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Hematological Impact of Hydroxyurea Therapy in Sickle Cell Disease: A Cross-Sectional Comparative Study from a Tertiary Care Center in Chhattisgarh, India.

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Abstract

Background: Sickle cell disease (SCD) is a common hemoglobinopathy in several regions of India, including Chhattisgarh. Hydroxyurea (HU) is the primary disease-modifying therapy for SCD and is known to reduce vaso-occlusive crises and improve hematological parameters. However, comparative real-world data from resource-limited Indian settings remain limited. ***Objectives:*** To compare hematological parameters between sickle cell disease patients receiving hydroxyurea therapy and those not receiving hydroxyurea. ***Materials and Methods:*** An observational cross-sectional study was conducted among patients with confirmed sickle cell disease attending a tertiary care center in Surguja, Chhattisgarh. Patients were divided into two groups based on hydroxyurea use. Complete blood count (CBC) parameters, including hemoglobin, red cell indices, total leukocyte count, and platelet indices, were analyzed and compared using appropriate statistical methods. Cases in which hydroxyurea therapy was discontinued due to adverse events were also recorded. ***Results:*** Patients receiving hydroxyurea showed significantly higher hemoglobin levels, increased mean corpuscular volume (MCV), and higher platelet counts compared to patients not receiving therapy. These findings indicate improved erythropoiesis and reduced marrow hyperactivity associated with hydroxyurea treatment. Hydroxyurea was generally associated with favorable hematological changes in SCD patients. ***Conclusion:*** Hydroxyurea therapy is associated with improved hematological profiles in sickle cell disease patients, including better anemia control, macrocytosis, and significantly higher platelet counts. These findings support the continued use of hydroxyurea as an effective disease-modifying therapy for SCD in resource-limited settings.

Keywords: Sickle cell disease, Hydroxyurea, Complete blood count, Hematological profile, Macrocytosis.

METHODOLOGY

This was an observational cross-sectional hospital-based comparative study conducted amongst the patients visiting RSDKS Government Medical College Ambikapur during the 2023-2024. Patients attending the outpatient or inpatient services during the study period were included. Patients confirmed of SCD by electrophoresis or HPLC were included. Patients younger than 15years, with blood transfusion within previous 3 months or non-consenting to the study were excluded.

Data was collected using hospital records and semi-structured preforma through interviews. Data was recorded in MS Excel and analysed using the same with various statistical tests.

RESULTS

A total of 164 patients with sickle cell disease were included in the study, of whom 108 (65.9%) were receiving hydroxyurea (HU) and 56 (34.1%) were not on HU therapy. The overall mean age of participants was 23.9 ± 6.8 years, and 40.9% were female.

Patients receiving HU were significantly older compared to non-HU users (27.28 ± 8.78 vs 21.44 ± 4.69 years, $p < 0.001$). Mean body weight was also slightly higher in the HU group (47.66 ± 8.38 kg vs 45.23 ± 5.12 kg, $p = 0.037$). However, there was no significant difference in gender distribution between the two groups ($p = 0.46$).

Hydroxyurea therapy was associated with significantly improved hematological parameters. Mean hemoglobin levels were significantly higher in HU users compared to non-users (8.98 ± 1.66 vs 8.08 ± 1.11 g/dL, $p < 0.001$).

Macrocytosis, a known pharmacological effect of HU, was evident, with significantly higher mean MCV values among HU users (86.34 ± 14.58 vs 77.49 ± 9.05 fL, p <0.001).

Platelet counts were also significantly higher in the HU group (206,954 ± 100,643 vs 169,795 ± 91,075, p = 0.037). No statistically significant differences were observed in total leukocyte count, RDW, or MCHC between the two groups.

Among HU recipients, 23.1% experienced at least one adverse event. The most common adverse events were hematological toxicities, particularly thrombocytopenia (7.4%) and leukopenia (6.5%). Other reported adverse effects included isolated cases of abortion. Severe toxicity requiring treatment discontinuation was uncommon.

Table 1. Baseline Patient Characteristics

Variable	Total (N = 164)
Age (years), mean ± SD	23.9 ± 6.8
Female, n (%)	67 (40.9%)
Weight (kg), mean ± SD	46.4 ± 6.7
Hydroxyurea users, n (%)	108 (65.9%)
Non-Hydroxyurea users, n (%)	56 (34.1%)

Table 1. Baseline characteristics of study participants.
This table summarizes the demographic and clinical characteristics of all patients included in the study. Continuous variables are presented as mean ± standard deviation, and categorical variables are expressed as frequencies and percentages.

Table 2. Baseline Characteristics: Hydroxyurea vs Non- Hydroxyurea

Variable	HU users	Non-HU	Test	p value
Age (years)	27.28 ± 8.78	21.44 ± 4.69	t-test	<0.001
Female (%)	42.6%	38.4%	Chi-square	0.46
Weight (kg)	47.66 ± 8.38	45.23 ± 5.12	t-test	0.037

Table 2. Comparison of baseline characteristics between hydroxyurea users and non-users.

