SONOGRAPHIC CORRELATION BETWEEN OBJECTIVE SPLEEN PARENCHYMAL ECHOTEXTURE AND HEMATOLOGICAL PARAMETERS IN CHILDREN WITH SICKLE CELL DISEASE

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ARTICLE INFO

ORIGINAL ARTICLE

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Vol: 4 | Issue: 1
ISSN Print: 2960-2580
ISSN Online: 2960-2599

Publisher:
Medical Research and Statistical Consultancy Training Centre (SMC-PRIVATE) Limited
CONTRIBUTION
Jamma M: Main idea, data collection, write up
Mohammed D: Data collection, data analysis
Keywords: spleen; sickle cell disease; ultrasound; echotexture; pixel intensity; hematological parameters

ABSTRACT

Background: Children with sickle cell disease (SCD) are frequently evaluated for spleen involvement using laboratory markers and subjective ultrasound interpretation. Quantitative ultrasound echotexture analysis could offer an objective way to assess spleen parenchymal alterations. Although its relationship with hematological markers of spleen function is not well established. **Objective:** The study assessed the relationship between selected hematological parameters and quantitative ultrasonography spleen parenchymal echotexture in children with sickle cell disease. **Methods:** In this cross-sectional study, children with SCD underwent standardized B-mode ultrasound scan of the spleen. Quantitative echotexture measures, including mean pixel intensity (MPI), were extracted from defined regions of interest using a validated MATLAB algorithm. Hematological parameters; white blood cell (WBC) count, red blood cell (RBC) count, and platelet count were obtained on the same day. Pearson correlation coefficients were used for analysis. **Results:** Mean Pixel Intensity showed a statistically significant moderate positive correlation with WBC count ($r = 0.53$, $p = 0.002$). Correlations between MPI and RBC count ($r = 0.09$, $p = 0.58$), platelet count ($r = 0.18$, $p = 0.27$) were weak and not statistically significant. **Conclusion:** Quantitative spleen echotexture, assessed via pixel intensity analysis, is meaningfully associated with WBC count in children with SCD. Mean pixel intensity may serve as a promising non-invasive imaging biomarker, complementing hematological assessment and enhancing the objectivity of spleen ultrasound evaluation.

INTRODUCTION

Chronic hemolytic anemia and vaso-occlusive episodes that cause progressive damage to many organs are the hallmarks of sickle cell disease (SCD)[1]. One of the first and most seriously impacted organs is the spleen, which has a consistent progression of acute sequestration, infarction, fibrosis, and finally atrophy (autosplenectomy)[2]. Leukocytosis and thrombocytosis, which are markers of growing functional hyposplenism, are typical laboratory results of this clinical development that directly affects hematological homeostasis[3]. The main imaging technique for assessing splenic morphology is ultrasound[4]. Although subjective terms like “coarse” and “heterogeneous”

are frequently used to describe echotexture, they are not objective or reproducible. Thanks to recent developments, parenchymal echotexture can now be quantified using pixel-intensity analysis, yielding an objective numerical metric called Mean Pixel Intensity (MPI) that is correlated with tissue density and architectural disruption like fibrosis[5].

Hematological measures, such as high WBC and platelet counts, are recognized substitute indicators of splenic dysfunction and disease severity in sickle cell disease[6]. The link between commonly measured hematological indices of spleen function and objective spleen echotexture parameters is still poorly understood in pediatric SCD populations, despite the increasing use of quantitative ultrasound techniques. A more comprehensive understanding of the course of the disease could be obtained by establishing such a link between imaging and laboratory studies. Therefore, the purpose of this study was to assess the relationship between quantitative spleen parenchymal echotexture and some important hematological parameters (WBC, RBC, and platelet count) in children with sickle cell disease.

MATERIALS and METHODS

Study Design: Cross sectional study

Duration: The study was done in 6 months (Jan – Aug 2025)

Settings: The study was done at the secondary healthcare facility in northeastern Nigeria

Sample size: A total of 45 children were taken, assuming correlation as 40.9%, at 5% and 80% power of test. The sample size was deemed sufficient for correlation analysis. Considering feasibility, availability of eligible patients, and consistency with prior neuroimaging and clinical studies, a final sample size of 45 was considered appropriate for the present study.[7–12]

Sampling technique: Non-probability consecutive sampling

Sample selection criteria

Inclusion criteria

- Patients with a confirmed diagnosis of sickle cell disease (HbSS or HbSC genotype) in a clinically stable state
- Patients with free from infection,
- Acute chest syndrome, or
- Vaso-occlusive crisis for at least four weeks before recruitment.

