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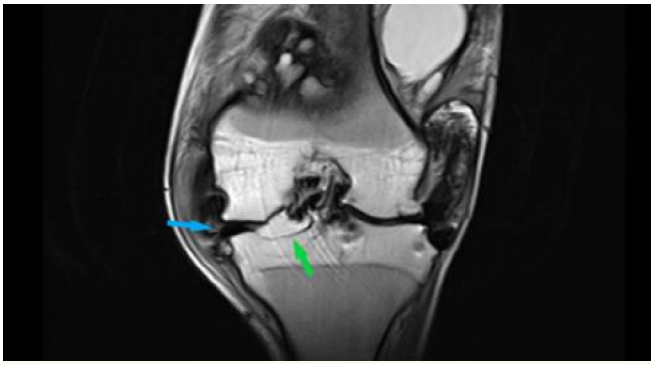
CLINICAL RESEARCH

Diagnostic performance of point-of-care ultrasonography (POC-US) in haemophilia joint health: a comparative study with MRI

Yash Duseja, Arnav Kashyap, Anupam Dutta, Dhrubajyoti Borpatragohain, Bhabani Dhal, Luish Borboruah

Introduction: Haemophilia presents challenges in joint pathology assessment, prompting exploration of point-of-care ultrasonography (POC-US) as a diagnostic tool. Aims: The study aimed to assess the diagnostic performance of point-of-care ultrasonography (POC-US) compared to magnetic resonance imaging (MRI) in detecting synovial hypertrophy, cartilage abnormality, and bony abnormality among people with haemophilia (PWH) treated at Assam Medical College Hospital. **Methods:** Forty-two PWH underwent POC-US and MRI for joint assessment. The POC-US and MRI imaging interpretation involved calculating diagnostic accuracy parameters for POC-US and MRI scores. This included sensitivity, specificity, positive predictive value, and negative predictive value. **Results:** POC-US demonstrated a sensitivity of around 97% and specificity of 92% for detecting synovial hypertrophy, while showing a sensitivity of 85% and specificity of 100% for bony abnormality. Cartilage abnormality assessment revealed a sensitivity of 55% and specificity of 100%. Knee joint involvement was observed in all patients, with 7% also exhibiting ankle joint pathology. Disease severity distribution



Coronal T2 weighted image of knee joint showing articular cartilage destruction (blue arrow) and bony erosion (green arrow) from a study in Assam, India, investigating POC-US as a diagnostic tool for joint pathology in people with haemophilia

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showed 57% with severe hemophilia, 24% with moderate, and 19% with mild disease. **Conclusion:** Our study highlights the diagnostic potential of POC-US in haemophilia management, particularly in detecting synovial hypertrophy and bony abnormality. Challenges in assessing cartilage abnormality warrant further investigation. These findings contribute to the discourse on POC-US in haemophilia management, emphasising the need for continued research to elucidate its clinical relevance.

Keywords: *Haemophilia, Point-of-care ultrasonography, MRI, Joint pathology, Diagnostic performance*

Haemophilia is an X-linked congenital disorder caused by mutations in clotting factor genes, leading to deficiency of factor VIII (haemophilia A) or factor IX (haemophilia B) [1]. It primarily affects males and is characterised by easy bruising, spontaneous bleeding into joints and muscles, and excessive bleeding following trauma or surgery. Family history may not always be present [2]. Severe factor deficiency can result in life-threatening bleeds, including bleeding into joints and muscles, gastrointestinal bleeding and intracranial haemorrhage. Recurrent joint bleeding can lead to disabling arthropathy [3].

Magnetic resonance imaging (MRI) examination is the gold standard investigation for evaluation of haemophilic arthropathy [3]. However, in India MRI is expensive and not widely accessible to the population in comparison to point-of-care ultrasonography (POC-US). This study evaluated joint status in PWH using sensitive techniques, focusing on the effects of haemorrhages on bones and joints, comparing MRI and POC-US findings to assess the accuracy of ultrasonography (USG) as a diagnostic tool. This evaluation was conducted regardless of age and gender, with the goal of improving the management of haemophilic arthropathy among PWH in our region.

AIMS AND OBJECTIVES

The aim of this study was to compare the ultrasonographic and MRI findings in the ankle and knee joints of PWH treated at Assam Medical College Hospital (AMCH). The primary objective of the study was to assess the diagnostic accuracy of POC-US for synovial hypertrophy in PWH compared with MRI, with secondary objectives of evaluating the diagnostic accuracy of POC-US for the presence or absence of cartilage abnormalities and bone surface irregularities.

