ORIGINAL ARTICLE

Prevalence and pattern of incidental sinus mucosal disease seen on 18F-FDG PET/CT imaging among cancer patients

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ABSTRACT

Objective: To study the incidental abnormalities of paranasal sinuses in cancer patients who underwent F18- Fluorodeoxyglucose (FDG) positron emission tomography-computed tomography (PET-CT) scan.

Subjects and Methods: A total of 342 patients were selected, out of which 101 patients have shown CT findings with F18-FDG avidity in paranasal sinuses. Mucosal thickening, retention cyst, and opacification were seen in one or multiple sinuses bilaterally. Mucosal thickening and opacification were labeled as active disease, while retention cyst as noninflammatory. Maximum standardized uptake values (SUV max) of all the involved sinuses on PET were calculated to assess the correlation between CT and PET findings to derive a cut-off value for sinusitis.

Results: Comparison of mean SUV between mucosal thickening and opacification with that of retention cyst showed significant difference with *p*-value of sample *t*-test as 0.001 and best cut-off value for sinusitis to be 1.82.

Conclusion: From the findings of this study, it can be concluded that incidental sinus findings are not seen uncommonly in cancer patients.

Keywords: Paranasal sinuses, FDG avidity, PET-CT, incidental findings, mucosal thickening.

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Introduction

The facial skeleton comprises buccal cavity, jaw bones, nose, and paranasal sinuses. Due to the anatomic connections between different facial structures, pathology in one component can easily affect others [1]. Sinus problems are one of the most commonly encountered diseases in the world, affecting more than 12% of the US population [2]. Paranasal sinuses are the four paired air-filled extensions with maxillary sinus being the largest one [3]. The paranasal sinus abnormalities can be either congenital disorders, inflammatory diseases, or malignancy [4]. Young adults are the most common victims of the elevated predominance of paranasal sinus pathologies [5-8]. This may be due to the reason that younger adults are more exposed to environmental factors such as pollution [9].

Due to the immunocompromised state of cancer patients, they are more liable to infections secondary to acute sinus conditions. Due to the sinus' close proximity to several facial and intracranial structures, the infection should be controlled and treated aggressively to prevent spread, especially to the brain. In one study, paranasal sinusitis affected 52 immuno-compromised cancer patients who were treated over 5 years at the University of Maryland Cancer Center [10].

The inflammatory conditions of paranasal sinuses include mucosal thickening, complete sinus opacification, polyp formation, mucous retention cyst, and antrolith. Mucosal thickening occurs as a result of inflammatory reaction with hyperplasia of the mucous lining of the sinus. Prolonged exposure to inspired allergens leads to chronic inflammation in the sinus mucosa, which is seen as mucosal thickening on computed tomography (CT). Mucous retention cysts are a common incidental finding on cross-sectional imaging with a prevalence of maxillary mucosal cyst between 12.4% and 35.6% [11]. They appear as rounded opacities on CT imaging and are not related to symptoms of chronic sinusitis. Nasal polyps are the non-cancerous, sac-like growths formed from the thickening

of chronically inflamed mucosa. The polyps can be single or multiple within the maxillary sinus [11].

Fluorodeoxyglucose positron emission tomography-computed tomography (FDG PET/CT) has been widely used for several indications [6]. Most of them include the evaluation of regional and distant metastases, assessment of unknown primaries and posttreatment follow-up of residual and recurrent diseases. In the course of these studies, FDG uptake in noncancerous inflammatory conditions has also been identified [12]. Incidental FDG-avid findings are also experienced in these investigations and most of them are of clinical importance [6,7]. 18F-FDG is moved into the cells by glucose transporters and is phosphorylated by hexokinase enzyme to 18F-2-FDG-6-phosphate but is not metabolized. The extent of cellular FDG uptake corresponds to the cellular metabolic rate and the number of glucose transporters. Higher FDG uptake in malignancies is likely due to the elevated number of glucose transporters in tumor cells. Almost the same condition is noted in inflammation. Activated inflammatory cells also exhibit elevated expressions of glucose transporters. Secondly, in inflammation, the affinity of glucose transporters for deoxyglucose is somehow raised by various cytokines and growth factors, a process that is not seen in malignancies [13]. The CT part of hybrid PET/CT scans gives clinically vital knowledge [7]. Previous studies on different population groups have shown the incidence of sinus abnormality on radiological imaging to range from 16% to 60% [14]. Incidental FDG uptake in the sinonasal region has been rarely discussed in the literature. So, in this study, we retrospectively studied the pattern, prevalence, and 18F-FDG uptake of incidental abnormalities of paranasal sinuses in cancer patients who have undergone PET/CT.

