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Research Article

Bone marrow biopsy as a new practice in a tertiary hospital center in Tirana Correlation with the literature and future perspective

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Abstract

Background: This study employed a retrospective, descriptive design. All variables were entered into a database using Microsoft Excel and subsequently analyzed using statistical methods to calculate frequencies and levels of statistical significance (*p*-values).
Objectives: The study aimed to examine the distribution of diagnostic categories across different years, develop an epidemiological database based on age, gender, and time periods, and evaluate diagnostic challenges by identifying the factors influencing them.
Materials and Methods: A total of 372 bone marrow biopsies collected over a three-year period (January 2019 to December 2021) were included in the study. Data obtained from biopsy reports were analyzed and compared in relation to clinical diagnosis, patient age, gender, and temporal distribution. Histopathological parameters assessed included cellularity, clonal maturation, fibrosis, and the application of immunohistochemical panels.
Results: The most frequent diagnosis was myeloproliferative disorders, accounting for 193 cases (52%, $p < .01$), followed by lymphoproliferative disorders with 78 cases (21%), of which non-Hodgkin lymphoma represented 69.2%. The annual distribution of myeloproliferative disorders demonstrated statistically significant differences for polycythemia vera ($p < .01$) and essential thrombocythemia ($p < .01$). The mean age of patients with hematologic disorders was 58.9 years, with the highest proportion of cases occurring in the sixth decade of life (33.2%). A slight male predominance was observed (male-to-female ratio 1.2:1), with a statistically significant variation in this ratio ($p < .01$), reaching 1.8:1 in 2021. Additionally, in 2021, a new category of biopsy reports (1%) characterized by reactive changes was identified. According to existing literature, such histological alterations have been observed in patients with severe COVID-19 infection.

Keywords: Bone marrow, biopsy, practice, tertiary hospital center, Tirana.

1. Introduction

Bone marrow biopsy (BMB) is a valuable diagnostic procedure commonly performed for evaluation of a wide spectrum of diseases including hematologic abnormalities, nonhematologic malignancies, metabolic abnormalities, and tumor treatment response such as chemotherapy and bone marrow transplantation, hematologic tumor staging, suspected infection in patients with fever of unknown origin and when the routine examination of a blood smear has failed (Tomasian & Jennings, 2022). As we know, bone marrow trephine biopsy offers a comprehensive view of the bone marrow architecture and although conventional morphology remains the gold standard for paraffin-embedded bone marrow trephines, with the addition of immunohistochemical (IHC) staining we can have a firm diagnosis. The bone marrow is one of the most common sites involved by metastatic tumor; nonhematologic and hematologic origin. The diagnosis of metastatic involvement of the bone marrow may have a profound effect on prognosis and treatment (Yan, Lv and Xiong et al., 2020). Furthermore, manual evaluation of BMB can be challenging and time-consuming and are highly dependent on examiner skill and experience, especially in unclear cases (Font et al., 2015). Hence, the number of high-quality histological examinations is limited by the availability and experience of trained experts, whereas examiner classifications have been found to be subject to substantial inter-variability (Briggs et al., 2009). Having a good knowledge of microscopic cellular morphology and bone marrow overall architecture implies the correct diagnosis and it requires also a good specimen preparation.

Bone marrow consists of functional units, composed of many cell-types arranged in an organized framework surrounding haemopoietic stem cells (HSCs) that constitute its microenvironment or niche (Thiele, 2005). The alterations between stroma and parenchyma of the bone marrow interferes with its normal functions activating mesenchymal stem cell to produce marrow fibrosis, a condition correlated especially with myeloproliferative neoplasms, myelodysplastic syndromes and lymphomas (Ghosh, Shome, Kulkarni et al., 2023).

BMB is often taken at the pelvic bone and is a painful procedure owing to the bigger bore of the needle and the collection of the material, and its processing takes at least 48-72 hours. Thus, performing trephine biopsies on all patients may not be cost-effective in terms of clinician and laboratory personnel's time, efforts, and patient discomfort (Egesie, 2009).

This study aims to assess the distribution of different diagnostic categories acquired from screening bone marrow biopsies received at our Pathology Department at the University Hospital Center of Tirana between 2019-2021, to correlate it with the literature and to create and epidemiologic data in relation to age, gender and different time periods. Furthermore, evaluate our diagnostic difficulties by determining the factors that influence them.