METHODS

This hospital-based observational study was conducted over a period of one year among all PWH attending the Haemophilia Outpatient Department (OPD) of AMCH. The study sample included all known and newly diagnosed registered patients attending the OPD during the study period. Patients were selected based on specific inclusion criteria, including known deficiency of factor VIII and IX, a history of at least one prior joint bleed in the knee or ankle, and consent to participate in the study. Exclusion criteria encompassed the presence of comorbidities that could confound joint findings, such as diabetes mellitus, osteoarthritis, rheumatoid arthritis and scurvy osteoporosis, and non-consent. Patients were recruited from the haemophilia clinic based on the inclusion criteria and their willingness to participate. Ankle and knee joints were scanned as these are most commonly involved joints in haemophilia.

Clinical findings were assessed and a restriction of joint movement examination was undertaken by a physiotherapist and medicine postgraduate using a goniometer; range of motion was calculated.

Imaging acquisition involved obtaining POC-US and MRI examinations with no more than 3 days between them. The POC-US method used a HEAD US protocol on a Samsung RS 80 A machine using 3-12 Hz linear probe performed by a postgraduate of the Radiology Department of Assam Medical College, with quality assurance undertaken by an Associate Professor of Radiology. Gray-scale ultrasound images were obtained in supine and prone positions using specific transducers. MRI images were acquired with a 1.5-T MRI unit. The total scanning time was approximately 40-50 minutes per joint. The protocol included sagittal, coronal, and axial 3D gradient-echo sequences (TR/ TE, 50/11; flip angle, 40°; slice thickness, 1.5 mm; matrix, 256 × 228 pixels); sagittal turbo spin-echo T2-weighted sequences (TR/TE, 4200/92; slice thickness, 3 mm; matrix, 256 × 224 pixels); sagittal proton density–weighted spin-echo sequences (TR/ TE, 3000/42; slice thickness, 3 mm; matrix, 320 × 256 pixels); and coronal spin-echo T1-weighted sequences (TR/TE, 517/12; slice thickness, 3 mm; matrix, 256 × 192 pixels). Additional sagittal and coronal 3D fast spoiled gradient-recalled echo images (radiofrequency amplitude ratios, 1:2:1; TR/ TE, 21.5/5.6; flip angle, 25°; slice thickness, 1.5 mm; matrix, 512 × 512 pixels) and sagittal spin-echo T1-weighted (TR/TE, 439/12; slice thickness, 3 mm; matrix, 256 × 184 pixels) images were obtained. The MRI images were interpreted by an Associate Professor of Radiology.

Table 1. Participant demographics (N=42)

AGE GROUP (YEARS)	NUMBER (N (%))
10–19	18 (42.8%)
20–29	18 (42.8%)
30–39	4 (9.5%)
40–49	2 (4.7%)
Mean ± S.D	21.2 ±7.6
HAEMOPHILIA TYPE	
Haemophilia A	35 (83.3%)
Haemophilia B	7 (16.6%)
HAEMOPHILIA SEVERITY	
Severe	24 (57.1%)
Moderate	10 (23.8%)
Mild	8 (19%)
FAMILY HISTORY	
Positive	24 (57.1%)
Negative	18 (42.8%)

Imaging interpretation involved calculating diagnostic accuracy parameters for POC-US and MRI scores, including sensitivity, specificity, positive predictive value, and negative predictive value. Statistical analysis was performed using MEDCALC STATISTICAL SOFTWARE, with data tabulated in Microsoft Excel and presented as proportions, percentages, and mean ± standard deviation for categorical and continuous variables, respectively.

Ethical clearance was obtained from the Institutional Ethics Committee (H) of Assam Medical College. Written informed consent was obtained from each participant.

RESULTS AND OBSERVATIONS

The study comprised 42 patients with an age range of 10 to 49 years (mean age 21.2 ± 7.6 years).The majority of patients (85.7%) were in the age groups 10-19 and 20-29 years. Haemophilia A was predominant (83.3%); 16.6% of participants had haemophilia B. Disease severity assessment showed 57.1% with severe haemophilia, 23.8% with moderate haemophilia, and 19.0% with mild haemophilia. Additionally, 57.1% of participants had a positive family history. Participant demographics are shown in Table 1.

