Original Article

Correlation between Mean Corpuscular Hemoglobin, Mean Corpuscular Hemoglobin Concentration, and Fetal Hemoglobin Levels in Sickle Cell Anemia Patients of Saurashtra Region in Gujarat

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Abstract

Introduction: Sickle cell anemia (SCA) is a genetic disorder characterized by abnormal hemoglobin S production. Fetal hemoglobin (HbF) levels and complete blood count (CBC) parameters are crucial in evaluating SCA. This study investigates the correlations between mean corpuscular hemoglobin (MCH), MCH concentration (MCHC), and HbF levels in SCA patients. **Materials and Methods:** A retrospective, observational study was conducted using data from 68 SCA patients. The study included patients with HbSS genotype, aged over 1 year, who had complete CBC and high-performance liquid chromatography data available between January 1, 2023, and January 1, 2024. Patients with incomplete data, pregnancy, recent blood transfusions, and concurrent conditions affecting blood parameters were excluded. Pearson's correlation analysis was performed to assess relationships between HbF, MCH, and MCHC. **Results:** The analysis revealed significant correlations among the studied parameters. A positive correlation was observed between HbF and MCH ($r = 0.243$, $P = 0.046$). A stronger positive correlation was found between HbF and MCHC ($r = 0.328$, $P = 0.006$). The strongest correlation was observed between MCH and MCHC ($r = 0.571$, $P < 0.001$). **Conclusion:** The study demonstrates significant positive correlations between HbF levels and both MCH and MCHC in SCA patients. These findings suggest that elevated HbF levels may influence red blood cell indices, potentially reflecting compensatory mechanisms in SCA. The relationships observed could have implications for understanding disease severity variability and treatment responses in SCA patients.

Keywords: Complete blood count, fetal hemoglobin, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, sickle cell anemia

Introduction

Sickle cell anemia (SCA) is a genetic disorder characterized by the production of abnormal hemoglobin S, leading to red blood cell (RBC) deformity and various clinical complications.[1] Among the various hematological parameters, fetal hemoglobin (HbF) has garnered increasing attention due to its potential role in modulating the severity of SCA.[2] Concurrently, the complete blood count (CBC) remains a cornerstone in the initial evaluation and monitoring of SCA, providing crucial information about the quantity and quality of blood cells.[3]

Recent advances in hematology have highlighted the complex interplay between different blood parameters in SCA and their potential implications for patient outcomes. The relationship between HbF levels and standard CBC parameters, such as mean corpuscular hemoglobin (MCH) and MCH Concentration (MCHC), has emerged as an area of particular interest.[4] Understanding these correlations could provide

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valuable insights into the underlying pathophysiology of SCA and potentially offer new avenues for prognostic evaluation and therapeutic interventions.

In SCA, elevated HbF levels have been linked to milder clinical phenotypes and improved outcomes in some patients.[5] Various studies have been done in various regions and documented in regions such as Nigeria[6] and Uganda,[7] but there is a scarcity of study in India.

This study aims to elucidate the correlations between MCH, MCHC, and HbF levels in a cohort of patients with SCA. By examining these relationships, we seek to:
1. Establish the nature and strength of correlations between HbF levels and MCH/MCHC in SCA patients
2. Investigate how these correlations may vary across different patient subgroups
3. Explore the potential of using these correlations as predictive tools for patient prognosis in SCA
4. Assess the implications of these findings for tailoring treatment strategies in SCA.

Understanding these correlations could significantly enhance our ability to interpret CBC results in the context of HbF levels for SCA patients, potentially leading to more accurate prognostic assessments. Moreover, insights gained from this study may inform the development of novel treatment approaches that leverage the protective effects of HbF or target the mechanisms underlying its regulation in SCA.[8]

Materials and Methods

Study design

A retrospective observational study was conducted to investigate the correlations between MCH, MCHC, and HbF levels in SCA patients. The research utilized existing patient data from medical records, covering from January 1, 2023, to January 1, 2024. The study protocol adhered to all relevant ethical guidelines and privacy regulations and the ethical approval number: (199/05/2022).