This is the first study of its kind in Pakistan.

Materials and Methods

This is the retrospective cross-sectional study. PET/CT reports of 342 patients with various types of cancers from December 2019 to March 2020 were reviewed for the presence of any abnormal finding in all four paranasal sinuses. Patients who were reported to have abnormal CT findings in the sinus area were categorized as having sinus disease and patients who exhibited comparatively increased FDG uptake in a sinus region were considered to have sinusitis. The objective and main focus of study was to categorize the frequency of involvement of different paranasal sinuses and to derive a cut-off value for diagnosing sinusitis on the basis of standardized uptake values (SUVs) on PET/CT.

In this cross-sectional study, we conducted a quantitative assessment with image analysis from the database of the Department of PET/CT, Armed Forces Institute of Radiology and Imaging, Military Hospital, Rawalpindi. This study was approved by the ethical research committee.

Selection of patient

The sample included all diagnosed cases of carcinomas referred for PET/CT of both genders and all age groups.

Acquisition and processing

Serum creatinine levels were measured for all patients and blood glucose was also noted at the time of injection. Personalized doses of 18F-FDG were administered intravenously to all patients via left arm. To allow for the distribution and uptake of radiotracer uptake, the patient was allowed to rest quietly for 65 minutes in a shielded room. Imaging was performed on an integrated 64-slice PET/CT scanner with scanning from head to thigh or whole body, according to patient's diagnosis. Axial, sagittal, and coronal CT images from all of the PET/CT studies were reviewed on picture archiving and communications system workstations and correlated with the findings from the accompanying PET and fused PET/CT images.

Data collection

Our data included age, gender, and diagnosis of the patient along with characterization of the pathological processes on CT findings as involvement of any of four sinuses alone or combined with unilateral or bilateral or multiple as either mucosal thickening, retention cyst, complete sinus opacification, or polyp. Mucosal thickening and opacification were labeled as active disease process/sinusitis and the presence of mucous retention cyst as non-inflammatory. SUVs as maximum standardized uptake values (SUV max) of all the involved sinuses on PET were calculated to assess the correlation between CT and PET findings. Although SUVs were calculated separately for all four involved sinuses, mean SUVs were calculated from the SUVs of all combined sinuses from CT findings of mucosal thickening along with complete opacification for sinusitis. Finally, a cut-off value was extracted from the above findings.

Statistical analysis

All data were entered into SPSS version 24.0 for statistical analysis. Continuous variables were expressed as mean value ± SD. We calculated the mean SUVs of involved sinuses and generated an receiver operating characteristic (ROC) curve to find out the best cut-off SUV value differentiating active sinus disease/sinusitis for various CT findings. Student's *t*-test was used for analysis of difference between the means of quantitative data. *p*-value less than 0.05 was considered statistically significant. The studies were reviewed, and the findings confirmed by a classified radiologist along with a nuclear physician.

Results

In our study, out of 342 patients, abnormal CT findings were seen in 101 patients (29%).

Male constituted majority of the patients (n = 66, 65.5%), with mean age 49.9, as shown in Figure 1.

The mean age for the female group was 49.5 (n = 35, 34.65%), as shown in Table 1.

Most of the patients (n = 25, 24.75%) were diagnosed case of Hodgkin's lymphoma, followed by non-Hodgkin's lymphoma (n = 22, 21.78%), breast carcinoma (n = 12, 11.88%), and Gastrointestinal (GI) tumors (n = 10, 9.90%), as shown is Table 2 and Figure 2.

Out of 101 patients, 87 patients (86.14%) had single sinus disease with maxillary sinus as the major involved sinus (n = 78, 77.23%), followed by ethmoid sinus (n = 8, 7.92%) and sphenoid sinus (n = 1, 0.99%). Other patients had involvement of simultaneous two or more sinuses, as shown in Table 3.

