TITLE: VALIDITY OF 18F FDG-PET/CT IN THE DETECTION OF BONE MARROW DISEASE IN HODGKIN'S AND NON-HODGKIN'S LYMPHOMA"

Author; Dr. Tooba Khan (This study was conducted at the Department of Nuclear Medicine, KIRAN, Karachi, Pakistan)

INTRODUCTION

Positron Emission Tomography with 18F-Fluorodeoxyglucose (18F FDG-PET/CT) is useful for diagnosing lymphomas, including Hodgkin's and non-Hodgkin's [1]. Its ability to detect bone marrow involvement is often compared to biopsy [2]. Traditional bone marrow biopsy has been the gold standard for diagnosing lymphomas. On the other hand, 18F FDG-PET/CT provides functional and anatomical data without surgery.

OBJECTIVE

To determine the validity of 18F FDG-PET/CT in the detection of bone marrow disease in Hodgkin's and non-Hodgkin's lymphoma taking bone marrow biopsy as gold standard.

STUDY DESIGN

Cross Sectional Study.

SETTING

This study was conducted at the Department of Nuclear Medicine, KIRAN, Karachi, Pakistan.

DURATION

Six months after the approval of the synopsis from January 31, 2023 to July 30, 2023.

MATERIALS AND METHODS

Patients meeting the inclusion criteria at KIRAN, Karachi, were included after getting informed consent, which explained the study protocol, hazards, and benefits. Contrast-enhanced PET/CT and bilateral/unilateral iliac crest marrow aspirate with trephine biopsy were done. Marrow biopsy was followed by PET/CT within two weeks. Interpreting Hodgkin's lymphoma marrow infiltration. PET/CT scans with localized or diffuse tracer uptake in bone/bone marrow were positive. The offered proforma was used to electronically record research data.

It is to be concluded that that 18F FDG-PET/CT holds potential for identifying bone marrow pathology in both Hodgkin's and non- Hodgkin's lymphoma. The results suggest that there is a promising ability to accurately detect patients with or without bone marrow involvement, which makes it a helpful method for assessing the condition and planning treatment without the need for intrusive procedures.

RESULTS

The mean ± standard deviation of age was 33.49±14.45 years. In the gender distribution, 55 (63.2%) were classified as male while 32 (36.8%) were classified as female. Diagnostic accuracy of 18 F-FDG-PET findings was 80.46% in diagnosis of bone marrow disease with sensitivity 92.00%, specificity 75.81%, PPV 60.53% and NPV was found to be 95.92% by using bone marrow biopsy as gold standard.

CONCLUSION

It is to be concluded that that 18F FDG-PET/CT holds potential for identifying bone marrow pathology in both Hodgkin's and non- Hodgkin's lymphoma. The results suggest that there is a promising ability to accurately detect patients with or without bone marrow involvement, which makes it a helpful method for assessing the condition and planning treatment without the need for intrusive procedures.

Background:

Bone marrow involvement (BMI) is a key prognostic factor in lymphoma, influencing staging, treatment decisions, and outcomes. Traditionally, bone marrow biopsy (BMB) has been the gold standard, but it provides limited sampling and may miss focal disease.

Problem:

Recent studies suggest that 18F-FDG PET/CT may detect BMI more effectively, particularly in Hodgkin lymphoma (HL) and diffuse large B-cell lymphoma (DLBCL), with reported sensitivities up to 100%. However, its performance in follicular lymphoma (FL) remains variable (31–68%).

Local data from Pakistan on PET/CT's diagnostic accuracy for BMI are scarce.

Key Findings from Literature:

BMI occurs in 50–80% of low-grade NHL, 25–40% of high-grade NHL, and 5–14% of HL.

PET/CT shows 100% sensitivity, 76.6% specificity, and 78.6% accuracy in detecting BMI.

International guidelines now recognize focal skeletal FDG uptake as a reliable indicator of BMI in aggressive lymphomas, potentially replacing BMB.

Rationale:

Given the high prevalence of lymphoma and late presentation among Pakistani patients, evaluating the validity of FDG-PET/CT for BMI detection is crucial. If proven accurate, PET/CT could replace invasive biopsy in many cases, enabling earlier diagnosis and improved prognosis.