Study setting

The study was conducted at a tertiary care center, Shri M P Shah Medical College and GG Hospital, in the Saurashtra Region of Gujarat. This center serves as a major referral hospital for SCA patients in the region. The study population consisted of patients diagnosed with SCA (HbSS genotype).

Sample size

As the retrospective nature of the study, universal sampling was employed. All participants who met the inclusion criteria were included in the study because the retrospective nature sample size was not calculated. The study included a total of 68 patients who met all inclusion criteria. These patients were selected through a comprehensive medical records screening process. Detailed data were collected for each participant, including demographic information, clinical data, and laboratory parameters. The laboratory data specifically focused on CBC parameters, with particular attention to MCH and MCHC, along with HbF levels. This sample size provided sufficient data points to conduct meaningful statistical analyses and draw reliable conclusions about the relationships between the studied parameters. Figure 1 illustrates the participant's recruitment process.

Study period

The study included medical records from January 23, 2023, to January 22, 2024, covering 1 year.

Study population

Patients with >1 year of age presenting with SCA.

Inclusion criteria

- Patients diagnosed with SCA (HbSS genotype)
- Age range: >1-year-old (This cut of age group was orbitally selected by authors by reviewing the last year's record of the institute as there are very few cases reported before 1 year)
- Complete CBC data and high-performance liquid chromatography (HPLC) data are available
- Data collected between January 1, 2023, and January 1, 2024.

Exclusion criteria

- Patients with incomplete CBC or HPLC data
- Pregnant women
- Patients who had received blood transfusions within 3 months before the CBC and HbF measurements[9]
- Patients with concurrent conditions that could significantly affect blood parameters.

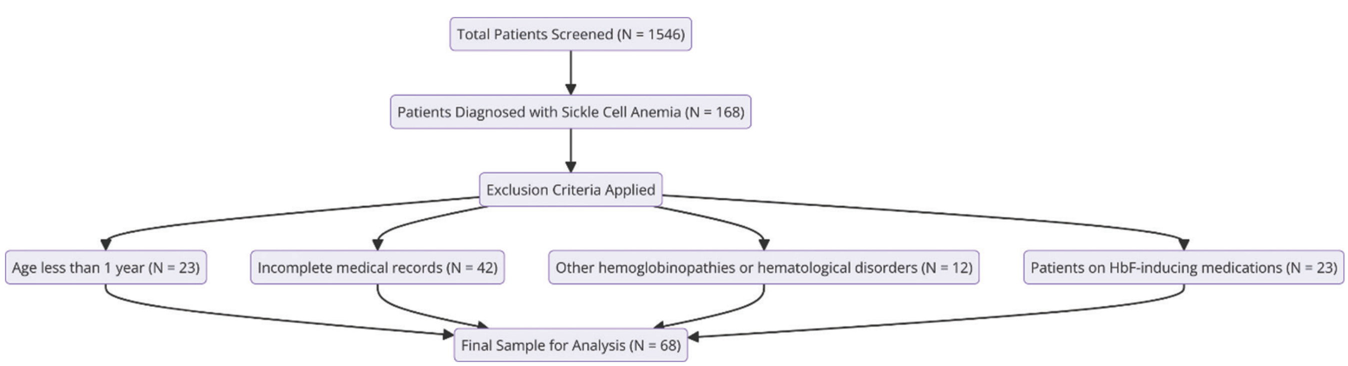

Figure 1: Participant requirement

Data collection

Source of data

Data were extracted from electronic medical records and paper-based patient files maintained at the Shri M P Shah Medical College, GG Hospital. A standardized data extraction form was developed and initially pilot-tested on 10 records to ensure reliability. Two trained research assistants independently extracted data from the medical records, with a third researcher cross-verifying 20% of the extracted data to ensure accuracy (NP) (PB). The collected data encompassed comprehensive demographic information, including age, sex, and ethnicity, along with detailed clinical data covering primary hematological diagnosis, date of diagnosis, treatment history, and comorbidities. Laboratory data included CBC parameters such as hemoglobin (Hb), hematocrit, RBC count, mean corpuscular volume, MCH, MCHC, red cell distribution width, white blood cell count and differential, and platelet count (Horiba Pentra XLR 5 Part Hematoloy Analyser). In addition, HbF (ADAMS A1c HA-8180T System) levels were recorded along with the dates of all laboratory tests. Treatment history data, including blood transfusions, pain management, and hospitalizations, were also documented. Following the manufacturer's protocol, hbF levels were determined using HPLC on an ADAMS A1c HA-8180T System analyzer.