2. Materials and methods

A hospital-based retrospective/descriptive study was conducted on 372 biopsies over a period of two years from 2019 to 2021 at the Department of Pathology, Mother Theresa University Hospital. The patients were admitted at the Hematology Department at the same hospital diagnosed with hematologic disorders. We analyzed the biopsies reports and compared with each other according to different diagnosis, age, sex and distribution in time. Furthermore, the histopathologic characteristics present in bone marrow biopsies such as cellularity, clonal maturation and fibrosis were compared in relation to different hematologic diseases. Most of the BM biopsies were performed on the anterior/superior (ASIS) or posterior iliac spine (PSIS). The tissue samples were fixed in 10% neutral buffered formaldehyde and were decalcified according to the ETDA method, the first two years for 24 hours and during 2021 only 4 hours (Choi, Hong & Yoon, 2015). Paraffin blocks were stained with H-E and with Silver Stain for reticular fibres and Masson's Trichrome Stain for collagen fibres, simultaneously.
Whenever necessary, IHC stains were used. IHC methodology is performed automatically with the Benchmark XT device from Ventana as well as with different IHC clone antibodies from Ventana.
The results were statistically analyzed using Excel and were statistically processed to calculate frequencies and statistical significance (P).

3. Results

3.1 Diagnosis distribution

Out of 372 biopsies were identified 193 cases (52%) with myeloproliferative disorders, 78(21%) lymphoproliferative disorders LPD, 13(3.5%) myelodysplasia MDS, 13(3.5%) hypoplasia/aplasia, 2(0.5%) metastases, 4(1.1%) infectious/metabolic diseases, 5(1.3%) reactive changes, 1(0.2%), macrophage activation syndrome and 62(16.7%) were unconclusive; Table 1. The most frequent diagnosis was the myeloproliferative disorders MPD with a significant difference in frequency from other diagnoses ($p < 0.01$), followed by lymphoproliferative disorders with 78 cases (21%).

Diagnosis	Nr. Cases	Percentage %
MPD	193	52%
LPD	78	21%
MDS	13	3.50%
Hypoplasia/Aplasia	13	3.50%
Metastasis	2	0.50%
Infectious/Metabolic D	4	1.10%
Reactive changes	6	1.60%

MAS	1	0.20%
*Unconclusive	62	16.70%
Total	372	100%

Table 1: Distribution of microscopic diagnosis
LPD, lymphoproliferative disorders; MPD, myeloproliferative disorders; MDS, myelodysplastic disorders; MAS, macrophage activation syndrome; *Unconclusive BMB: Inadequate tissue/incompatible with clinical diagnosis

The years-wise distribution of myeloproliferative disorders (MPD) diagnoses, had a significant difference from polycythemia vera (PV) ($p<0.01$) and essential thrombocythemia (ET) ($p<0.01$). In a three-year period, we observed, in relation to the other diagnoses, included in the MPD, that essential thrombocythemia (ET) predominates with 41% of cases, followed by PV with 29%, primary myelofibrosis (PMF) 24% and chronic myeloid leukemia (CML) and (MPD NOS) only 3%; Table 2. According to a large population-based study in Singapore that collected 2557 individuals from 1968 to 2017, diagnosed with MPN, identified 1031 diagnosed with chronic myeloid leukemia (CML), 424 with polycythemia vera (PV), 389 with essential thrombocythemia (ET) and 134 primary myelofibrosis (PMF) (Htun, Lian, Wong, Tan, Foo, Ong & Lim, 2022) which is compatible with the data from our study (Marchetti, Carobbio, Capitoni, & Barbui, 2018). In another study the incidences of CML, PV, and ET were relatively similar at 1.0-2.0 per 100,000 person-years, while PMF is rarer with an incidence of 0.3 per 100,000 person-years but in our study even if PMF was present in just 24% of the cases, CML was only described in 3% of our biopsies.

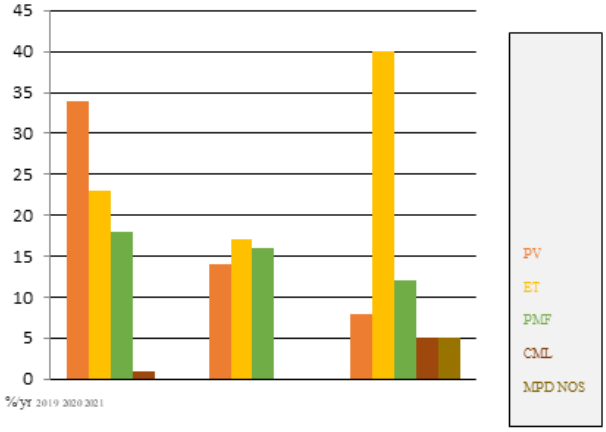
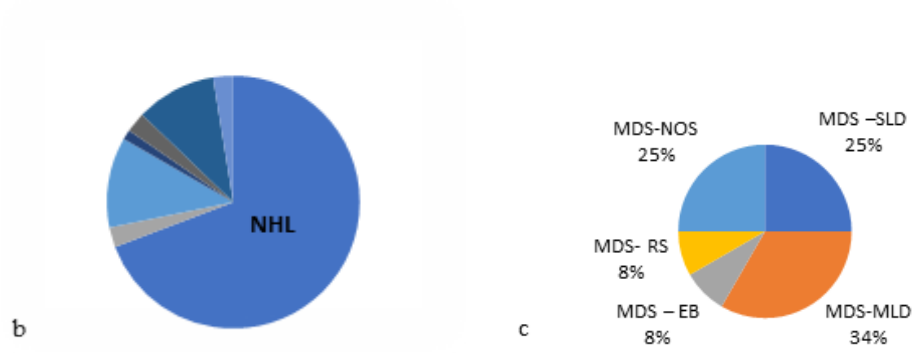