MATERIALS & METHODS

Study Design

Cross-sectional study

Conducted at the **Department of Nuclear Medicine, KIRAN, Karachi**

Duration: **January 31 – July 30, 2023 (6 months)**

Sample

Total: 87 suspected lymphoma patients

Sampling: Non-probability, consecutive sampling

Inclusion criteria:

- **Biopsy-proven Hodgkin's and Non-Hodgkin's lymphoma**
- **Age 18–70 years, either gender**

Exclusion criteria:

- **Prior treatment**
- **PET–biopsy interval > 2 weeks**

Data Collection

Ethical approval: CPSP Ethical Review Committee

PET/CT Protocol:

- **Radiotracer: ^{18}F-FDG (150–250 MBq IV)**
- **Fasting: 4–6 hours (glucose <150 mg/dL)**
- **Scanner: Siemens Biograph LSO PET/CT**
- **Acquisition: 60 min post-injection, head to mid-thigh**
- **CT for attenuation correction & anatomical localization**
- **Reconstruction: 3D RAMLA algorithm**

Bone Marrow Biopsy:

- **Iliac crest aspirate + trephine biopsy**
- **Staining: H&E, Reticulin, IHC (CD3, CD20, CD15, CD30, CD45)**
- **Reviewed by two blinded pathologists**

Interpretation

Abnormal marrow uptake: ≥ liver uptake

PET/CT positive: focal or diffuse tracer uptake in bone/bone marrow

Data Analysis

Software: **SPSS version 21**

Quantitative data: Mean ± SD or Median (IQR)

Qualitative data: n (%)

Diagnostic metrics: Sensitivity, Specificity, PPV, NPV, Accuracy

Effect modifiers: Age, gender, symptoms, Hb, WBC, platelets, LDH

18F-FDG PET/CT studies of two patients-one with B symptoms (A) and one without (B)-showing that the bone marrow uptake of 18F-FDG was greater in the patient with B symptoms