Data analysis

All collected data were entered and analyzed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). The analysis comprised both descriptive and inferential statistical methods. Continuous variables were summarized for descriptive statistics using means, standard deviations, medians, and interquartile ranges, while categorical variables were presented as frequencies and percentages. The primary analytical approach involved calculating Pearson's correlation coefficients to assess the relationships between HbF levels and each CBC parameter. Statistical significance was set at $P < 0.05$. The strength of correlations was interpreted using a standardized scale where coefficients of 0.00–0.19 were considered "very weak," 0.20–0.39 "weak," 0.40–0.59 "moderate," 0.60–0.79 "strong," and 0.80–1.0 "very strong."[10] This comprehensive statistical approach allowed for a thorough examination of the relationships between the key variables while maintaining statistical rigor and interpretability of the results.

Results

Table 1 presents the analysis of three key hematological parameters in SCA patients, with descriptive statistics revealing distinct patterns in their distribution. The mean HbF level was found to be 15.3, with a standard deviation of 5.93, indicating considerable variation among patients. MCH values averaged 23.2 with a standard deviation of 3.24, notably lower than the typical normal range of 27–31 pg, which is consistent with expectations in SCA. MCHC measurements showed a mean of 30.6 with a standard deviation of 1.69, positioning at the lower end of the normal range (31–36 g/dL) while demonstrating less variability compared to HbF and MCH parameters.

The correlation analysis, presented in Table 2, revealed significant relationships between all three parameters. A weak but significant positive correlation was observed between HbF and MCH ($r = 0.243$, df = 66, $P = 0.046$). A stronger positive correlation emerged between HbF and MCHC ($r = 0.328$, df = 66, $P = 0.006$), suggesting that higher HbF levels are associated with increased MCHC values. The most robust relationship was identified between MCH and MCHC ($r = 0.571$, df = 66, $P < 0.001$), demonstrating a substantial positive correlation between these two variables. All correlations proved statistically significant with $P < 0.05$, indicating these relationships were unlikely to have occurred by chance.

The distribution patterns of HbF and MCHC are further illustrated through box-and-whisker plots in Figures 2 and 3, respectively. Figure 2 displays the HbF distribution, showing a median of approximately 15, with the interquartile range spanning from 11 (25^{th} percentile) to 19 (75^{th} percentile). The plot demonstrated relative symmetry, suggesting a normal distribution of HbF values, with whiskers extending from 4 to 29. Similarly, Figure 3, shows the MCHC box plot, revealing a median of about 30.5, with an interquartile range from 29.5 to 32. The MCHC distribution also appeared symmetrical, with whiskers ranging from 27 to 34, indicating a normal distribution pattern.

Table 1: Mean and standard deviations of fetal hemoglobin, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration

Parameters	Mean	SD
HbF	15.3	5.93
MCH	23.2	3.24
MCHC	30.6	1.69

HbF: Fetal haemoglobin, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, SD: Standard deviation

Table 2: Correlation matrix for fetal hemoglobin, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration

	HbF	MCH	MCHC
HbF			
Pearson's *r*	-	0.243	0.328
df	-	66	66
P	-	0.046*	0.006*
MCH			
Pearson's *r*	0.243	-	0.571
df	66	-	66
P	0.046*	-	<0.001
MCHC			
Pearson's *r*	0.328	0.571	-
df	66	66	-
P	0.006*	<0.001	-

*P<0.05 - statistically significant. HbF: Fetal haemoglobin, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration

Figure 4 presents the relationship between HbF and MCHC through a scatter plot, which displays individual patient data points and a fitted linear regression line. The plot's X-axis ranged from 0 to 30 for HbF values, while the Y-axis spanned from 27 to 34 for MCHC measurements. The upward slope of the regression line confirmed the positive correlation between these parameters, though the moderate scatter of points around the line indicated variability in the relationship. Data points showed higher concentration in the HbF range of 10–20, with fewer observations at extreme values. This visualization supported the statistical findings while providing additional insight into the distribution and relationship patterns between these crucial hematological parameters in SCA patients.