Exclusion criteria

- Children with an ongoing infection or a history of splenectomy were not included.

Data collection procedure

The study was done after approval from the institutional review board (NREC/040/11/19B/2021/020), and participants/parents informed consent was acquired. A curvilinear transducer was used to conduct a systematic ultrasound examination of the spleen. To provide the best possible sound energy transfer between the individual and the probe, coupling gel was first applied to the abdomen wall in the left hypochondriac region while the subjects were in a supine position. The individual was now instructed to elevate their left side while lying in the right lateral posture. The 3.5 MHz transducer was then positioned between the eighth and ninth ribs at a right angle to the skin, and contact compound scanning was carried out parallel to the ribs from the rear to the front. To reduce lung masking, a measurement of the spleen was made during deep inhalation. On a longitudinal coronal plane, the splenic length was measured from the dome to the tip via the hilum. DICOM format was used to store a single longitudinal image that displayed the maximum splenic length. To reduce grayscale intensity variability, all images were obtained with the same machine presets. A previously validated internal algorithm created in MATLAB (MathWorks Inc.) was used to conduct quantitative echotexture analysis. MATLAB R2022a was used to construct the main algorithm. The following consecutive steps made up the workflow, which is depicted in Figure 1: A graphical user interface (GUI) was developed to enable the user to manually design a rectangular ROI within the splenic parenchyma after the DICOM image was imported using the “dicomread” function. In order to prevent the hilum, visible vessels, and acoustic shadows from ribs, the operator was directed to position the ROI in a uniform area. Every pixel value inside the specified rectangle ROI was retrieved by the algorithm. The Mean Pixel Intensity (MPI) was the main quantitative metric computed. The algorithm produced the computed MPI value and showed the original image with the ROI overlay.

Hematological Parameter Assessment

On the same day as the ultrasound examination, venous blood samples were drawn and placed in an EDTA bottle. An automated hematology analyzer was used to perform a complete blood count. For analysis, the following parameters were noted:

- WBC (white blood cell count) (x109/L)
- RBC (red blood cell count) ($x10^{12}$/L)
- The platelet count (x109/L)

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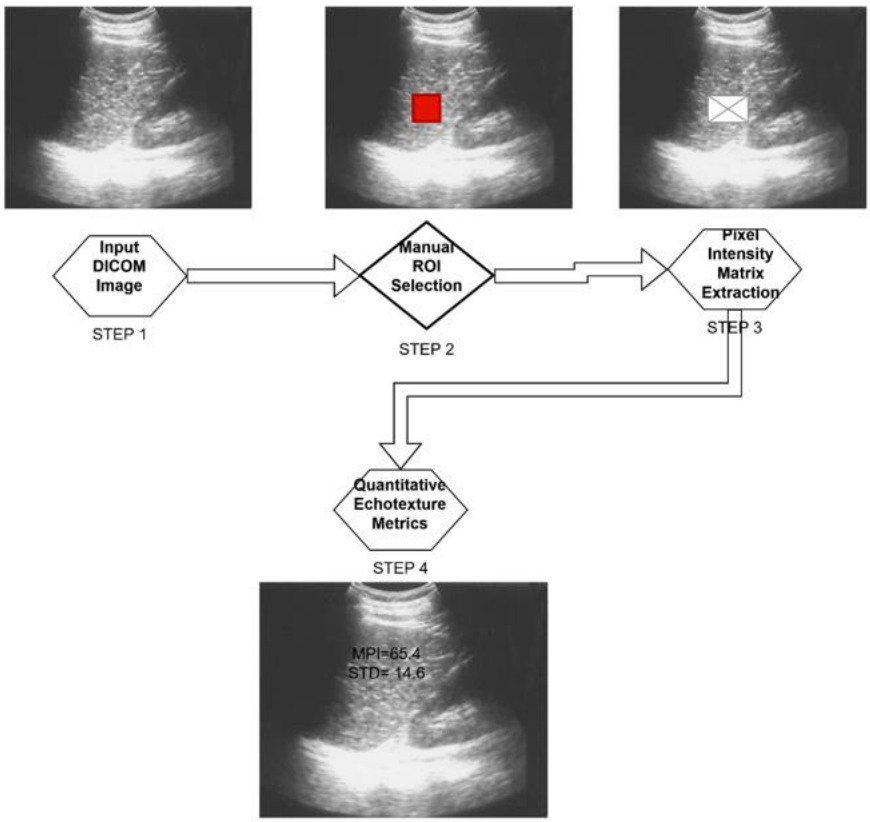

