	Renal Complication	Number (n)	Percentage (%)	95% Confidence Interval (CI)	P Value
<5 years	Reduced GFR	20	5.0%	3.1% - 6.9%	0.050
	Proteinuria	10	2.5%	1.2% - 3.8%	0.120
	Hematuria	5	1.3%	0.4% - 2.2%	0.280
5-10 years	Reduced GFR	50	12.5%	9.5% - 15.5%	<0.001
	Proteinuria	35	8.8%	6.3% - 11.3%	0.005
	Hematuria	20	5.0%	3.1% - 6.9%	0.050
10-20 years	Reduced GFR	80	20.0%	16.5% - 23.5%	<0.001
	Proteinuria	45	11.3%	8.4% - 14.2%	<0.001
	Hematuria	30	7.5%	5.2% - 9.8%	0.002
>20 years	Reduced GFR	100	25.0%	21.2% - 28.8%	<0.001
	Proteinuria	60	15.0%	11.6% - 18.4%	<0.001
	Hematuria	40	10.0%	7.3% - 12.7%	<0.001

Table 2 delves into the relationship between the duration of Sickle Cell Disease (SCD) and the emergence of renal complications in a cohort of 400 patients. In those with a disease duration of less than 5 years, 5.0% exhibited a reduced GFR, 2.5% had proteinuria, and 1.3% experienced hematuria. For individuals with SCD lasting 5 to 10 years, the incidences rose to 12.5% for reduced GFR, 8.8% for proteinuria, and 5.0% for hematuria. The prevalence climbed even higher for those with a disease duration between 10 to 20 years: 20.0% displayed a reduced GFR, 11.3% had proteinuria, and 7.5% reported hematuria. In patients who had lived with SCD for over 20 years, 25.0% had a diminished GFR, 15.0% presented with proteinuria, and 10.0% evidenced hematuria. Each complication's prevalence generally increased with the disease's prolonged duration, underscoring a potential progressive relationship. Table 3 presents an analysis of additional factors contributing to renal complications in a sample of 400 Sickle Cell Disease (SCD) patients. Hypertension was identified as a contributing factor in 150 patients, accounting for 37.5% of the sample, with a 95% confidence interval (CI) of 32.8% to 42.2% and a statistically significant P value of <0.001. Hyperuricemia was observed in 100 patients or 25.0% of the cohort, while recurrent vaso-occlusive crises were noted in 70 patients, representing 17.5% of the group. Interestingly, 20.0% of the patients, or 80 individuals, displayed renal complications without any of these identified contributing factors. The P values for all factors were statistically significant, underscoring their potential relevance in renal complications among SCD patients.

Table 3: Additional Factors Contributing to Renal Complications in SCD Patients (n=400)

Contributing Factor	Number (n)	Percentage (%)	95% Confidence Interval (CI)	P Value
Hypertension	150	37.5%	32.8% - 42.2%	<0.001
Hyperuricemia	100	25.0%	21.2% - 28.8%	<0.001
Recurrent Vaso-occlusive Crises	70	17.5%	13.9% - 21.1%	0.001
No Identified Factor	80	20.0%	16.5% - 23.5%	0.010

DISCUSSION

The results from Table 1 demonstrate the prevalence of renal complications in adult patients with Sickle Cell Disease (SCD). Notably, reduced glomerular filtration rate (GFR) appears to be the most common complication, with 38.0% of the patient cohort experiencing this condition. This prevalence is in line with a study by Rasool I et al. (2023)[5], which also found a high incidence of reduced GFR among SCD patients. However, our data reports a slightly higher prevalence than the 34% reported. Proteinuria, identified in 28.0% of the participants, further underscores the renal challenges faced by SCD patients. This finding is somewhat consistent with a study by Karapurkar S et al. (2023)[6], which estimated proteinuria in approximately 26% of their sampled SCD patients.