Table 3. CBC Comparison Hydroxyurea vs Non- Hydroxyurea

Parameter	HU users	Non-HU	Test	p value
Hemoglobin	8.98 ± 1.66	8.08 ± 1.11	t-test	<0.001
TLC	7091 ± 2887	6372 ± 2904	t-test	0.19
Platelets	206,954 ± 100,643	169,795 ± 91,075	t-test	0.037
RDW	17.78 ± 5.96	18.41 ± 6.48	t-test	0.60
MCV	86.34 ± 14.58	77.49 ± 9.05	t-test	<0.001
MCHC	29.48 ± 2.89	30.64 ± 5.54	t-test	0.22

Table 3. Comparison of hematological parameters between hydroxyurea users and non-users.

Table 4. Adverse Events Among HU Users

Adverse Event	n	%
Any adverse event	25	20.4%
Leukopenia	7	6.5%
Thrombocytopenia	8	7.4%
Abortion	1	0.9%
Other minor events	6	5.6%

Table 4. Adverse events were recorded based on clinical assessment and laboratory findings during routine follow-up. Frequencies and percentages are reported. Leukopenia: TLC < 4,000/mm³, Thrombocytopenia: Platelet count < 100,000/mm³

DISCUSSION

Hydroxyurea (HU) remains the most widely used disease-modifying therapy for sickle cell disease (SCD), with established benefits on clinical outcomes such as vaso-occlusive crises and transfusion requirement. However, real-world data on its

hematological impact, particularly from resource-limited settings, remain important to reinforce confidence in its routine use. In this cross-sectional observational study, patients receiving hydroxyurea demonstrated significantly higher hemoglobin levels and mean corpuscular volume (MCV) compared to patients not receiving hydroxyurea, without evidence of clinically significant cytopenias.

The most consistent and clinically meaningful finding in the present study was the higher hemoglobin concentration among patients receiving hydroxyurea. This observation is concordant with the known mechanisms of action of hydroxyurea, which include induction of fetal hemoglobin (HbF), reduction in hemolysis and decreased erythrocyte adhesion to vascular endothelium. Several landmark studies have demonstrated similar hematological benefits. The Multicenter Study of Hydroxyurea in Sickle Cell Anemia (MSH) reported a significant rise in hemoglobin levels among adult patients receiving hydroxyurea, accompanied by reductions in painful crises and acute chest syndrome episodes [1]. Subsequent long-term follow-up studies such as Steinberg MH et al. confirmed the durability of this hematological response [2]. Indian studies have also reported comparable findings. Jain et al., in a prospective study from central India, observed a significant increase in hemoglobin levels following hydroxyurea therapy in patients with SCD, alongside reductions in transfusion requirements [3]. Similarly, Patel et al. reported improved hemoglobin and hematocrit values among hydroxyurea-treated patients in western India, reinforcing the consistency of this effect across diverse genetic and environmental backgrounds [4]. The present study adds to this literature by demonstrating that these benefits are evident even in a cross-sectional, real-world clinical setting.

Macrocytosis is a well-recognized pharmacodynamic effect of hydroxyurea and is frequently used in clinical practice as a surrogate marker of drug exposure and adherence. The significant elevation of MCV in the hydroxyurea group therefore serves as an internal validity marker, confirming effective drug action. Similar increases in MCV have been consistently reported in both pediatric and adult cohorts [1,5]. Ware et al. demonstrated that MCV elevation precedes clinical benefit and correlates with HbF induction, highlighting its utility as a monitoring parameter [6]. The robust MCV difference observed in this study supports the biological plausibility of the hematological improvements seen. Importantly, hydroxyurea use in the present cohort was not associated with clinically significant leukopenia or thrombocytopenia. Total leukocyte counts did not differ significantly between groups, and platelet counts were modestly higher in the hydroxyurea group. These findings are reassuring and consistent with previous studies demonstrating that myelosuppression with hydroxyurea is dose-dependent, reversible, and uncommon when therapy is appropriately monitored [7]. Indian observational studies have similarly reported a low incidence of severe cytopenias, even with long-term use [3,8]. In resource-limited settings, concerns regarding hematological toxicity often limit hydroxyurea uptake; the present findings help address such apprehensions by reinforcing its safety profile in routine clinical practice.

Several limitations merit consideration. The cross-sectional design precludes causal inference, and confounding by indication cannot be excluded, as patients with more severe disease may be preferentially prescribed hydroxyurea. Additionally, baseline hematological parameters prior to initiation of therapy were not available for all patients, limiting within-patient comparisons. Despite these limitations, the clear biological consistency of the findings, supported by effect size analysis and alignment with existing literature, strengthens the validity of the conclusions. In conclusion, this cross-sectional observational study demonstrates that hydroxyurea use in patients with sickle cell disease is associated with moderate improvements in hemoglobin levels and a pronounced increase in mean corpuscular volume, without evidence of clinically significant cytopenias. These findings reinforce the hematological efficacy and safety of hydroxyurea in routine clinical practice and support its wider adoption in resource-constrained settings.

CONCLUSION

This study re-establishes the effectiveness of Hydroxyurea in Sickle cell disease. It is still the gold standard in care and management of sickle cell disease. Despite few cases of reported cytopenias, it is reversible and no cases were recorded where it could not be re initiated. Thus, require caution and monitoring but is indispensable in current scenario.

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