FREQUENCY AND RISK FACTORS FOR HEMATOMA FORMATION FOLLOWING BONE MARROW BIOPSY IN PATIENTS WITH SEVERE AND VERY SEVERE THROMBOCYTOPENIA

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ABSTRACT

OBJECTIVES

To determine the frequency and risk factors of hematoma formation after bone marrow biopsy in patients with severe and very severe thrombocytopenia.

METHODOLOGY

This cross-sectional study was conducted at Hayatabad Medical Complex, Peshawar, from 1st April 2024 to 31st January 2025. Patients over the age of 18 years with severe and very severe thrombocytopenia who underwent bone marrow biopsy were included. Age, gender, clinical bleeding at presentation, history of bone marrow biopsy at the same site, body mass index, and platelet count at the time of biopsy were documented. Participants were screened for hematoma twenty-four hours after the procedure. Data analysis was carried out in SPSS.

RESULTS

Most patients had severe thrombocytopenia (60.3%, n = 132), while the remaining patients had very severe thrombocytopenia (39.7%, n = 87). Only eight patients (3.7%) developed a hematoma. Patients who had clinical bleeding (95% CI: 1.93 – 168.45; p = 0.011) and who had repeat biopsy from a site of previous biopsy (AOR: 18.03; 95% CI: 1.93 – 168.45; p = 0.011) were significantly more likely to develop hematoma. The development of hematoma was not influenced by age, gender, body mass index, or the severity of thrombocytopenia.

CONCLUSION

Hematoma formation after bone marrow biopsy is uncommon. Patients with clinical bleeding and previous biopsy at the same site have a higher risk. Factors like age, gender, body mass index, and severity of thrombocytopenia did not significantly impact hematoma formation. Prophylactic platelet transfusion before bone marrow biopsy may largely be unnecessary and can be avoided.

KEYWORDS: *Bone Marrow, Biopsy, Thrombocytopenia, Hematoma, Bleeding, Risk Factors, Pakistan*

INTRODUCTION

Bone marrow biopsy is a commonly performed procedure. It is invasive but indicated for unexplained pancytopenia, anemia, leucopenia, thrombocytopenia, and to evaluate cases of fever of undetermined origin, lymphoma and leukemia.[1] It is almost always performed percutaneously. There are many sites for percutaneous bone marrow biopsy, like sternum, posterior iliac crest, anterior iliac crest, tibia, femur, vertebral bodies and ribs. The preferred site is the posterior iliac crest as it is accessible and less traumatic.[2,3] Bleeding at the biopsy site is an expected complication of bone marrow biopsy. The frequency of biopsy site bleeding ranges from 0.03% to 0.2%.[4,6] It is mostly encountered in patients with thrombocytopenia, platelet function disorders, and coagulation disorders.[7] There is disagreement on the minimum platelet count at which bone marrow biopsy can be performed safely without bleeding at the biopsy site.[8] Some authorities do not consider thrombocytopenia, regardless of its severity, as a contraindication to bone marrow biopsy.[9,10] However, others recommend a platelet count of at least 20,000/mcL for safely performing a bone marrow biopsy.[11,12] A survey of 104 hematologists revealed that before bone marrow biopsy, 48% do not transfuse platelets, 49% selectively transfuse platelets, and 3% routinely transfuse platelets to increase the platelet count to 20,000/mcL.[12] A retrospective study comparing patients with platelet counts of less than 20,000/mcL with those with platelet counts between 20,000 to 50,000/mcL demonstrated no difference in post-procedure biopsy site hematoma frequency.[13] Given the infrequent occurrence of hematoma formation following bone marrow biopsy in thrombocytopenic patients, existing data on this subject

are limited, and expert opinions vary. The inconsistencies in recommendations contribute to prolonged hospital stays and delays in diagnosing patients who undergo transfusions to achieve a safer platelet count before biopsy. Additionally, these patients are exposed to the risks associated with transfusions. This study aims to establish the frequency of hematoma formation after bone marrow biopsy in patients with severe (20,000 - 50,000/mcL) and very severe thrombocytopenia (< 20,000/mcL), and to identify risk factors associated with hematoma formation. The findings of this study will assist in generating evidence-based guidelines for institutions or local practices, thereby helping physicians avoid unnecessary platelet transfusions before performing bone marrow biopsies. Consequently, this would facilitate earlier diagnosis of bone marrow disorders and result in shorter hospital stays.