Table 2: Distribution in time of MPD, LPD and MDS 2019-2021
PV polycythemia vera; ET essential thrombocythemia; PMF primary myelofibrosis; CML chronic myeloid leukemia
NHL non-Hodgkin lymphoma; MDS myelodysplastic syndrome; MDS-RS ring

sideroblastic; MDS-EB excess blasts; MDS-SLD single lineage dysplasia; MDS-MLD multilineage dysplasia; MDS-SLD single lineage dysplasia



No significant change in years was found in the distribution of LPD category diagnoses. During the three years, NHL prevails (69.2 %) (Thandra, Barsouk, Saginala, Padala, & Rawla, 2021).

In the subcategories of myelodysplasias, we see that multilineage myelodysplasia disease MDS-MLD is the most frequent with 34% of cases, followed by single lineage myelodysplasia disease MDS-SLD and unspecified MDS with 25% each. According to literature was also found that MDS-MLD was the most frequently encountered subtype, 19/50 (38%) followed by MDS-SLD; 11/50 (22%) (Elnahass & Youssif, 2018).

3.2 Age and gender variation

Among all the patients with bone marrow biopsies analyzed,168 were men and 142 were women. A slight predominance of men is observed over women with ratio M:F 1.2:1. A significant difference in the distribution of diagnoses by gender was found only for lymphoproliferative disorders (LPD) (p=0.01), where the M:F ratio is 1.8:1 (50 males, 28 females). The average age of patients with hematological disorders was 58.9 years (interval 50yr-69yr). There is a predominance of cases in the 6-th decade of life (33.2%), followed by the 5-th decade (25.1%) and the 7-th decade (19.4%). No significant difference was found in the age distribution group between MPD and LPD (p=0.3). They both prevail in the 6th decade of life (average age 62 years). In our study MDS appeared to be present at a younger age, mean age 46.3 years, while in literature the average age of patients with MDS is 53 years. Aul et al. found a strong correlation between the proportion of elderly patients and the relative frequency of MDS diagnoses. Furthermore, Zeidan at al., an epidemiologic study, confirmed a high incidence of MDS between 60-90 years of age; Figure 1. The reasons for this age discrepancy in MDS was not investigated further.

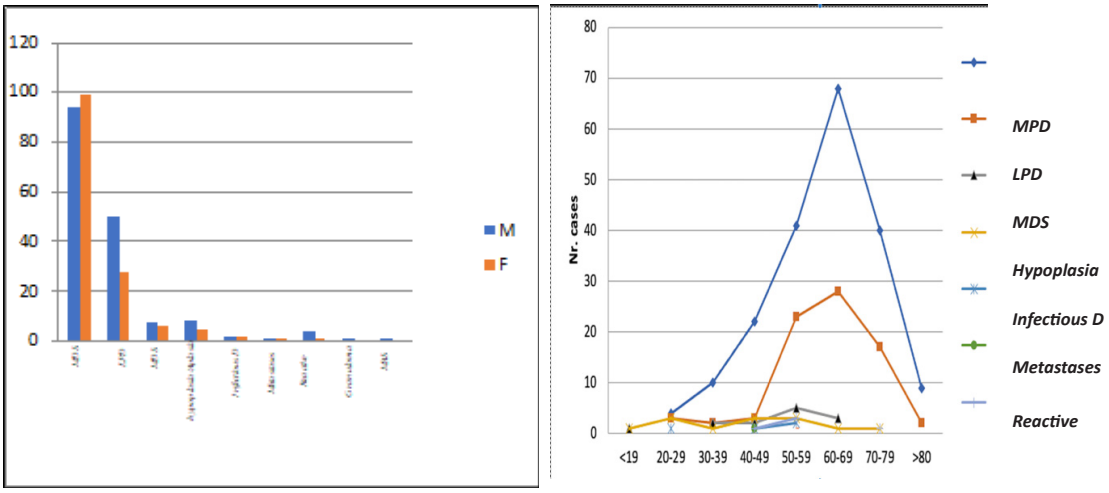


Figure 1: Gender and Age-wise distribution of final diagnosis

LPD lymphoproliferative disorders; MPD myeloproliferative disorders; MDS myelodysplastic disorders; MAS macrophage activation syndrome; Infectious D infectious disease

3.3 Cellularity, maturation and fibrosis distribution

In our study, 73% of biopsies diagnosed with myeloproliferative disorders MPD were hypercellular, 22% normocellular and only 5% hypocellular. According to literature myeloproliferative disorders are characterized by mutations in hematopoietic stem cells that results in clonal expansion in myeloid cells; polycythemia vera PV and primary myelofibrosis PMF show significant hypercellularity in contrast with essential thrombocythemia ET with mild hypercellularity. Cellular maturity was not reported.