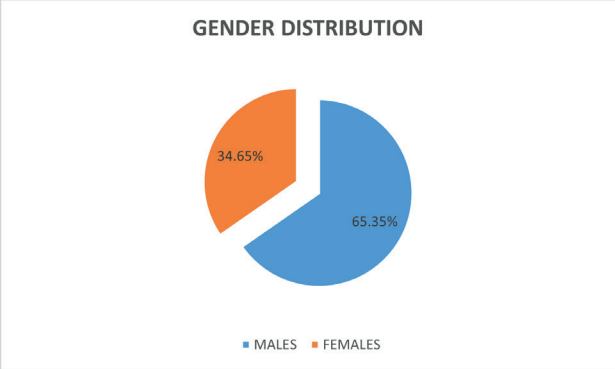

Figure 1. *Gender distribution.*

Table 1. *Age distribution.*

Gender	n	Mean Age (Years)	Std.dev
Males	66	49.9	18.7
Females	35	49.5	17.1
Total	101	49.8	18.1

Mucosal thickening was the most common finding (n = 127) seen in all four sinuses, followed by retention cyst (n = 55) and then complete opacification (n = 11). SUVs of involved sinuses were calculated as shown in Table 5. No retention cyst was seen in ethmoid and frontal sinuses and complete opacification was not seen in any ethmoid sinus. Complete opacification and retention cysts were noted with high numbers (n = 7 and n = 54, respectively) in the maxillary sinus, as shown in Table 4.

A total of 138 sinuses demonstrated abnormal CT findings of mucosal thickening and complete opacification along with increased FDG uptake, with mean SUV of 2.22. A total of 55 sinuses showed retention cyst with comparatively much lower SUVs, and mean SUV was 1.06, as shown in Table 5

Comparison of mean SUVs showed significant difference with p-value of sample t-test = 0.001, as shown is Table 6 and Figure 3.

Table 2. *Diagnosis of patients.*

Diagnosis	Frequency	Percent
Hl	25	24.75%
Nhl	22	21.78%
Cabreast	12	11.88%
Gitumors	10	9.90%
Calung	9	8.91%
Sarcomas	6	5.94%
Melanoma	4	3.96%
Head and neck caner	3	2.97%
Cabladder	3	2.97%
Cacervix	3	2.97%
Others	4	3.96%
Total	101	100.00%

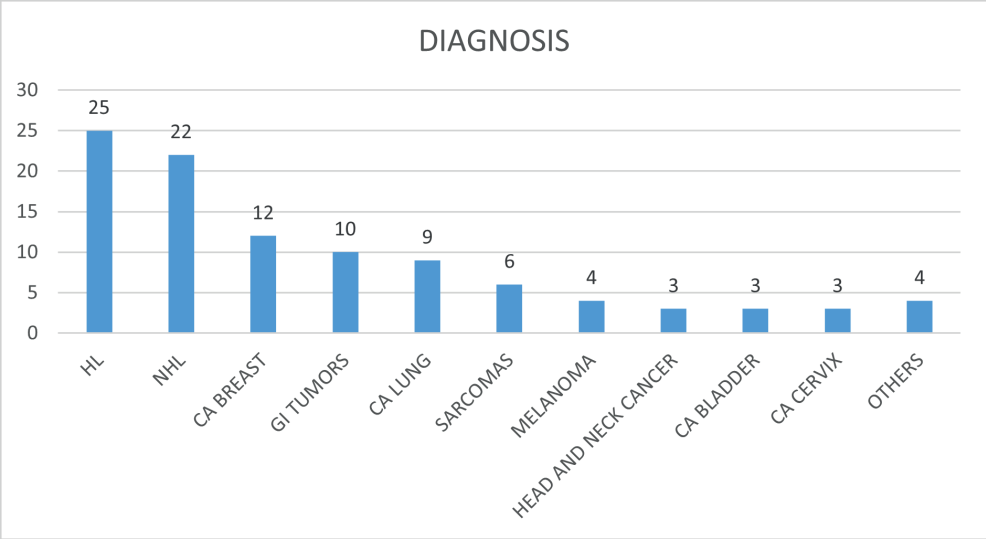

Figure 2. *Diagnosis of patients.*

Table 3. *Involved sinuses.*

Involved sinuses	Frequency	Percent
Maxillary	78	77.23%
Ethmoid	8	7.92%
Maxillary and ethmoid	5	4.95%
Maxillary And Frontal	3	2.97%
Maxillary And Sphenoid	3	2.97%
Maxillary, Ethmoid And Sphenoid	2	1.98%
Sphenoid	1	0.99%
Maxillary, Ethmoid And Frontal	1	0.99%
Total	101	100.00%