METHODOLOGY

This cross-sectional study was approved by the Institutional Review and Ethical Board (IREB) of Hayatabad Medical Complex, Peshawar. It was conducted from 1st April 2024 to 31st January 2025. Patients, 18 years and older, with severe thrombocytopenia (platelet count between 20 × 10^9 per mm^3 and 50 × 10^9 per mm^3) and very severe thrombocytopenia (platelet count below 20 × 10^9 per mm^3) who underwent bone marrow biopsy at Hayatabad Medical Complex, Peshawar, were included in the study after informed consent. Those having coagulopathy (defined as International Normalized Ratio > 1.5), renal failure (defined as serum creatinine > 1.5 mg/dl), a history of platelet function disorders, or those who have had antiplatelet and/or anticoagulant medications within the last 7 days were excluded from the study. A total of 219 patients met the inclusion and exclusion criteria and were enrolled in the study. All bone marrow biopsies were performed by the same operator under the supervision of a clinical hematologist. All patients received standard care guided by their clinical condition before and after the bone marrow biopsy. None of the patients were transfused with platelets before or after the biopsy. Participants were screened for hematoma at the biopsy site via ultrasound by the same radiologist twenty-four hours after the procedure. Age, gender, history of bleeding at presentation, history of bone marrow biopsy at the same site, body mass index, platelet count at the time of biopsy, and the presence or absence of hematoma were documented on a structured proforma. Data was analyzed through the Statistical Package for Social Sciences, version 21. Descriptive statistics were performed for all the variables and presented as mean ± standard deviation, and frequency/percentages. The presence of post-biopsy hematoma was stratified by mean age, mean BMI, and mean platelet count; the statistical significance of between-group differences was estimated using the Mann-Whitney Test. Similarly, the significance of the association between hematoma formation and risk factor categories like gender, degree of thrombocytopenia, BMI category, bleeding at admission, and previous biopsy from the same site was determined by Fisher's Exact test. Multivariate logistic regression analysis was used to identify independent predictors of hematoma formation by controlling for confounders. A p-value of less the 0.05 was considered significant for all analyses.

RESULTS

Most of the study participants (55.3%, n = 121) were males. The mean age was 41.1 ± 19.1 years, and the mean platelet count was 28.9 ± 16.7 × 10^9 per mm^3. Most patients had severe thrombocytopenia (60.3%, n = 132), while the remaining patients had very severe thrombocytopenia (39.7%, n = 87). All biopsies were performed from the posterior superior iliac spine. Out of 219 patients, only eight (3.7%) developed a hematoma after undergoing a bone marrow biopsy. The characteristics of the study participants are summarized in Table 1.

Table 1: Comparison of Electric Pulp Testing (EPT) Readings between Maxillary and Mandibular Teeth

Variables	Mean ± SD / No. (%)
Age, (Years)	41.1 ± 19.1
Body mass index, (kg/m^2)	26.1 ± 4.0
Platelet count, (× 10^9 per mm^3)	28.9 ± 16.7
Gender	
Male	121 (55.3%)
Female	98 (44.7%)
BMI category, (g/dl)	
Normal	99 (45.2%)
Overweight & obese	120 (54.8%)
Bleeding at admission, No. (%)	
Yes	58 (26.5%)
No	161 (73.5%)
Previous bone marrow biopsy, No. (%)	
Yes	08 (3.7%)
No	211 (96.3%)
Degree of thrombocytopenia, No. (%)	
Severe thrombocytopenia	132 (60.3%)
Very severe thrombocytopenia	87 (39.7%)
Post-biopsy hematoma, No. (%)	
Yes	08 (3.7%)
No	211 (97.3%)

There was no significant difference in the mean age (36.6 ± 8.0 versus 41.3 ± 19.4 years, p = 0.737) and the mean body mass index (25.2 ± 4.4 versus 28.1 ± 4.0 Kg/m^2, p = 0.591) between those with and without hematoma. Those with hematoma had a lower platelet

count at the time of biopsy (19.1 ± 17.5 × 10^9 per mm^3) than those without hematoma (29.3 ± 16.6 × 10^9 per mm^3), but the difference was not significant (p = 0.057). Univariate analysis showed that a significantly higher proportion (10.3%) of patients who presented with bleeding at the time of admission developed hematoma than those without bleeding (1.2%) (p = 0.005). Patients with severe thrombocytopenia and very severe thrombocytopenia experienced similar rates of hematoma formation after biopsy (3.0% vs 4.6%, respectively, p = 0.716). Likewise, factors like gender, body mass index, and prior bone marrow biopsy at the same site did not significantly impact the frequency of hematoma formation. (Table 2)