Clinical findings revealed joint swelling (78.5%), tenderness (52.3%), and restriction of movement (50%). All 42 cases exhibited knee joint involvement, with 3 cases also involving the ankle joint. POC-US findings for knee joints included synovial hypertrophy in 30 cases, cartilage abnormality in 6 cases, and bony abnormality in 6 cases. For ankle joints, 3 cases showed synovial hypertrophy without cartilage or bony abnormality (Table 2). MRI findings for knee joints revealed synovial hypertrophy in 30 cases, cartilage abnormality in 10 cases, and bony abnormality in 6 cases. In ankle joints, 3 cases showed synovial hypertrophy, with 1 case showing cartilage and bony abnormality (Table 3). POC-US demonstrated a sensitivity of around 97% and specificity of 92% for detecting synovial hypertrophy, while showing a sensitivity of 85% and specificity of 100% for bony abnormality. Cartilage abnormality assessment revealed a sensitivity of 55% and specificity of 100%. Knee joint involvement was observed in all patients, with 7% also exhibiting ankle joint pathology.

The comparison of USG and MRI examination findings for 45 involved joints yielded the following results: for synovial hypertrophy, there were 32 true positives, 11 true negatives, 1 false positive, and 1 false negative. MRI was used as gold standard. The calculated sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were derived using appropriate statistical software. The kappa value for the correlation between point of care ultrasound and MRI for synovial hypertrophy was found to be 0.89. For cartilage abnormality, there were 6 true positives, 34 true negatives, 0 false positives, and 5 false negatives, with a resulting kappa value of 0.64. Lastly, for bony abnormality, there were 6 true positives, 38 true negatives, 0 false positives, and 1 false negative, with a calculated kappa value of 0.91.(Tables 4 and 5).

DISCUSSION

A previous study by Foppen et al. comparing POC-US and MRI demonstrated high sensitivity and specificity for synovial hypertrophy in both knee and ankle joints [4], aligning closely with the current study's findings. Specifically, they reported a sensitivity of 89% (67-99%) and a specificity of 99% (93-100%) for synovial hypertrophy, indicating the robustness of POC-US in detecting this condition. Similarly, a study by Sierra Aisa et al. evaluating the sensitivity and specificity of synovial hypertrophy reported high values, with a sensitivity of 97% (94-100%) and a specificity of 96% (82-100%) [5]. Again, these results closely mirror the current study's findings, reinforcing the reliability of POC-US in identifying synovial hypertrophy in PWH.

Findings by Foppen et al. also revealed a lower sensitivity for cartilage abnormality [4]. This perspective was also presented in a study by Doria et al., whose findings indicated a lower sensitivity of 50% (7-93%) and a specificity of 10% (95-100%) for cartilage abnormality, highlighting potential challenges in using

Table 2. Point-of-care ultrasound (POC-US) results for knee and ankle joints in the study cohort (n=42)

	SYNOVIAL HYPERTROPHY	CARTILAGE ABNORMALITY	BONY ABNORMALITY
Knee	30	6	6
Ankle	3	0	0
Total	33	6	6

Table 3. Magnetic resonance imaging (MRI) results for knee and ankle joints in the study cohort (n=42)

	SYNOVIAL HYPERTROPHY	CARTILAGE ABNORMALITY	BONY ABNORMALITY
Knee	30	10	6
Ankle	3	1	1
Total	33	11	7

Table 4. Comparision of the POC-US and MRI findings of the involved knee and ankle joints

		KNEES (N =)		ANKLES (N =)		OVERALL (N =)	
		MRI–	MRI+	MRI–	MRI+	MRI–	MRI+
Synovial hypertrophy	POC-US–	11	1	0	0	11	1
	POC-US+	1	29	0	3	1	32
Bone irregularities	POC-US–	35	1	3	0	38	1
	POC-US+	0	6	0	0	0	6
Cartilage abnormalities	POC-US–	31	5	3	0	34	5
	POC-US+	0	6	0	0	0	6

Table 5. Diagnostic performance of POC-US for evaluation

	SYNOVIAL HYPERTROPHY	CARTILAGE ABNORMALITY	BONY ABNORMALITY
True positive	32	6	6
True negative	11	34	38
False positive	1	0	0
False negative	1	5	1
Sensitivity	96.9	54.5	85.7
Specificity	91.6	100.0	100.0
PPV	96.9	100.0	100.0
NPV	91.6	87.1	97.4
Diagnostic accuracy	95.5	88.8	97.7
Kappa value	0.89	0.64	0.91

POC-US for this aspect of joint evaluation [6]. These comparative studies underscore the variability in POC-US performance across different aspects of joint pathology. While POC-US demonstrates consistent strength in detecting synovial hypertrophy, the assessment of cartilage abnormality appears to present more variability, as evidenced by the differing sensitivity and specificity values reported [7].