In lymphoproliferative disorders LPD was found a significant difference in the distribution according to cellularization ($p<0.01$). The presence of hyper-cellularization prevails in 75% of cases. Hypo-cellularization was not observed in any case. Cellularization was normal in MM (66.7%). According to the literature (Park, Park, Jeong et al., 2016), LPD have more frequent hypercellular marrow, with cells that are difficult to differentiate. Immunochemistry is required[22]. Hodgkin lymphoma HL, multiple myeloma MM and hairy-cell leukemia HCL presented 100% tissue maturation; Figure 2.

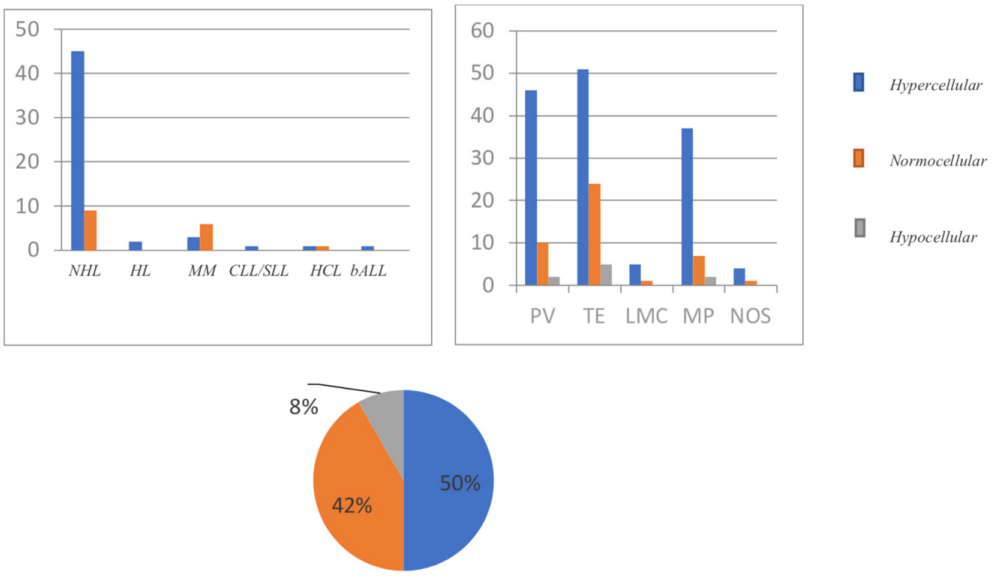
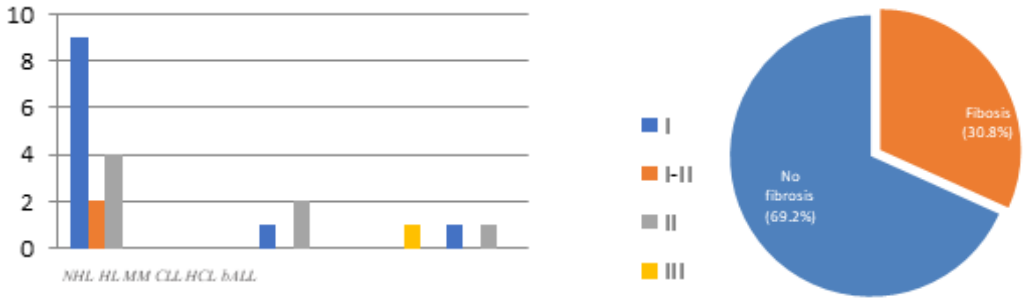


Figure 2: Distribution of cellularity in BOM 2019-2021: a. LPD; b. MPD; c. MDS

NHL non-Hodgkin lymphoma; HL Hodgkin lymphoma; MM multiple myeloma; HCL hairy cell leukemia; CLL chronic lymphocytic leukemia; bALL Acute lymphoblastic leukemia.

In myelodysplastic syndromes MDS, the majority of the BOM, 42% were hypercellular and 8% (1) hypocellular. MDS biopsies were characterized by ineffective hematopoiesis of one or more major myeloid cell lineages, with the potential to evolve into acute myeloid leukemia. In the study by Kini J et al (2001), 84% of patients had hypercellular marrow, 68% of patients had trilinear dysplasia. We identified 13 biopsies diagnosed with aplastic anemia AA, 72.7% of them presented severe low cellularity.

