Baseline FDG PET CT for Evaluation of Primary Extranodal Lymphoma: A Multi Center Cross Sectional Study

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ABSTRACT

Extranodal lymphoma comprises 20-30% of all lymphomas, and diagnosis at presentation is a challenge due to the wide range of presentations. To see the pattern of disease involvement at presentation as well as to assess the role of 18F-FDG PET-CT in diagnosing extranodal lymphoma. This cross-sectional study was conducted in the Institute of Nuclear Medicine and Allied Sciences, Dhaka, along with one well-equipped private PET-CT center from January 2021 to December 2023 among 98 patients having pathologically and immunohistochemistry-proven primary extranodal lymphoma without a history of prior treatment. Maximum patients (22) were in the 50–59-year age group with male predominance (56%). 96% were non-Hodgkin's lymphoma histopathologically. Among the non-Hodgkin's group, 29% of patients presented with gastrointestinal involvement and 10% with skeletal lesions. 8% showed orbital primary, and another 8% had tonsil as the primary site of involvement. The rest of the primary sites included thyroid (6%), bone marrow (5%), thymus (2%), brain (2%), nasopharynx (5%), tongue (4%), other head and neck regions (3%), vagina (2%), ovary (2%), spleen (5%), liver (1%), muscular (2%), and cutaneous (2%). Hepatosplenomegaly was present in 32% of patients, while the rest did not have any organomegaly. No FDG-avid lymph nodes were found in 76% of the patients. The SUV max of FDG-avid lesions ranged from 5 to 40. 52% of FDG-avid lesions had an SUV max from 11 to 20. FDG PET-CT enables accurate detection of involvement of unusual organs with lymphomatous infiltration even without morphologic change.

Keywords: Extra nodal lymphoma, 18F-FDG PET-CT, Primary Presentation, Pattern

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INTRODUCTION

Lymphoma is a neoplastic proliferation of lymphoid cells at various stages of differentiation. It affects lymph nodes and commonly infiltrates into the bone marrow, spleen and thymus. However, extranodal involvement is seen in 20–30% of all lymphoma cases (1). Extranodal disease might be part of lymphomatous involvement (secondary lymphoma) or the primary site where lymphoma arises (primary lymphoma) (2). The route of spread to the extranodal site is either regional spread from nodal disease or hematogenous dissemination (3). Diagnosing involvement sites with extent of disease is crucial in choosing therapy options (1, 4, 5). PET/CT is a hybrid scan providing both anatomic and functional natures of the disease and covers a wide area of scanning, thus may have a pivotal role. Key roles of 18F-FDG PET-CT lie in accurate staging, superior sensitivity than other imaging modalities and detecting disease in unusual sites (6). It is also crucial for accurate assessment of metabolic response to therapy and distinguishing residual viable tumors from post-treatment fibrotic tissue.

PATIENTS AND METHODS

This cross-sectional study was conducted in the Institute of Nuclear Medicine and Allied Sciences, Dhaka, along with one well-equipped private PET-CT center from January 2021 to December 2023 among 98 patients having pathologically and immunohistochemistry-proven primary extranodal lymphoma without a history of prior treatment. Samples were collected through the "purposive sampling technique." Patients with uncontrolled diabetes, pregnant and lactating mothers, and concurrent malignancy were excluded. Informed written consent was taken from all patients.

A whole-body FDG PET-CT scan was acquired from vertex to mid-thigh in a whole-body PET-CT scanner (Philips 128-slice Ingenuity TF PET-CT, USA) one hour after intravenous injection of 5 to 10 mCi of 18F-FDG. Semi-quantitative estimation of FDG uptake was performed by calculating the SUVmax value, corrected for dose administered and body weight.