Overall, current literature and comparative studies emphasisie the strength of POC-US in detecting synovial hypertrophy while also highlighting the need for further research to enhance its capabilities in assessing cartilage abnormality [8]. These insights contribute to the ongoing dialogue surrounding the optimal use of POC-US in the comprehensive evaluation of joint health in PWH.

Our study builds upon the existing literature by focusing on a specific patient population with a history of joint bleeds or acute joint episodes, providing a targeted investigation into the diagnostic performance of POC-US in this context [9]. The inclusion of patients with a documented history of joint bleeds adds a unique dimension to our study, offering insights into the utility of POC-US in a population with a higher likelihood of joint pathology. Furthermore, its emphasis on both knee and ankle joints aligns with the common sites of haemophilic joint involvement, allowing for a comprehensive evaluation of POC-

US performance in areas most frequently affected in PWH. By contextualizing our findings within the broader landscape of existing research, we contribute evidence to the ongoing discourse on the role of POC-US in haemophilia management, particularly in the assessment of synovial hypertrophy and cartilage abnormality [10].

While our study provides valuable insights into the diagnostic performance of POC-US in haemophilia management, several limitations warrant consideration. Firstly, the relatively small sample size of 42 patients may limit the generalisability of our findings to broader populations of PWH. A larger, more diverse cohort would enhance the robustness and applicability of our results. Additionally, the exclusion of patients with comorbidities that could confound joint findings, while necessary for methodological rigor, may have limited the representation of real-world clinical scenarios. MRI is used as a comparison tool as it is considered as gold standard in joint screening.

Furthermore, the focus on knee and ankle joints, while aligned with the common sites of haemophilic joint involvement, may not fully capture the spectrum of joint pathology observed in haemophilia. Future studies could benefit from a more comprehensive assessment encompassing a wider range of joint locations, e.g. the elbow, to provide a more holistic understanding of POC-US performance in PWH.

Another critical consideration is the potential for inter-operator variability in POC-US interpretation. Addressing this limitation through rigorous training and inter-rater reliability assessments would strengthen the validity of our findings [11].

Lastly, the absence of long-term follow-up data in our study limits our ability to assess the prognostic implications of POC-US findings on disease progression and joint outcomes. Longitudinal studies tracking the evolution of joint pathology over time would provide valuable insights into the clinical relevance of POC-US findings in hemophilia management.

In light of these limitations, a critical appraisal of our study underscores the need for future research endeavors to address these constraints and further elucidate the role of POC-US in haemophilia management. Despite these limitations, our study contributes valuable insights to the existing body of literature and sets the stage for continued exploration of POC-US as a diagnostic tool in haemophilic joint assessment. POC-US can be used in developing countries as a diagnostic tool in hemophilic where MRI is not accessible and affordable.

CONCLUSION

Our study provides valuable insights into the diagnostic performance of POC-US in haemophilia management, particularly in the assessment of synovial hypertrophy and bony abnormality. While our findings underscore the reliability of POC-US in detecting synovial hypertrophy, the challenges associated with assessing cartilage abnormality highlight the need for further research to enhance the capabilities of this modality. The inclusion of patients with a history of joint bleeds adds a unique dimension to our study, offering insights into the utility of POC-US in a population with a higher likelihood of joint pathology. Despite limitations such as sample size and the potential for inter-operator variability, our study contributes valuable evidence to the ongoing discourse on the role of POC-US in haemophilia management. Moving forward, addressing these limitations and conducting longitudinal studies will further elucidate the clinical relevance of POC-US findings in haemophilia management.

ACKNOWLEDGEMENTS

The authors have advised no interests that might be perceived as posing a conflict or bias.

Informed consent has been obtained from the participants in the study reported in this paper.

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HOW TO CITE THIS ARTICLE:
Duseja Y, Kashyap A, Dutta A, Borpatraohain D, Dhal B, Borboruah L. Diagnostic performance of point-of-care ultrasonography in haemophilia joint health: a comparative study with MRI. *J Haem Pract* 2024; 11(1): 123-128. *https://doi.org/10.2478/jhp-2024-0018*