A significant difference was found in the distribution of fibrosis in LPD according to diagnose and the fibrosis grade ($p<0.01$). Most cases of LPD, (47) 69.2% did not present fibrosis while 30.8% of them presented fibrosis ($p<0.01$). In total, stage I fibrosis predominates with (11)17.5% of the total, followed by stage II with (7) 11.1% of the total and only (1) 1.6% stage I-II and stage III. The most frequent diagnosis of LPD associated with fibrosis was NHL (in 27.8% of cases). In two cases of hairy cell leukemia HCL only one of them had developed secondary fibrosis; Figure 3.



Secondary myelofibrosis occurred in 33.3% of chronic myeloid leukemia CML, 26.8% of PV, 11.25% of ET and zero cases of MPD-NOS. According to the literature, myeloproliferative lesions that are most often associated with secondary myelofibrosis are PV and chronic myeloid leukemia CML. ET is not usually associated with MF even if according to Tefferi et al (2021) approximately 15% of patients with ET or PV might progress into a PMF-like phenotype (post-ET/PV MF) during their clinical course. According to the literature in secondary MF the most frequent causes are metastatic tumor and malignant lymphoma. It also occurs relatively often in the course of chronic myeloproliferative disorders, such as chronic myeloid leukemia and polycythemia vera. We studied also the different grades of fibrosis in primary myelofibrosis PMF and our results are 22% stage pre-fibrotic, 15% grade I, 6% grade II and 9% grade III.

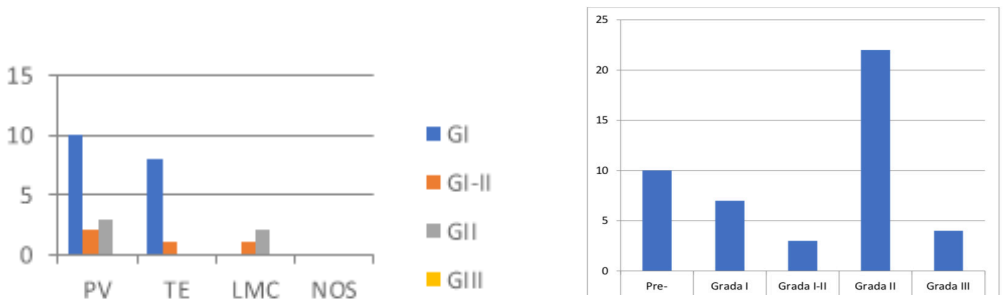


Figure 3: Distribution of bone marrow fibrosis; a/b. LPD; c. MPD; d. PMF grade fibrosis

NHL non-Hodgkin lymphoma; HL Hodgkin lymphoma; MM multiple myeloma; HCL hairy cell leukemia; CLL/SLL chronic lymphocytic leukemia; bALL Acute lymphoblastic leukemia.

4. Discussion

Evaluation of bone marrow trephine biopsy specimens is critical to the diagnosis of benign and malignant hematologic conditions. Most of hematologic patients that underwent bone marrow needle biopsy and were screened in our laboratory were diagnosed myeloproliferative neoplasms (MPNs) that are clonal diseases originating from a single hematopoietic stem cell that cause excessive production of mature blood cells. The 7 seven subcategories are: chronic myeloid leukemia, chronic neutrophilic leukemia, polycythemia vera (PV), primary myelofibrosis (PMF), essential thrombocythemia (ET), chronic eosinophilic leukemia-not otherwise specified and MPN, unclassifiable (MPN-U) according to the World Health Organization (WHO) and international consensus classification (ICC) criteria (Barbui, Thiele, Gisslinger et al. 2018. In our study, we screened 372 bone marrow biopsies, from which 52% with myeloproliferative disorders (MPD), 41% with essential thrombocythemia (ET), 29% with polycythaemia vera (PV) and 24% with primary myelofibrosis (PMF). Morphological features of bone marrow of patients with myeloproliferative neoplasms may initially be difficult for pathologists to recognize, especially in cases where the experience lacks, as in our case, as we started examining BOM in 2018 for the first time. Another problem in our facility that is confirmed in other studies, was the fact that most of the bone marrow biopsies were viewed in isolation, without clinical and laboratory information. According to the literature, the discovery of the Janus Kinase 2 mutation (JAK2V617F) has changed the diagnostic approach for myeloproliferative disorders, unfortunately in our university hospital center molecular examination are not performed. Molecular testing has become a critical diagnostic tool in the evaluation of patients with suspected PV. *JAK2*-p. V617F is present in >95% of PV patients, and also in about half of the patients with ET or PMF. Also, in MPN with nonmutated *JAK2* and *MPL*, somatic mutations in the gene for calreticulin (*CALR*) was identified according to Nangalia et al. (2013) that sequenced exomes from 151 patients with MNP and concluded that *CALR* mutations were found in 70 to 84% of samples of myeloproliferative neoplasms with nonmutated *JAK2*. Thus, when BCR-ABL1-negative myeloproliferative neoplasia is suspected, in addition to markers of hematopoietic cells of the three lineages; erythroid lineage (CD71); granulocyte lineage (myeloperoxidase) megakaryocytic lineage (CD42b) and hematopoietic stem cells (CD34), CAL2 monoclonal antibody immunostaining should be performed. The discovery of recently identified molecular features has yielded new perspectives regarding diagnostic and prognostic markers that provide novel insights for the understanding of the pathobiology of these disorders (Arber, Orazi, Hasserjian et al., 2016). Current diagnostic challenges of chronic myeloproliferative disorders (MPD) include the differentiation of essential thrombocythemia (TE) from its mimics: early polycythemia vera (PV) and/or "pre-fibrotic"/early primary myelofibrosis (pre-PMF) which was recognized as a separate entity in the 2016 revised WHO classification of myeloproliferative neoplasms. This distinction is important, because the frequency of complications such as progression to "overtly fibrotic" myelofibrosis, blast crisis and