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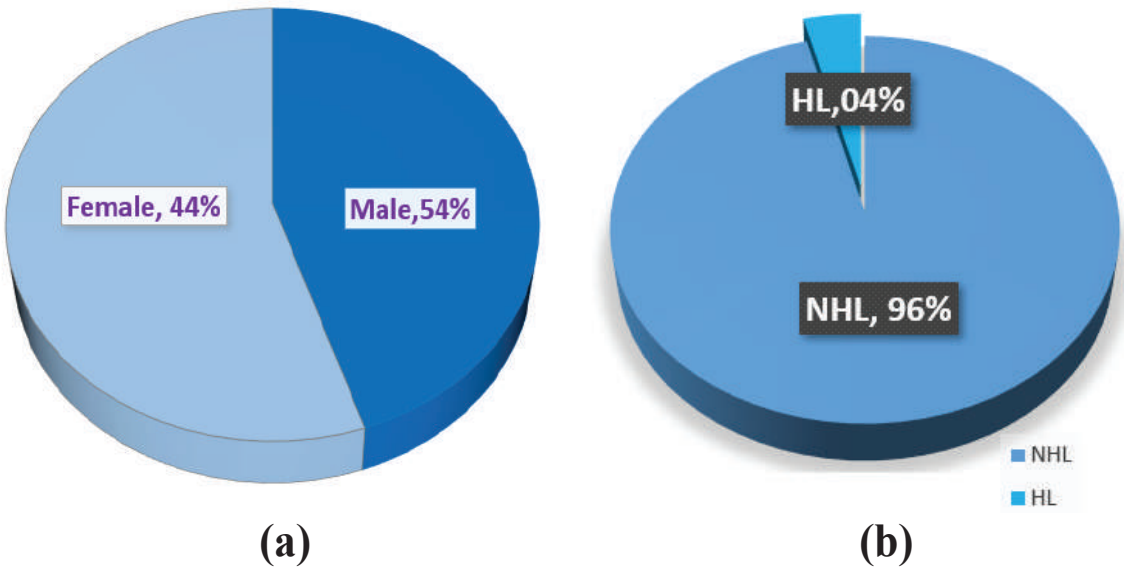

NHL: Non-Hodgkin's lymphoma, HL = Hodgkin's lymphoma.

Figure 1: (a) Gender Distribution of Study Participants (N=98) (b) Histological and Immunohistochemical Profile of the Study Cohort (N = 98)

RESULT

Among the 98 patients, 56% were male, 44% were male. The patient demographics by age group are presented in Table 1. Maximum 22 patients were in the 50–59-year age group. The histological classification and immunohistochemical expression patterns for the 98 cases are summarized in Figure 1 (B). Histopathological analysis revealed that 97 patients (96%) had non-Hodgkin's lymphoma, while the remaining cases were diagnosed as Hodgkin's lymphoma.

Table 1: The age distribution of the study patients.

Age (in Years)	Number of patients
10-19	08
20-21	20
30-39	16
40-49	06
50-59	22
60-69	16
70-79	08
80-89	02

Within the non-Hodgkin's lymphoma subgroup, diffuse large B-cell lymphoma (DLBCL) accounted for 36% of cases. High-grade lymphoma constituted 15%, low-grade lymphoma 12%, intermediate-grade lymphoma 14%, and B-cell lymphoma 15%, while the remaining 8% comprised other histopathological subtypes.

Regarding disease distribution, gastrointestinal involvement was observed in 29% of patients, skeletal lesions in 10%, orbital primary involvement in 8%, and tonsillar involvement in another 8% of cases.

Table-2: Extranodal Lymphoma Involvement Sites on baseline 18F FDG PET-CT.

Location of primary site of extranodal lymphoma by baseline FDG PET-CT	Percentage
Gastrointestinal Tract	29%
Bones	10%
Orbit	08%
Tonsils	08%
Thyroid	06%
Bone marrow	05%
Nasopharyngeal	05%
Tongue	04%
Testis	04%
Other head neck regions	03%
Vagina	02%
Ovary	02%
Spleen	05%
Liver	01%
Muscular	02%
Cutaneous	02%
Thymus	02%
Brain	02%

The remaining primary sites included thyroid (6%), bone marrow (5%), thymus (2%), brain (2%), nasopharynx (5%), tongue (4%), other head and neck regions (3%), vagina (2%), ovary (2%), spleen (5%), liver (1%), muscle (2%), and cutaneous sites (2%). Hepatosplenomegaly was observed in 32% of patients, while the remainder showed no evidence of organomegaly.

On 18F-FDG PET-CT, no FDG-avid lymph nodes were identified in 76% of patients. The SUVmax of FDG-avid lesions ranged from 5 to 40, with 52% of lesions demonstrating an SUVmax between 11 and 20.