Fig. 1: Algorithm work flow

SPSS version 23.0 was used to analyze the data. For the normally distributed data, descriptive statistics were displayed as mean ± standard deviation (SD). The Shapiro-Wilk test was used to determine whether continuous variables were normal. The degree and direction of the linear relationship between MPI and each hematological parameter were evaluated using Pearson's correlation coefficient (r). To verify linearity assumptions, scatter plots were examined. Negligible (0.00–0.19), weak (0.20–0.39), moderate (0.40–0.59), strong (0.60–0.79), and very strong (0.80–1.00) were the interpretations of correlation strength. Statistical significance was defined as a p-value of less than 0.05.

RESULTS

The 45 children with SCD had an age range 1–14 years, comprises of 26 (57.8%) male and 19 (42.2%) female. The mean splenic Mean Pixel Intensity (MPI) among the study participants was 63.5 ± 14.7, ranging from 30.7 to 95.1. The mean WBC count was 14.8 ± 14.9 $\times 10^9$/L with values ranging from 7.9 to 47.7 $\times 10^9$/L. The mean RBC count was 3.9 ± 0.93 $\times 10^{12}$/L, ranging between 2.2 and 6.3 $\times 10^{12}$/L. Similarly, the mean platelet count was 218 ± 88.0 $\times 10^9$/L with a range of 66 to 474 $\times 10^9$/L. Pearson's correlation analysis demonstrated a statistically significant moderate positive

correlation between splenic Mean Pixel Intensity and WBC count (r = 0.52, p = 0.002), indicating that higher MPI values were associated with increased WBC levels. However, platelet count (r = 0.10, p = 0.49) and RBC count (r = 0.10, p = 0.52) showed no statistically significant correlation with splenic MPI.

Table 1: Descriptive Statistics of Quantitative Echotexture and Hematological Parameters in Children with SCD (n=45)

Parameter	Mean ± SD	Range
Mean Pixel Intensity (MPI)	63.5 ± 14.7	30.7 – 95.1
WBC ($\times 10^9$/L)	14.8 ± 14.9	7.9 – 47.7
RBC ($\times 10^{12}$/L)	3.9 ± 0.93	2.2 – 6.3
Platelets ($\times 10^9$/L)	218 ± 88.0	66 – 474

Table 2: Pearson's Correlation (r) Between Splenic Mean Pixel Intensity and Hematological Parameters

Hematological Parameter	Correlation Coefficient (r)	p-value	Strength of Correlation
WBC count	0.52	0.002	Moderate Positive
Platelet count	0.10	0.49	No Correlation
RBC count	0.10	0.52	No Correlation

DISCUSSION

This study examined the association between specific hematological parameters in children with sickle cell disease (SCD) and quantitative spleen parenchymal echotexture, as determined by an ultrasound algorithm based on pixel intensity. The results show that whereas correlations with red blood cell (RBC) and platelet counts were weak and not statistically significant, mean pixel intensity (MPI) exhibits a statistically significant, positive correlation with white blood cell (WBC) count. These findings demonstrate the potential utility of quantitative ultrasound echotexture as an additional imaging indicator of splenic involvement in children with sickle cell disease.