Table 4. *Detail of the sinus abnormalities.*

Sinus		Mucosal Thickening	Retention Cyst	Complete Opacification	Total
Maxillary	Right Left	37 37	25 29	2 5	65 71
Ethmoid	Right Left	19 17	0 0	0 0	19 17
Sphenoid	Right Left	3 7	0 0	1 1	4 8
Frontal	Right Left	4 3	1 0	1 1	5 4

Table 5. *Standardize uptake values (SUVs).*

Sinuses		Suvs			
		Minimum	Maximum	Mean	Std.dev
Maxillary	Right Left	0.20 0.48	3.61 3.62	1.58 1.60	0.89 0.85
Ethmoid	Right Left	0.97 0.74	7.23 5.70	2.66 2.31	1.54 1.07
Sphenoid	Right Left	1.21 0.79	3.29 2.86	2.35 1.90	0.77 0.71
Frontal	Right Left	0.77 1.20	4.06 2.07	1.90 1.63	1.29 0.46

Table 6. *Comparison of mean SUVs.*

Sinusitis	N	Mean Suv	Std.dev	P-Value T-Test
Present	138	2.22	1.04	0.001*
Absent	55	1.06	0.57	

The ROC curve showed the best cut-off value predicting sinusitis to be 1.82, with sensitivity = 64.5%, specificity = 90.8%, and area under the curve (AUC) = 0.869, as shown in Figure 4.

Figure 5a and b significant FDG uptake in a patient with an incidental finding of bilateral maxillary sinus mucosal thickening. 57-year-old female patient with a known case of Non Hodgkin's Lymphoma (NHL) with bilateral maxillary sinus mucosal thickening. SUV on right side was 3.40 and on left side was 3.58.

Figure 6a-c insignificant uptake in incidental finding of maxillary sinus mucosal retention cyst. 50-year-old male patient with a diagnosed case of Hodgkin's Lymphoma (HL) with bilateral maxillary mucous retention cyst. SUV on right side was 0.74 and on left side was 0.92.

Discussion

In this study, we found that 101 out of 342 (29%) patients who underwent PET/CT for oncological purposes had abnormal incidental findings in paranasal sinuses with

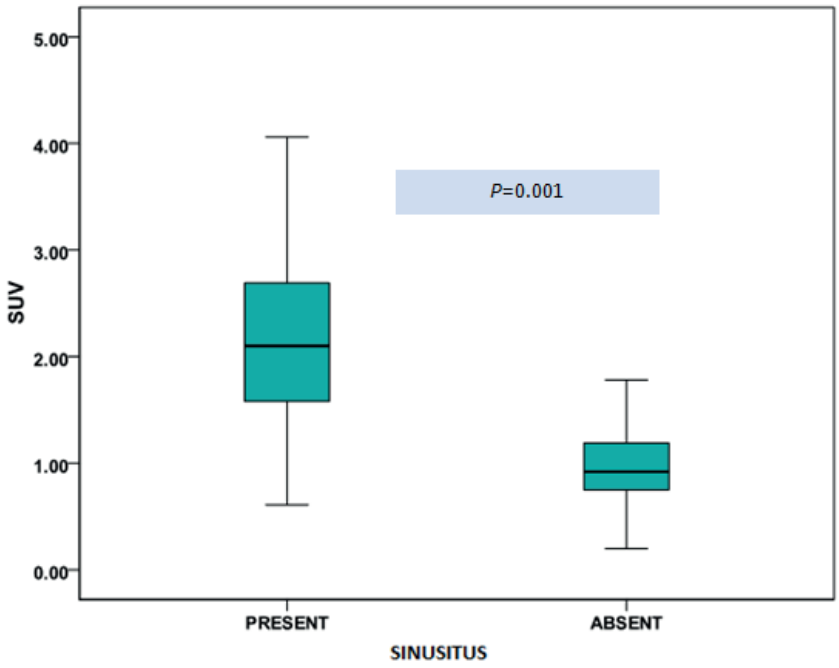

Figure 3. *Box plots showing significant differences in mean SUVs in sinusitis (mucosal thickening plus opacification) and in retention cyst.*