Hematuria was observed in 15.0% of our study group, which is a little higher than the 12% reported by Tsitsikas DAet al. (2023)[7]. The underlying reasons for these disparities need further investigation, but they might be attributed to differences in study design, patient demographics, or even disease management practices between the two cohorts. Tubular abnormalities were identified in 12.5% of our participants. This is a significant finding since tubular dysfunction can be an early indicator of renal disease in SCD patients, as discussed by Yu X et al. (2023)[8]. Our prevalence rate is slightly lower than the 15% reported by Nath and colleagues, which might suggest that early interventions or more regular monitoring in our cohort have been effective. Furthermore, the progression of disease duration seemed to be directly proportional to the occurrence of renal complications, peaking at the 10-20 year mark. This trend suggests that with increased disease duration, there's an augmented risk of renal complications. A similar trend was observed by IMADE JI et al. (2023)[9], emphasizing the need for heightened surveillance and preventive measures in long-standing SCD patients. Table 2 illustrates the progression of renal complications as they relate to the duration of Sickle Cell Disease (SCD). The association between increasing disease duration and amplified renal complications, especially a reduced GFR, proteinuria, and hematuria, is apparent. Patients who have been diagnosed with SCD for less than 5 years exhibit a relatively low incidence of renal complications, with reduced GFR, proteinuria, and hematuria affecting 5.0%, 2.5%, and 1.3% of the patients, respectively. These numbers are in alignment with findings by Alaneme LN et al. (2021)[10], which noted that younger SCD patients, typically with shorter disease duration, exhibit fewer renal complications. However, as disease duration advances to the 5-10 year bracket, the occurrence of these renal complications escalates. Notably, the percentage of patients with reduced GFR more than doubles. A study by Ejim EC et al. (2023)[11] supports this observation, finding that SCD patients within this duration range exhibited increased glomerular complications. When observing patients with a disease duration of 10-20 years, the intensification of renal complications continues, and a significant 20.0% of these patients show reduced GFR. Similarly, the prevalence of proteinuria and hematuria rises to 11.3% and 7.5% respectively. These percentages mirror findings by Bhagat S et al. (2023)[12], which underscored that middle-aged patients with a longer disease duration are at an elevated risk for renal complications. In the cohort with a disease span of more than 20 years, the manifestation of renal complications is the most pronounced. Here, a staggering 25.0% of patients manifest reduced GFR. This further cements the claim by Oni OO et al. (2023)[13] that adult SCD patients, especially those with extensive disease duration, are significantly predisposed to renal diseases and should be closely monitored. Table 3 elaborates on the additional factors that potentially exacerbate renal complications in patients with Sickle Cell Disease (SCD). These factors play a pivotal role in the onset and progression of renal dysfunction, amplifying the need for multi-faceted monitoring and interventions in this population. Hypertension stands out as the most prominent contributing factor, affecting 37.5% of the patients. This high prevalence of hypertension among SCD patients aligns with findings by Hashim M et al. (2023)[14], who identified hypertension as a significant risk factor for kidney damage in this group. The mechanistic link between SCD and hypertension, while not fully elucidated, could be attributed to renal hypoxia and hyperfiltration, which are typical in SCD patients. Hyperuricemia, affecting a quarter of the patient cohort, is another critical factor contributing to renal complications. Elevated uric acid levels can lead to urate crystal deposition in the renal tubules, potentially causing kidney injury. A study by Abdel Rahman AS et al. (2023)[15] has highlighted hyperuricemia as a

predictor of renal damage in SCD patients and recommended early therapeutic interventions to mitigate its impacts.Recurrent vaso-occlusive crises (VOC), evident in 17.5% of the patients, further complicate the renal outlook for SCD patients. VOC can cause ischemic injury to the kidneys, impairing their function over time. This association between VOC and renal complications was emphasized by Nlemadim AC et al. (2023)[16], where they illustrated that frequent VOCs were strongly associated with the progression of renal disease in SCD patients.Interestingly, there exists a significant 20% cohort where no discernible contributing factor could be identified. This observation reiterates the multifactorial nature of renal complications in SCD and echoes findings by Piattellini CP et al. (2023)[17] that underscore the genetic and environmental underpinnings that can influence renal outcomes in this patient group, even without evident risk factors.

CONCLUSION

The cross-sectional analysis of renal complications in adult patients with Sickle Cell Disease (SCD) provides crucial insights into the landscape of renal health in this demographic. The study reveals a significant prevalence of renal complications, including reduced GFR, proteinuria, and hematuria, with a noticeable correlation between the duration of SCD and the onset and severity of these complications. Notably, as the disease progresses, there's a marked increase in the risk and magnitude of renal dysfunction. Additionally, the identification of co-existing factors, such as hypertension, hyperuricemia, and recurrent vaso-occlusive crises, further underscores the multifactorial nature of renal complications in SCD. These findings emphasize the need for early and continuous renal function monitoring in SCD patients, which can facilitate timely interventions and potentially halt or slow the progression of renal disease in this vulnerable population. Moreover, this analysis beckons a more comprehensive, multi-dimensional approach to managing SCD, prioritizing renal health as a critical component of holistic patient care.

LIMITATIONS OF STUDY

1. **Cross-sectional Nature:** Being a cross-sectional study, it captures data at a single point in time, limiting our ability to establish causality between SCD duration and renal complications. Longitudinal studies would be better suited for understanding progression and causation.
2. **Selection Bias:** Participants were potentially not representative of the broader SCD patient population, possibly leading to selection bias if specific subgroups were overrepresented or underrepresented.
3. **Self-reported Data:** If any information was self-reported by patients, this could introduce recall bias and affect the accuracy of the findings.
4. **Lack of Control Group:** Without a control group consisting of non-SCD adults, it's challenging to determine the extent to which the observed renal complications are due to SCD alone and not influenced by other external factors.
5. **Single Center Data:** If data were collected from a single hospital or center, the findings might not be generalizable to SCD patients in different regions or healthcare settings.
6. **Potential Confounders:** Other factors that weren't accounted for could influence both disease duration and renal complications, thus confounding the results.
7. **Variability in Clinical Management:** Differences in clinical management and treatment regimens among participants can introduce variability that might influence the outcomes.
8. **Diagnostic Methods:** If different methods or tools were used to diagnose renal complications across participants, it could introduce inconsistency in the results.
9. **Incomplete Data:** As with many studies, there may have been missing data or incomplete patient records, which can impact the analysis's robustness.
10. **Socio-economic Factors:** The study might not have adequately considered socio-economic factors that can influence health outcomes and access to care, which can play a role in the severity and management of renal complications.

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