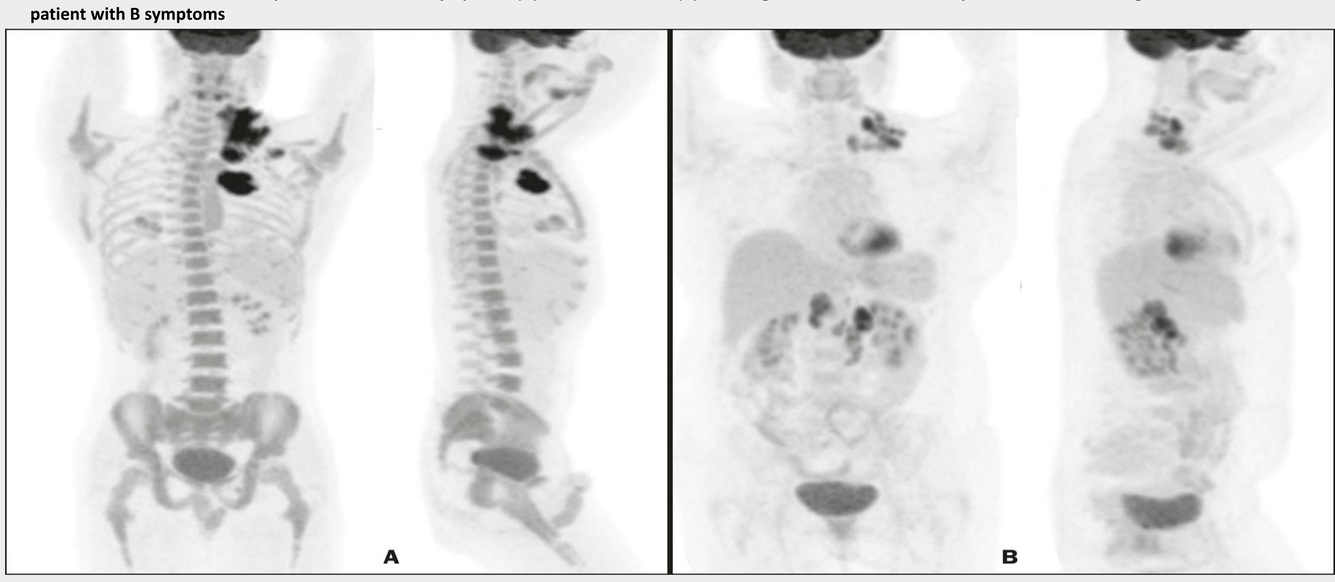


FIGURE # 1
FREQUENCY OF GENDER n=87

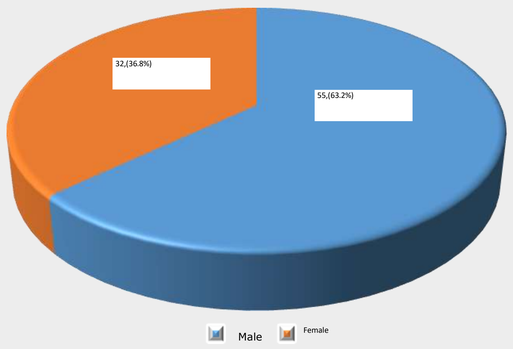


FIGURE # 2 FREQUENCY OF FEVER n=87

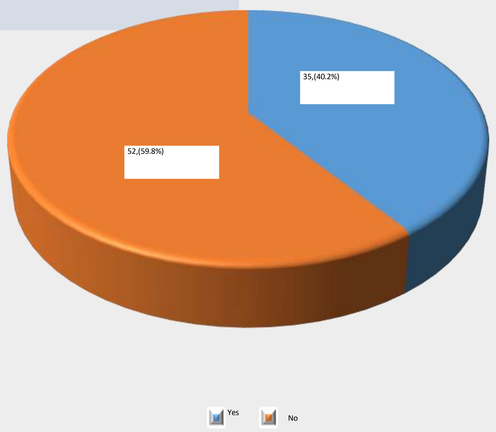


FIGURE # 3 FREQUENCY OF DRENCHING SWEATS n=87

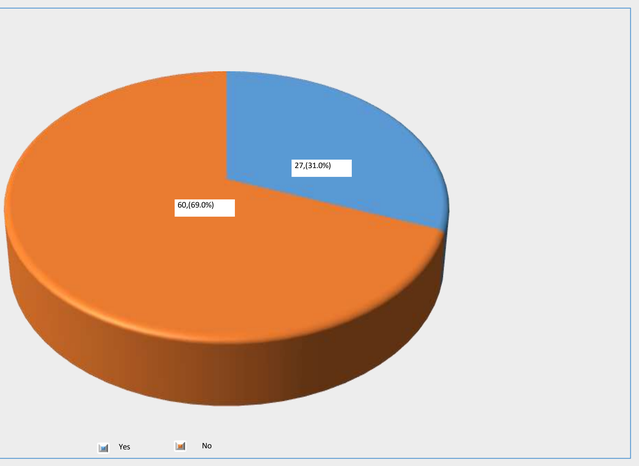


FIGURE # 4 FREQUENCY OF WEIGHT LOSS n=87

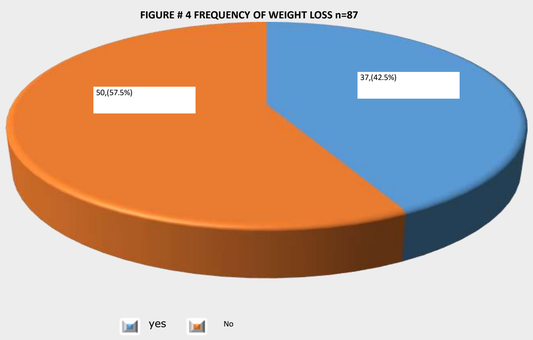


FIGURE # 5
FREQUENCY OF BONE MARROW DISEASE ON ^{18} F-FDG-PET FINDINGS n=87

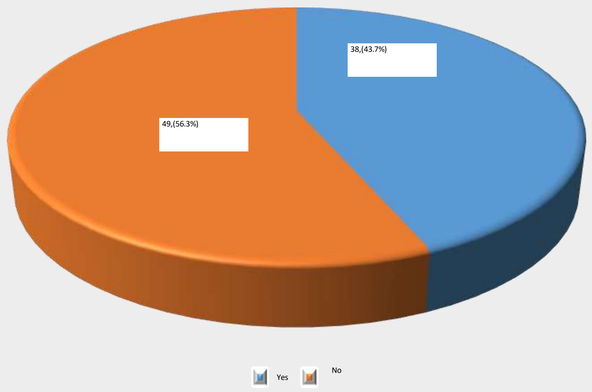
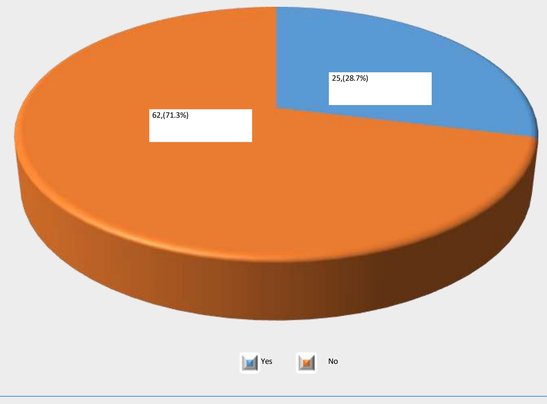


FIGURE # 6
FREQUENCY OF BONE MARROW DISEASE ON BONE MARROW BIOPSY n=87



RESULTS

In the gender distribution, 55 (63.2%) were classified as male while 32 (36.8%) were classified as female as shown in **FIGURE 1**.

Fever was observed in 40.2% of the patients, totaling 35 individuals as shown in **FIGURE 2**.

Drenching sweats were documented in 31.0% of the patient population, affecting a total of 27 individuals as shown in **FIGURE 3**.

Weight loss was noted in 37 (42.5%) patients as shown in **FIGURE 4**.

On 18F-FDG-PET/CT findings, bone marrow disease was noted in 38 (43.7%) patients as shown in **FIGURE 5**.

Bone marrow disease was detected in 28.7% of the patients based on biopsy as (gold standard) as shown in **FIGURE 6**.

In our study, diagnostic accuracy of 18 F-FDG-PET findings was 80.46% in diagnosis of bone marrow disease with sensitivity 92.00%, specificity 75.81%, PPV 60.53% and NPV was found to be 95.92% by using bone marrow biopsy as gold standard. Several studies have reported sensitivities ranging between 31% and 68% [19,22-24] while in another