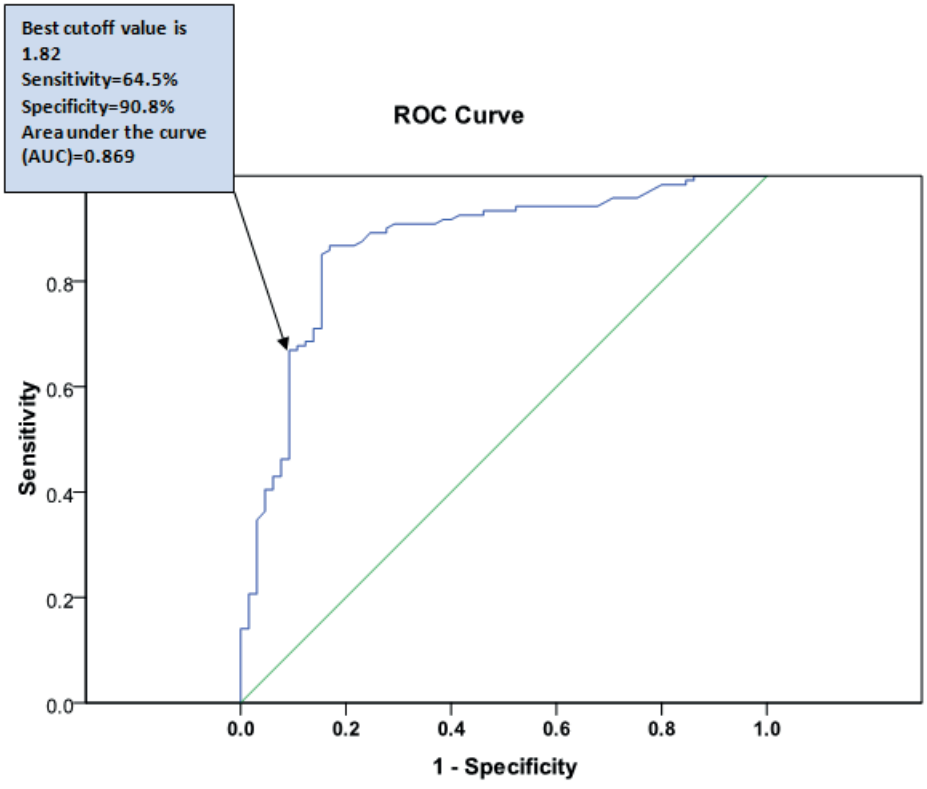

Figure 4. *ROC curve showing best cut-off value predicting sinusitis and the AUC.*

majority of the patients being male (65.34%). Maxillary sinus was the most commonly involved sinus alone in 78 patients (77.23%), with simultaneous involvement of other sinuses in 14 patients (13.86%). The least involved sinus was sphenoid. Mucosal thickening was the most common abnormal finding in all of the four sinuses (n = 127), followed by retention cyst (n = 55). Comparison of mean SUV for mucosal thickening plus opacification with that of retention cyst showed significant difference with p-value for t-test to be 0.001, which is statistically highly significant. The best cut-off value for sinusitis was calculated to be 1.82, with specificity of 90.8% implicating that SUVs above this cut-off value will likely represent sinusitis which will aid clinicians in timely treatment of

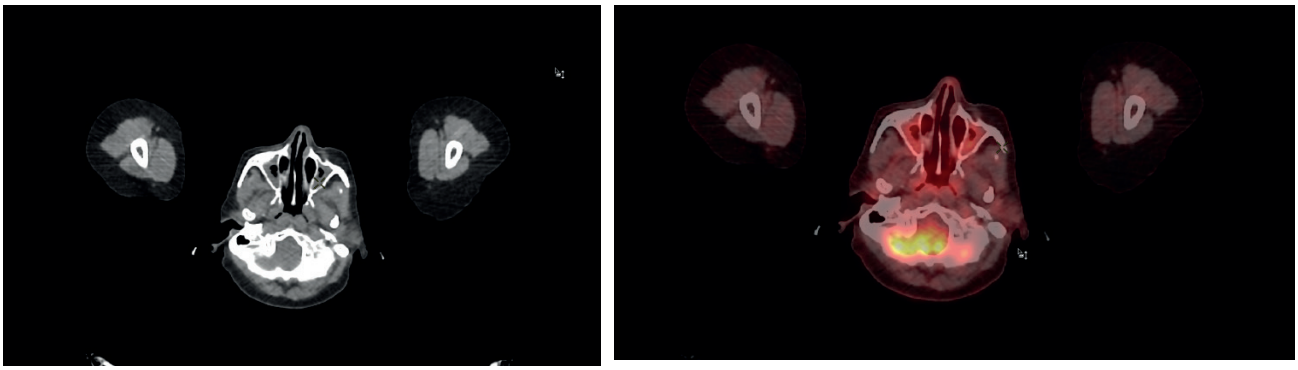

Figure 5. *(a) Axial CT image of bilateral mucosal thickening. (b) Fused PET/CT image demonstrating bilateral mucosal thickening with significant FDG uptake.*