overall prognosis are markedly different in the two conditions. The progression to the fibrotic phase is 0-1% in TE vs 10-12% in PMF, and leukemic transformation is 1-2% in TE vs 2-6% in PMF. Furthermore, about 15% of patients with ET or PV develop a PMF-like phenotype over time, referred to as post-ET or post-PV myelofibrosis and according to the same study over a total of 125 patients with secondary myelofibrosis, after a 3-year follow-up were documented 86(69%) deaths and 10(8%) leukemic transformations (Thiele, Kvasnicka, Müllauer et al., 2011). According to another study the median survival in these cases were 9.3 years (95% CI: 8-not reached-NR-). Furthermore, bone marrow screening is important for lymphoma staging. Haematological disorders are complex and require additional techniques such as hemogram, immunophenotyping and molecular examinations for the diagnostic needs and the clinical scenario. Technical preparation of BMB specimen for histologic samples is specific and important for the correct interpretation of histopathologic samples. Bone marrow trephine biopsy can appear altered and show a variety of changes that do not match the clinical diagnosis for a variety of technical problems. In our cases, a study was made on the technical problems of the period October - December 2021, were requested new slides preparations in13% of the BOM, due to problems of biopsies preparation. According to the literature, other problems related to technical issues in the interpretation of the BOM are also the fact that occasionally, in patients who undergo frequent repeat biopsies, a specimen can be obtained from a recently biopsied site. In these cases, the presence of granulation tissue in the biopsy may result in misinterpretation of the sample. Furthermore, the bone marrow biopsy taken bilaterally at the posterior iliac bone offers the advantage of doubling the sample size and allows examination of specimens from separate sites, thus increasing the number of cases diagnosed as positive for NHL by biopsy. From this data we can say that the material, despite being optimal and technically suitable, may not be representative to evaluate it as compatible with NHL infiltration. On the other hand, involvement of the bone marrow by Hodgkin's lymphoma is rare with an average incidence of 10%. However, the incidence of bone marrow involvement has been shown to be less than 1% in patients with clinical stage IA or IIA disease. Usually marrow involvement in a patient with Hodgkin's lymphoma represents stage IV disease.

We identified 62 BMB (16.7%) that were classified as inconclusive due to inappropriate material (suboptimal, hemorrhagic, subcortical, damaged material), incompatible with the clinical diagnosis and require further examinations to conclude. The most frequent reason for material inadequacy in three-year period was subcortical material (with 40%), followed by suboptimal material reason (27%). According to the literature an adequate biopsy specimen should contain at least five to six intertrabecular spaces. It should be at least 1.5 - 2cm in length after processing. Since bone marrow involvement in NHL is focal, the volume of biopsy material may account for their underdiagnosis. In the difficulties encountered in the histopathologic diagnosis was simultaneous coexistence of lymphoproliferative and myeloproliferative lesions presented clinically as a myeloproliferative lesion, in our study we identified two cases. Myeloid and lymphoid malignancies are assumed to have different pathogenetic

mechanisms. The recent observation that patients with a myeloproliferative neoplasia have an increased risk of developing lymphoproliferative malignancies has challenged this assumption. Another issue that we encountered was the evaluation of bone marrow biopsy in patients after treatment for lymphoproliferative disorders. The difficulties were due to the fact that the pathologist had to consider a vast number of heterogeneous diseases, for which different treatments may have been applied. Furthermore, different clinical issues usually need to be addressed for which the diagnostic strategies performed are also different and are usually performed in different laboratories by different investigators. To minimize difficulties, a systematic, an integrative and interdisciplinary approach is suggested, which includes prior knowledge of the primary diagnosis and previous therapy.