There is a physiologically and clinically plausible link between MPI and WBC count. Chronic inflammation and recurrent vaso-occlusive events cause increasing splenic parenchymal damage, fibrosis, and functional impairment in sickle cell disease (SCD)[13]. Leukocytosis frequently results from decreased sequestration and

clearance of white blood cells as splenic filtration and immunological control deteriorate [14]. Quantitative echotexture alterations may reflect underlying splenic dysfunction, which is also shown systemically by inflammatory and immunological markers, according to the positive correlation between rising MPI and WBC count. The multifactorial modulation of these parameters in SCD, on the other hand, may be reflected in the lack of substantial relationships between MPI and RBC or platelet counts. While thrombocytosis frequently only becomes noticeable in severe functional asplenia, anemia in SCD is predominantly caused by persistent hemolysis and bone marrow compensation rather than splenic function alone [15]. Leukocytosis may be a more sensitive early signal of splenic compromise than changes in RBC or platelet counts, according to the differential pattern seen in this study, supporting the usefulness of MPI as an early imaging diagnostic. The subjective interpretation of parenchymal echogenicity, which is vulnerable to inter-observer variability and has poor sensitivity for early illness, is a major component of traditional sonographic evaluation of the spleen[16]. Mean Pixel Intensity (MPI) provides a standardized method that can improve uniformity in ultrasound reporting by offering an objective numerical assessment of splenic echotexture. The use of quantitative echotexture analysis as a link between structural imaging results and systemic hematological illness symptoms is supported by the established correlation between MPI and WBC count.

Crucially, the goal of quantitative ultrasonography is to supplement laboratory research rather than to replace it. Children who are at risk of developing progressive splenic dysfunction and who might benefit from closer clinical monitoring, preventative measures, or long-term follow-up may be identified using Mean Pixel Intensity (MPI). This is especially important in environments with low resources, where ultrasonography is still the major diagnostic method and access to more sophisticated imaging modalities is limited. Prior research on splenic evaluation in sickle cell disease (SCD) has mostly concentrated on splenic size, morphology, or the existence of autosplenectomy [17–19], but parenchymal texture measurement has received less attention. Although echotexture analysis has been investigated in other organs like the liver and testis [20,21] there hasn't been much use of it in the pediatric spleen. By proving that pixel-intensity based echotexture analysis is both practical and clinically useful in pediatric SCD, the current study expands on previous research. The found moderate strength of correlation is consistent with imaging laboratory interactions, where measured parameters are influenced by a variety of biological and technical factors. This emphasizes how crucial it is to interpret MPI not as a stand-alone diagnostic parameter but rather in the context of a larger clinical and laboratory setting. This study's main advantages are the same day acquisition of ultrasound and hematological data, which reduces temporal variability, the use of a verified internal MATLAB program, and a standardized ultrasound acquisition process. By verifying linear trends and ruling out erroneous connections, scatter plot analysis adds even more evidence to the correlation finding's power.

There are a few limitations to be aware of; Causal inference is limited by the cross-sectional design, which makes it unable to evaluate temporal changes in hematological parameters and echotexture. The sample size may have less power to identify weaker relationships, especially for platelet and RBC counts, even though it is sufficient for exploratory correlation analysis. Furthermore, the peculiarities of the ultrasound system can affect pixel-intensity readings, highlighting the necessity of cross-platform validation prior to broad clinical implementation. Even though it may be repeated, manually placing the region of interest is still rather subjective and could be automated in the future.

CONCLUSION

In children with sickle cell disease, quantitative evaluation of splenic parenchymal echotexture utilizing pixel-intensity based ultrasound analysis shows a significant correlation with white blood cell count. A novel non-invasive imaging biomarker that enhances the objectivity of splenic ultrasound assessment and supplements hematological examination is mean pixel intensity. This strategy may enhance the early identification and tracking of splenic dysfunction in children with sickle cell disease. To determine whether changes in MPI precede or coincide with changes in hematological markers and clinical outcomes, future research should use longitudinal approaches. Diagnostic accuracy may be further improved by combining quantitative echotexture analysis with Doppler indices, splenic stiffness measurements, and automated segmentation methods. To test the generalizability of these findings and create generally applicable thresholds, larger, multi-center investigations spanning several ultrasound systems are also required.

ACKNOWLEDGMENTS

The authors acknowledged all the pediatric staff for their hard work and support toward the process of data collection. However, we also thank the patient's guardian for the support, cooperation during ultrasound procedures.

FUNDING:

The research work was funded by Tertiary Education Trust Fund (TETFund) Nigeria, under the Institutional Based Research (IBR) grantsmanship, through the Federal University of Health Sciences (FUHSA), Azare, with grant number: TETF/DR&D/CE/UNI/AZARE/IBR/2024

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