Discussion

The present study's correlation analysis between HbF, MCH, and MCHC in SCA patients reveals intriguing relationships warranting further exploration.

The correlation analysis of HbF, MCH, and MCHC in SCA patients reveals interesting relationships that warrant further discussion.

The positive correlation between HbF and MCH ($r = 0.243$, $P = 0.046$) suggests a weak but significant association in SCA patients. This is comparable to the previous study's findings ($r = 0.12$, $P = 0.243$),[6] though it is not significant. This relationship may be attributed to the fact that HbF can influence the overall hemoglobin content per cell in SCA.[11] The presence of HbF in SCA patients might contribute to slight increases in MCH values, potentially reflecting a compensatory mechanism.[12,13]

A stronger positive correlation was found between HbF and MCHC ($r = 0.328$, $P = 0.006$) in SCA patients. This is comparable to the previous study's findings ($r = -0.16$, $P = 0.104$),[6] in contrast to our study. This finding is intriguing as it implies that higher levels of HbF are associated with increased hemoglobin concentration within RBCs in SCA. This relationship could be explained by the unique properties of HbF, which has a higher oxygen affinity compared to HbS.[14] The increased oxygen affinity might lead to compensatory mechanisms that result in higher hemoglobin concentrations within the cells of SCA patients.[15-17]

The strongest correlation in the matrix was observed between MCH and MCHC ($r = 0.571$, $P < 0.001$) in SCA patients. This strong positive relationship is expected, as both parameters are measures of hemoglobin content in RBCs. The strong correlation suggests that changes in one parameter are likely to be reflected in the other, consistent with their physiological relationship, even in the context of SCA.[18]

Clinical implications

The findings of this study have several important clinical implications for the management of SCA patients. The positive correlations between HbF levels and both MCH and MCHC suggest that these parameters could serve as valuable markers in assessing disease severity and treatment response.

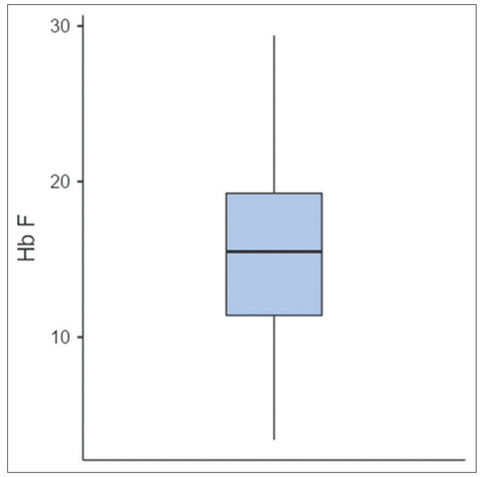

Figure 2: Box-and-whisker plot for fetal haemoglobin mean corpuscular hemoglobin concentration. HbF: Fetal haemoglobin, MCHC: Mean corpuscular hemoglobin concentration

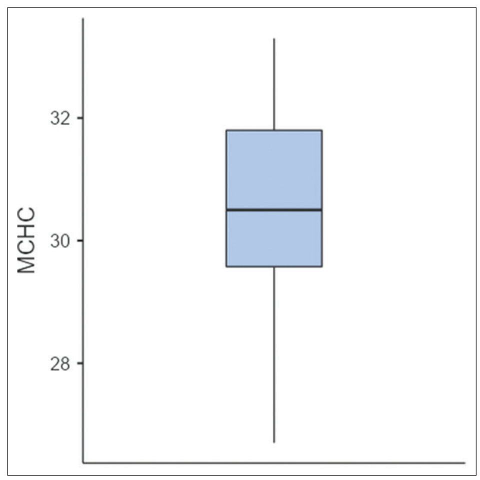

Figure 3: Box-and-whisker plot for mean corpuscular hemoglobin concentration. MCHC: Mean corpuscular hemoglobin concentration