5. Conclusion

In conclusion in our laboratory, between 2019 to 2021 we screened in total 193 BMB, most of them were myeloproliferative disorders, the most frequent was essential thrombocythemia followed by lymphoproliferative disorders, among them non-Hodgkin lymphoma leaded. In a three-year period, we observed that, in relation to the other diagnoses, included in the MPD, essential thrombocythemia (ET) predominates with 41% of cases, followed by PV with 29%, primary myelofibrosis (PMF) 24% and chronic myeloid leukemia (CML) and (NOS) only 3%. In 2021, a new category of biopsy reports (small category 1%) is observed with data consisting of reactive changes with trilinear hyperplasia, predominance of histiocytes and plasma cells. Based on literature data, these alterations could be found in patients after a severe infection of COVID 2019, and we could say that this new category is probably a consequence of the COVID 19 pandemic[39]. The average age of patients with bone marrow biopsies was 58.9 years old. There is a predominance of cases in the sixth decade of life (33.2% of cases), followed by the fifth decade (25.1%) and the seventh decade with 19.4%. In our study MDS appeared to be present at a younger age, mean age 46.3 years, while in literature the average age of patients with MDS is 53 years. A slight predominance of men is observed over women in the ratio M:F 1.2:1. Significant change in the ratio M:F ($p<0.01$) in the ratio 1.8:1.

The technical challenges and diagnostic complexity of bone marrow biopsy specimens usually arise as a result of scarce information accompanying the specimen, poor specimen quality, inadequate sections and stains, lack of experience in the histological interpretation of BMB, furthermore, from being in the first steps of bone marrow histopathologic interpretation that we started only in 2018, as well as the lack of access to more advanced studies such as genetic and molecular biology examinations. Overcoming these challenges requires a high degree of collaboration between histopathologists, hematologists, samplers, laboratory technicians and other scientific personnel. Relying on more advanced techniques such as those of genetics and molecular biology are a hope for easing our diagnostic challenges in the evaluation of BMB.

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Conflict of interest
Conflict of interest e authors declare that they have no conflict of interest**.**

References

Alyamany, R., El Fakih, R., Alnughmush, A., Albabtain, A., Kharfan-Dabaja, M. A., & Aljurf, M. (2024). A comprehensive review of the role of bone marrow biopsy and PET-CT in the evaluation of bone marrow involvement in adults newly diagnosed with DLBCL. *Frontiers in Oncology, 14*, 1301979. https://doi.org/10.3389/fonc.2024.1301979

Arber, D. A., Orazi, A., Hasserjian, R., et al. (2016). The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood, 127*(20), 2391–2405. https://doi.org/10.1182/blood-2016-03-643544

Aul, C., Gattermann, N., & Schneider, W. (1992). Age-related incidence and other epidemiological aspects of myelodysplastic syndromes. *British Journal of Haematology, 82*(2), 358–367. https://doi.org/10.1111/j.1365-2141.1992.tb06430.x

Barbui, T., Thiele, J., Gisslinger, H., et al. (2018). The 2016 WHO classification and diagnostic criteria for myeloproliferative neoplasms. *Blood Cancer Journal, 8*(2), 15

Briggs, C., Longair, I., Slavik, M., Thwaite, K., Mills, R., Thavaraja, V., Foster, A., Romanin, D., & Machin, S. J. (2009). Can automated blood film analysis replace the manual differential? *International Journal of Laboratory Hematology, 31*(1), 48–60. https://doi.org/10.1111/j.1751-553X.2007.01002.x

Choi, S. E., Hong, S. W., & Yoon, S. O. (2015). Proposal of an appropriate decalcification method of bone marrow biopsy specimens. *Journal of Pathology and Translational Medicine, 49*(3), 236–242. https://doi.org/10.4132/jptm.2015.03.16

Egesie, O. J. (2009). Epidemiology of anaemia necessitating bone marrow aspiration cytology in Jos. *Nigerian Journal of Medicine, 50*, 61

Elnahass, Y., & Youssif, L. (2018). Cytogenetic features in primary myelodysplastic syndrome Egyptian patients. *Journal of Advanced Research, 10*, 77–83. https://doi.org/10.1016/j.jare.2018.02.002

Font, P., Loscertales, J., Soto, C., Ricard, P., Novas, C. M., Martín-Clavero, E., López-Rubio, M., García-Alonso, L., Callejas, M., Bermejo, A., Benavente, C., Ballesteros, M., Cedena, T., Calbacho, M., Urbina, R., Villarrubia, J., Gil, S., Bellón, J. M., Díez-Martín, J. L., & Villegas, A. (2015). Interobserver variance in myelodysplastic syndromes with less than 5% bone marrow blasts. *Annals of Hematology, 94*(4), 565–573. https://doi.org/10.1007/s00277-014-2252-4

Ghosh, K., Shome, D. K., Kulkarni, B., et al. (2023). Fibrosis and bone marrow: Understanding causation and pathobiology. *Journal of Translational Medicine, 21*, 703. https://doi.org/10.1186/s12967-023-04393-z