study conducted on 142 patients, PET identified a higher number of nodal areas in 32% [25]. In a study by Muzahir S, et al, the sensitivity of FDG PET/CT was 100%, the specificity was 76.57%, the negative predictive value was 76.57%, the positive predictive value was 29.72%, and the diagnostic accuracy was 78.62 [28].

Future research could focus on optimizing imaging protocols, exploring new radiotracers, and refining criteria for interpreting 18F FDG-PET/CT findings in lymphomas. Additionally, prospective studies with larger patient cohorts and long-term follow-up could provide further insights into the clinical utility and prognostic value of 18F FDG-PET/CT in the detection of bone marrow disease in Hodgkin's and non-Hodgkin's lymphoma. 18F FDG-PET/CT is a valuable tool for the detection of bone marrow disease in Hodgkin's and non-Hodgkin's lymphoma. Its diagnostic performance, when carefully interpreted in conjunction with clinical and histological data, can contribute to more informed decision-making in the management of these lymphomas. However, the limitations and challenges associated with false positives and negatives should be considered in the overall context of patient care.

CONCLUSION

It is to be concluded that that 18F FDG-PET/CT holds potential for identifying bone marrow pathology in both Hodgkin's and non- Hodgkin's lymphoma. The results suggest that there is a promising ability to accurately detect patients with or without bone marrow involvement, which makes it a helpful method for assessing the condition and planning treatment without the need for intrusive procedures.