Table 2: Univariate Analysis Comparing Risk Factors for Post Biopsy Hematoma Formation

Variables	Post-biopsy hematoma		P-value
	Yes (n = 08)	No (n = 211)	
Age, (Years)	36.6 ± 8.0	41.3 ± 19.4	0.737*
Body mass index, (kg/m^2)	25.2 ± 4.4	28.1 ± 4.0	0.591*
Platelet count, (× 10^9 per mm^3)	19.1 ± 17.5	29.3 ± 16.6	0.057*
Degree of thrombocytopenia, No. (%)			
Severe thrombocytopenia	04(3.0%)	128(97%)	0.716#
Very severe thrombocytopenia	04(4.6%)	83(95.4%)	
Gender			
Male	02(1.7%)	119(98.3%)	0.144#
Female	06(6.1%)	92(93.9%)	
BMI category, (g/dl)			
Normal	03(3.0%)	96(97%)	0.732#
Overweight & obese	05(4.2%)	115(95.8%)	
Bleeding at admission, No. (%)			
Yes	06(10.3%)	52(89.7%)	0.005#
No	02(1.2%)	159(98.8%)	
Previous bone marrow biopsy, No. (%)			
Yes	01(12.5%)	07(87.5%)	0.261#
No	07(3.3%)	204(96.7%)	

*Mann-Whitney U test
#Fisher's Exact test

On multivariate logistic regression analysis, patients who presented with bleeding had an 18 times higher likelihood (95% CI: 1.93 – 168.45; p = 0.011) of developing post-biopsy hematoma compared to those who did not have bleeding at admission. Likewise, patients who underwent a repeat biopsy at the site of a previous biopsy were more likely to develop a hematoma than those without a history of biopsy at the same site (AOR: 18.03; 95% CI: 1.93 – 168.45; p = 0.011). The gender, platelet category, and BMI category remained insignificant. (Table 3)

Table 3: Multivariate Logistic Regression Analysis of the Factors Predicting Post-Biopsy Hematoma

Variables		AOR	95% CI	P-value
Gender	Female*			
	Male	0.43	0.08–2.33	0.326
Platelet category	Severe thrombocytopenia*			
	Very severe thrombocytopenia	0.67	0.15–3.11	0.610
BMI category	Normal*			
	Overweight & Obese	1.68	0.34–8.27	0.523
Bleeding at present ation	No*			
	Yes	18.03	1.93 – 168.45	0.011
History of biopsy	No*			
	Yes	26.41	1.28 - 546.51	0.034

*Reference category

DISCUSSION

Bone marrow biopsy is a routine medical procedure. Although it is invasive, it is frequently necessary. One common reason for the procedure is unexplained thrombocytopenia, either alone or alongside bicytopenia or pancytopenia. Bleeding after a bone marrow biopsy is a concern for both patients and clinicians. The optimal platelet count threshold for a safe bone marrow biopsy is not well established. The lack of clear guidelines often leads to unnecessary platelet transfusions before a bone marrow biopsy, which can result in adverse effects, increased costs, and longer hospital stays. This study aimed to identify the frequency and risk factors for biopsy site bleeding in patients with severe and very severe thrombocytopenia. Hematoma after bone marrow biopsy was observed in eight patients, accounting for 3.7% of cases. A low rate of bleeding complications following the procedure has been consistently reported. Bain et al., in a review of 19,259 bone marrow biopsy procedures performed in 2003, found that only 11 cases (0.06%) developed local hematoma.[4] Likewise, in a similar review of bone marrow biopsies performed between 1995 and 2001, hematoma was reported in 14 out of 54,890 biopsies.[5] Similarly, Salem et al. stated that biopsy site hematoma rarely complicates bone marrow biopsy, occurring in one out of 500 cases.[6] The frequency of hematoma in this study is notably higher than that reported previously. Multiple factors might have contributed to this. These include patient-related factors: a higher proportion of our patients may have had platelet dysfunction; procedure-related factors: variation in bone marrow biopsy technique and post-procedure compression time, in addition to the operator's