Holst, J. M., Plesner, T., & d'Amore, F. (2020). Myeloproliferative and lymphoproliferative malignancies occurring in the same patient. *Haematologica, 105*(10), 2432–2439

Htun, H. L., Lian, W., Wong, J., Tan, E. J., Foo, L. L., Ong, K. H., & Lim, W. Y. (2022). Classic myeloproliferative neoplasms in Singapore. *Cancer Epidemiology, 79*, 102175. https://doi.org/10.1016/j.canep.2022.102175

Irons, R. D., Wang, X., Gross, S. A., et al. (2006). Prevalence of MDS subtypes in Shanghai, China. *Leukemia Research, 30*(7), 769–775. https://doi.org/10.1016/j.leukres.2005.10.018

Jawed, M. A., Paswan, M. K., Mahto, S. K., Patra, S., Ashok, C., Ansari, M. A., Priya, A., & Shome, A. (2024). Analysis and comparison of bone marrow aspiration and trephine biopsy. *Cureus, 16*(6), e62661. https://doi.org/10.7759/cureus.62661

Kini, J., Khadilkar, U. N., & Dayal, J. P. (2001). A study of the haematologic spectrum of myelodysplastic syndrome. *Indian Journal of Pathology and Microbiology, 44*(1), 9–12

Marchetti, M., Carobbio, A., Capitoni, E., & Barbui, T. (2018). Lymphoproliferative disorders in patients with chronic myeloproliferative neoplasms. *American Journal of Hematology, 93*(5), 698–703. https://doi.org/10.1002/ajh.25049

Merzianu, M., Groman, A., Hutson, A., et al. (2018). Trends in bone marrow sampling and biopsy specimen adequacy. *American Journal of Clinical Pathology, 150*(5), 393–405. https://doi.org/10.1093/ajcp/aqy066

Nangalia, J., Massie, C. E., Baxter, E. J., et al. (2013). Somatic CALR mutations in myeloproliferative neoplasms. *New England Journal of Medicine, 369*(25), 2391–2405. https://doi.org/10.1056/NEJMoa1312542

OECD. (2019). *Digital government index 2019 results*.

Park, Y., Park, B. B., Jeong, J. Y., et al. (2016). Assessment of bone marrow involvement in lymphoma. *Korean Journal of Internal Medicine, 31*(6), 1030–1041. https://doi.org/10.3904/kjim.2015.006

Raskin, R. E., & Messick, J. B. (2012). Bone marrow cytologic and histologic biopsies. *Veterinary Clinics of North America: Small Animal Practice, 42*(1), 23–42. https://doi.org/10.1016/j.cvsm.2011.10.001

Shallis, R. M., Wang, R., Davidoff, A., Ma, X., Podoltsev, N. A., & Zeidan, A. M. (2020). Epidemiology of myeloproliferative neoplasms. *Blood Reviews, 42*, 100706. https://doi.org/10.1016/j.blre.2020.100706

StatPearls Publishing. (2024). *Myeloproliferative neoplasms*.

Tefferi, A. (2021). Primary myelofibrosis: 2021 update. *American Journal of Hematology, 96*(1), 145–162. https://doi.org/10.1002/ajh.26050

Thandra, K. C., Barsouk, A., Saginala, K., Padala, S. A., & Rawla, P. (2021). Epidemiology of non-Hodgkin lymphoma. *Medical Sciences, 9*(1), 5. https://doi.org/10.3390/medsci9010005

Thiele, J., Kvasnicka, H. M., Facchetti, F., Franco, V., van der Walt, J., & Orazi, A. (2005). European consensus on grading bone marrow fibrosis. *Haematologica, 90*(8), 1128–1132

Thiele, J., Kvasnicka, H. M., Müllauer, L., et al. (2011). Essential thrombocythemia vs early primary myelofibrosis. *Blood, 117*(21), 5710–5718. https://doi.org/10.1182/blood-2010-07-293761

Tomasian, A., & Jennings, J. W. (2022). Bone marrow aspiration and biopsy. *Skeletal Radiology, 51*(1), 81–88. https://doi.org/10.1007/s00256-021-03882-w

Yan, Y., Lv, R., Xiong, W., et al. (2020). Subtype distribution, clinical features, and survival in B-cell chronic lymphoproliferative disorders in China: A review of 1,592 cases. *Clinical Lymphoma, Myeloma & Leukemia, 20*(6), e270–e283. https://doi.org/10.1016/j.clml.2019.11.002

Zeidan, A. M., Shallis, R. M., Wang, R., Davidoff, A., & Ma, X. (2019). Epidemiology of myelodysplastic syndromes. *Blood Reviews, 34*, 1–15. https://doi.org/10.1016/j.blre.2018.09.001