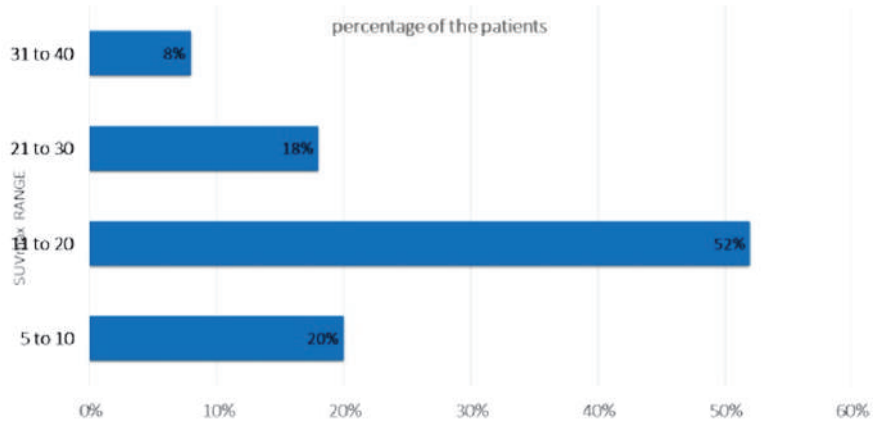

Figure 2: Frequency Distribution of SUVmax at Primary Extranodal Lymphoma Sites

DISCUSSION

Lymphoma is a histologically heterogeneous group of cancers of the immune system accounting for about 5–6% of all malignancies (7). Management varies according to histologic type as well as the pattern of involvement. Identification of extranodal lymphomatous involvement is crucial in prognosis [8]. In the current study PET-CT played a critical role in detecting unusual sites of disease involvement, e.g., the orbit and vagina, thus aiding the clinicians to a proper management path.

Unlike traditional imaging modalities such as CT or MRI, PET-CT covers a wide area of scanning along with delineation of metabolic characteristics of diseased tissue. Its ability to detect hypermetabolic foci provides an edge in identifying elusive tumors, particularly in cases where structural changes are minimal or absent.