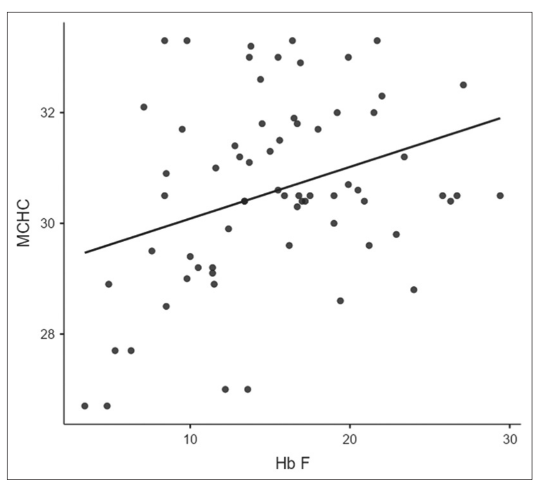

Figure 4: Scatter plot for fetal haemoglobin versus mean corpuscular hemoglobin concentration. HbF: Fetal haemoglobin, MCHC: Mean corpuscular hemoglobin concentration

The relationship between these hematological indices might help clinicians in predicting disease outcomes and tailoring treatment approaches. Particularly, patients with higher HbF levels showing correspondingly higher MCH and MCHC values might represent a subset requiring different monitoring strategies or treatment intensities. These correlations could potentially be incorporated into routine clinical assessments to provide a more comprehensive evaluation of SCA patients. The positive correlations of HbF with both MCH and MCHC suggest that elevated HbF levels might influence RBC indices in SCA. This could be particularly relevant in understanding the variability of disease severity among SCA patients.[19] These correlations might serve as additional markers for disease severity or treatment response in SCA. Patients with higher HbF levels and correspondingly higher MCH and MCHC values might experience milder disease courses, although this hypothesis requires further investigation.[20]

Recommendations

Based on our findings, we propose several key recommendations for clinical practice and research:

1. Regular monitoring: Implement systematic monitoring of HbF, MCH, and MCHC levels as part of routine care for SCA patients, with particular attention to their correlative patterns
2. Treatment strategy: Consider these correlations when making treatment decisions, especially regarding HbF-inducing therapies like hydroxyurea
3. Risk stratification: Develop and validate a risk assessment tool incorporating these parameters to better predict disease severity and guide management decisions
4. Healthcare provider education: Enhance awareness among healthcare providers about the significance of these correlations in SCA patient management
5. Future research: Conduct longitudinal studies to evaluate how these correlations change over time and their relationship with clinical outcomes.

Limitations

This study has several limitations that should be considered when interpreting the results:

1. Sample size: The relatively modest sample size of 68 patients may limit the generalizability of the findings to the broader SCA population
2. Single-center study: Data collection from a single center in the Saurashtra region may not represent the diversity of SCA patients across different geographical locations
3. Cross-sectional design: The cross-sectional nature of the study prevents the assessment of temporal relationships and causal associations between the parameters
4. Confounding factors: Despite careful exclusion criteria, some confounding factors such as environmental conditions, dietary habits, and genetic modifiers might not have been fully accounted for
5. Limited parameters: The study focused on specific hematological parameters, while other potentially important markers were not evaluated.

Conclusion

This study revealed significant positive correlations between HbF levels and both MCH and MCHC in SCA patients, with the strongest correlation between MCH and MCHC ($r = 0.571$, $P < 0.001$). These relationships suggest that elevated HbF levels may influence RBC indices, potentially reflecting compensatory mechanisms in SCA. These correlations could serve as valuable markers for disease monitoring and prognostic assessment.

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Ethical compliance

This study was conducted by the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Shri M P Shah Medical College. As this was a retrospective study using anonymized patient data, the requirement for individual patient consent was waived by the ethics committee.

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Conflicts of interest

There are no conflicts of interest.

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