REFERENCES

1. Sehn LH, Berry B, Chhanabhai M, Fitzgerald C, Gill K, Hoskins P, et al. The revised International Prognostic Index (R-IPI) is a better predictor of outcome than the standard IPI for patients with diffuse large B-cell lymphoma treated with R-CHOP. Blood. 2007; 109(5):1857-61.
2. Zhou Z, Sehn LH, Rademaker AW, Gordon LI, Lacasce AS, Crosby-Thompson A, et al. An enhanced International Prognostic Index (NCCN-IPI) for patients with diffuse large B-cell lymphoma treated in the rituximab era. Blood. 2014;123(6):837-42.
3. Federico M, Bellei M, Marcheselli L, Luminari S, Lopez-Guillermo A, Vitolo U, et al. Follicular lymphoma international prognostic index 2: a new prognostic index for follicular lymphoma developed by the international follicular lymphoma prognostic factor project. J Clin Oncol. 2009;27(27):4555-62.
4. Solal-Celigny P, Roy P, Colombat P, White J, Armitage JO, Arranz-Saez R, et al. Follicular lymphoma international prognostic index. Blood. 2004;104(5):1258-65.
5. Hasenclever D, Diehl V. A prognostic score for advanced Hodgkin's disease. International Prognostic Factors Project on Advanced Hodgkin's Disease. N Engl J Med. 1998;339(21): 1506-14.
6. Barrington SF, Mikhaeel NG. PET scans for staging and restaging in diffuse large B-cell and follicular lymphomas. Curr Hematol Malig Rep. 2016;11(3):185-95.
7. Salles G, Seymour JF, Offner F, Lopez-Guillermo A, Belada D, Xerri L, et al. Rituximab maintenance for 2 years in patients with high tumour burden follicular lymphoma responding to rituximab plus chemotherapy (PRIMA): a phase 3, randomised controlled trial. Lancet. 2011;377(9759):42-51.
8. Marcus R, Davies A, Ando K, Klapper W, Opat S, Owen C, et al. Obinutuzumab for the first-line treatment of follicular lymphoma. N Engl J Med. 2017;377(14):1331-44.
9. Federico M, Luminari S, Dondi A, Tucci A, Vitolo U, Rigacci L, et al. R-CVP versus R-CHOP versus R-FM for the initial treatment of patients with advanced-stage follicular lymphoma: results of the FOLLOS trial conducted by the Fondazione ItalianaLinfomi. J Clin Oncol. 2013;31(12):1506-13.
10. Bachy E, Seymour JF, Feugier P, Offner F, L6pez-Guillermo A, Belada D, et al. Sustained progression-free survival benefit of rituximab maintenance in patients with follicular lymphoma: long-term results of the PRIMA Study. J Clin Oncol. 2019;37(31):2815-24.
11. El-Galaly TC, d'Amore F, Mylam KJ, de Nully Brown P, Bogsted M, Bukh A, et al. Routine bone marrow biopsy has little or no therapeutic consequence for positron emission tomography/computed tomography-staged treatment-naive patients with Hodgkin lymphoma. J Clin Oncol. 2012;30(36):4508-14
12. Weiler-Sagie M, Kagna O, Dann EJ, Ben-Barak A, Israel O. Characterizing bone marrow involvement in Hodgkin's lymphoma by FDG-PET/CT. Eur J Nucl Med Mol Imaging. 2014; 41(6):1133-40.
13. Zwarthoed C, El-Galaly TC, Canepari M, Ouvrier MJ, Viotti J, Ettaiche M, et al. Prognostic value of bone marrow tracer uptake pattern in baseline PET scans in Hodgkin lymphoma: results from an international collaborative study. J Nucl Med. 2017;58(8): 1249-54.
14. Voltin CA, Goergen H, Baues C, Fuchs M, Mettler J, Kreissl S, et al. Value of bone marrow biopsy in Hodgkin lymphoma patients staged by FDG PET: results from the German Hodgkin Study Group trials HD16, HD17, and HD18. Ann Oncol. 2018;29(9):1926-31.
15. Adams HJ, Kwee TC, Fijnheer R, Dubois SV, Nievelstein RA, de Klerk JM. Bone marrow 18F-fluoro-2-deory-D-glucose positron emission tomography/computed tomography cannot replace bone marrow biopsy in diffuse large B-cell lymphoma. Am J Hematol. 2014;89(7):726-31.