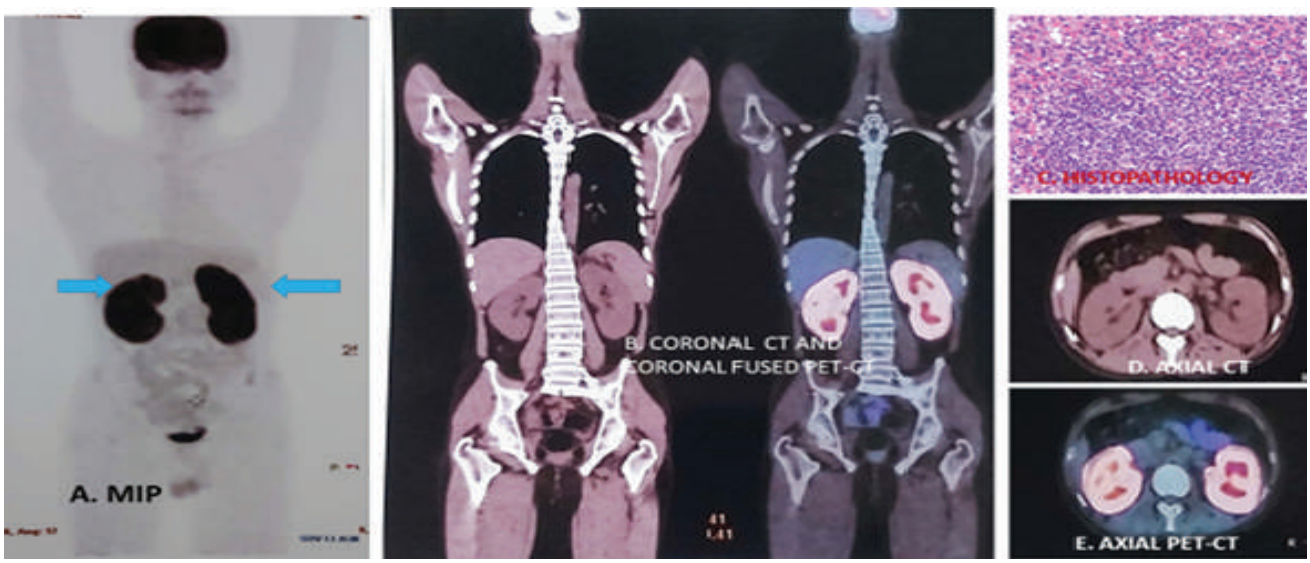

Figure 3: Primary extranodal lymphoma of intermediate grade NHL involving both the Kidneys in a male patient presented with hematuria. FDG PET-CT showed mild enlargement of both kidneys with intense and diffuse FDG uptake (SUVmax:20) (A, B, E), no definite mass in CT (B, D). No other hypermetabolic visceral, nodal or skeletal lesion.

In this study, PET- CT was performed to detect extranodal involvement at primary presentation, before any therapy. A total of 96 patients were diagnosed with non-Hodgkin's lymphoma (NHL), which represents 96% of the sample, a significantly higher percentage compared to Omar et al. (68.2%) and Das et al. (65.8%) (6, 8). This study indicates a male predominance of 56%, consistent with prior research, and identifies the highest patient count in the 50-59 age group. DLBCL was the most common histological subtype of non-Hodgkin's lymphoma in this study (35%). Similar studies have reported DLBCL frequencies of 43.6% and 44.1%, which are consistent with the present findings. (6, 8).