experience; and differences in the study protocol: discrepancies in the operational definitions used to diagnose hematoma and the inherently higher likelihood of reporting a hematoma when patients are monitored systematically for complications compared to a retrospective review of records. Age, gender, and body mass index were not significantly associated with the risk of hematoma formation. There is limited literature assessing the association of age and gender with hematoma formation. A case report highlights age as a risk factor, but none of the comparative studies or reviews have mentioned age or gender as risk factors for hematoma formation.[14] In contrast, obesity has been identified as a risk factor for bleeding complications by some researchers, owing to technical difficulties posed by the weight of the patient.[5,15,16] Computed tomography-guided biopsy has been proposed as a safer alternative to manual biopsy in obese patients.[15,17] Although lower in patients who developed hematoma, the mean platelet count was not significantly different between those with and without hematoma. Likewise, patients with severe thrombocytopenia and very severe thrombocytopenia had comparable rates of hematoma formation in univariate and multivariate analysis. Opinions are divided on the risk of post-biopsy hematoma posed by low platelet count. A case report by Salem et al. and reviews by Bain et al. have reported thrombocytopenia as a risk factor.[4,6] In contrast, Story et al. did not identify thrombocytopenia as a risk factor for hematoma.[18] Imaging-guided biopsy has been determined safe in patients with platelet count as low as 20×10^9 per mm^3 without the need for pre-procedural platelet transfusions. Clinical bleeding at the time of presentation increased the risk of post-biopsy bleeding. It was an independent predictor of hematoma formation, as this association remained significant after adjustment for the degree of thrombocytopenia and other confounders in multivariate analysis. There is a paucity of literature comparing patients with and without bleeding at presentation for post-bone marrow biopsy hematoma. Myeloproliferative disorders and functional abnormalities of platelets have been reported as predictors of post-biopsy bleeding.[4,5] It is possible that the subset of patients who presented with clinical bleeding might have had an underlying diagnosis of myeloproliferative disorder, leading to an acquired von Willebrand syndrome or had impaired platelet function secondary to the primary disease, which resulted in both clinical as well as post-biopsy bleeding despite reasonable platelet counts. Comparing patients stratified by platelet function for post-biopsy bleeding can be an area for further research. Patients who had a repeat biopsy at the site of a previous biopsy were more likely to develop a hematoma at the biopsy site. Reviews of bone marrow biopsies carried out between 1995 and 2001, and in 2003 in the United Kingdom, have not described previous bone marrow biopsy among the risk factors for post-biopsy bleeding.[4,5] Risk of post-biopsy bleeding at the site of a previous biopsy is a relevant concern, especially in patients undergoing repeated biopsies for hematological monitoring. Scarring and fibrosis following a previous biopsy and the subsequent reduced vascularity may theoretically reduce the risk of bleeding. On the other hand, it may make the procedure technically more difficult, potentially increasing the chances of trauma to the nearby vessels, leading to hematoma formation. This needs further evaluation in large-scale comparative studies.

LIMITATIONS

Most literature on the topic is limited to case reports or retrospective reviews. It is one of the few studies, and the first in Pakistan, to assess risk factors of biopsy site hematoma formation in thrombocytopenic patients undergoing bone marrow biopsy in a cross-sectional design. We consider this the primary strength of this study. It has identified some risk factors and given future research directions for novel risk factors. Moreover, advanced analysis, like multivariate logistic regression analysis, was used to mitigate the effects of confounders. We consider the single-center nature, relatively small sample, exclusion of certain patient groups, and the lack of a longer follow-up as limitations of the study, which might limit the generalizability of the study‘s findings.

CONCLUSIONS

Hematoma formation after bone marrow biopsy in patients with severe and very severe thrombocytopenia is relatively rare, occurring in only 3.7% of cases. Clinical bleeding at the time of presentation and a history of previous biopsy at the same site were significant risk factors for post-biopsy hematoma formation. However, factors like age, gender, body mass index, and the degree of thrombocytopenia did not significantly impact the frequency of hematoma formation. The findings suggest that unnecessary platelet transfusions before bone marrow biopsy can be avoided, potentially leading to early diagnosis of bone marrow disorders and shorter hospital stays. Large-scale, multi-center studies are recommended to validate the findings of this study to help shape guidelines for optimal peri-procedure care of patients undergoing bone marrow biopsy.

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AUTHORS CONTRIBUTION

Ayesha Bangash - *Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Critical Revision; Final Approval*
Fawad Rahim - *Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Critical Revision; Final Approval*
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The authors accept responsibility for all aspects of the work and will ensure that any concerns regarding the accuracy or integrity of any part are properly investigated and resolved.