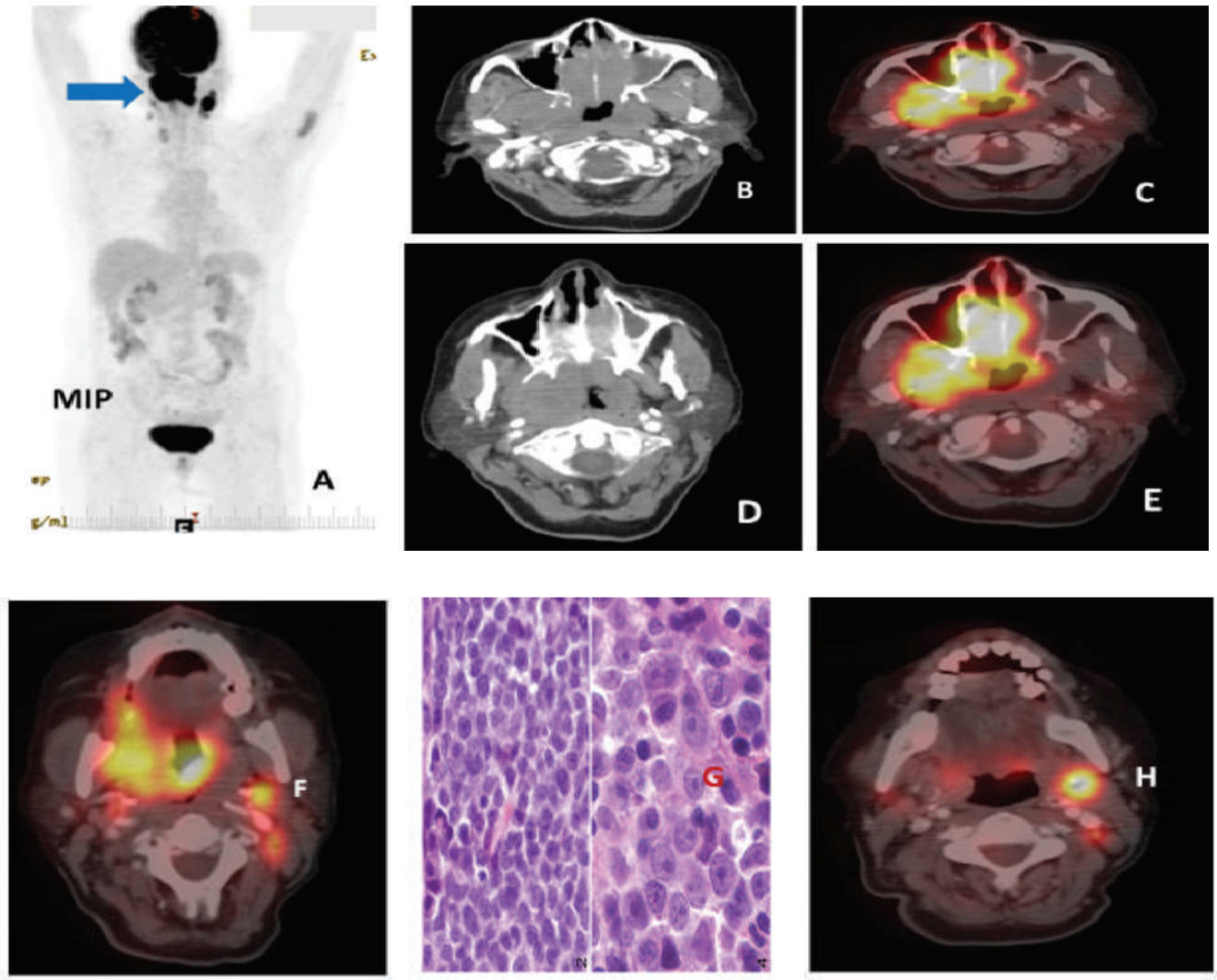

Figure 4: A 55 years old female patient presented with epistaxis and nasal obstruction. Nasopharyngeal laryngoscopy revealed bilateral nasal mass that's bleeds on touch occupying and obstructing both posterior choana. Nasopharyngeal biopsy from the lesion confirmed DLBCL. FDG PET-CT showed hypermetabolic enhancing irregular soft tissue mass involving the nasopharynx, nasal cavity (A-E). The mass also involving right pterygopalatine fissure, right pterygopalatine fossa, pterygomaxillary fissure (B, C, D) foramen rotundum, adjacent pharyngeal wall and hypopharynx (G). Hypermetabolic few enlarged left cervical lymph nodes. No other hypermetabolic visceral, nodal or skeletal lesion.

The most common site of primary lymphoma was the gastrointestinal tract (29%), followed by skeletal involvement (10%), which is consistent with the findings reported by Barbara et al. The orbit and tonsil were the next most frequent sites (8% each). Other primary sites included the thyroid (6%), bone marrow (5%), thymus (2%), brain (2%), nasopharynx (5%), tongue (4%), other head and neck regions (3%), vagina

(2%), ovary (2%), spleen (5%), liver (1%), muscle (2%), and cutaneous sites (2%). The site of initial presentation may have important prognostic implications, with certain locations, such as the brain and testis, requiring site-specific therapeutic strategies. The present study also identified less common sites of involvement, including the orbit and thyroid gland, at an early stage before significant anatomical changes became evident. The wide spectrum of primary tumor locations highlights the diagnostic complexity of lymphoma and underscores the value of hybrid PET imaging in guiding clinical decision-making.

The presence of hepatosplenomegaly in diffuse large B-cell lymphoma (DLBCL) is associated with poor overall survival, estimated at approximately 8–12 months (11). In the present study, 69% of patients demonstrated hepatosplenomegaly, suggesting an adverse prognostic implication. Approximately 24% of patients demonstrated FDG-avid lymph nodes. In the setting of extranodal lymphoma, the presence of FDG-avid nodal involvement indicates disseminated disease, resulting in disease upstaging and potential modification of the management strategy.

A higher baseline SUVmax has been reported as a predictor of shorter progression-free survival (PFS) in certain lymphoma subtypes, including mucosa-associated lymphoid tissue (MALT) lymphoma (12). Although histopathological examination of biopsy specimens remains the gold standard for diagnosis, ^{18}F-FDG PET-CT plays an increasingly important role in staging and subsequent monitoring of non-Hodgkin's lymphomas (13, 14). In the present study, SUVmax values ranged from 5 to 37, with 52% of patients demonstrating values between 11 and 20, corresponding predominantly to intermediate- to high-grade histopathological subtypes.

CONCLUSION

Primary extranodal lymphoma can affect any organ or system making diagnosis at initial presentation a challenge. 18F-FDG PET-CT can be a valuable tool in tackling the obstacle. FDG PET-CT enables accurate detection of involvement of unusual organs with lymphomatous infiltration even without morphologic change in contrast enhanced CT. It also helps differentiating lymphomatous infiltration from benign causes of increased FDG uptake and subsequent disease staging which furthermore helps in treatment planning.

CONFLICT OF INTEREST

Authors have no financial, personal, or professional conflicts that could inappropriately bias this work.

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