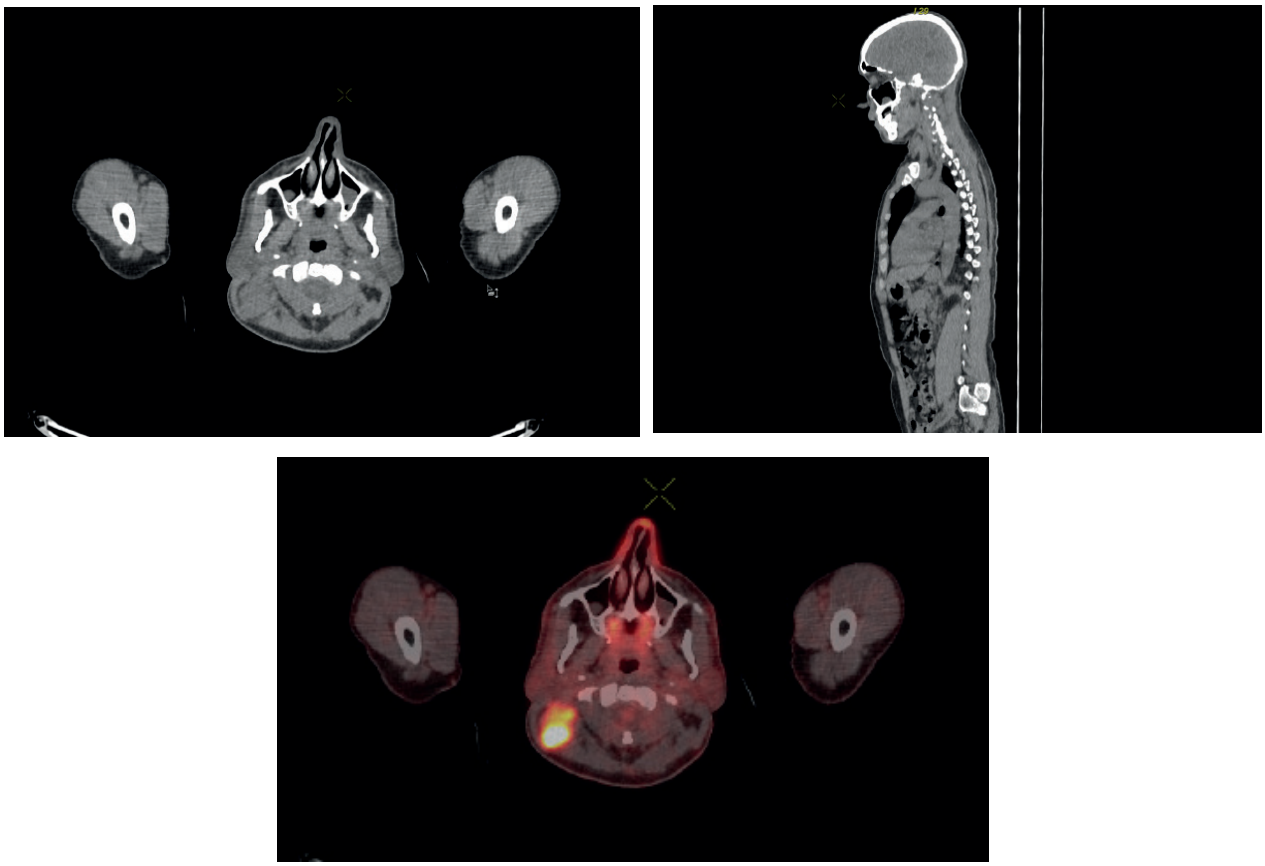

Figure 6. *(a) Axial CT showing bilateral retention cysts. (b) Sagittal CT image showing bilateral retention cysts. (c) Fused PET/CT image demonstrating bilateral retention cysts with insignificant FDG uptake.*

the disease, especially in cancer patients who are already immunocompromised and are at more risk of developing sinusitis and its complication.

The results of our study are almost similar to other studies on radiological imaging. Maxillary sinus mucosal thickening was the most commonly reported pathology in the sinuses, with a higher prevalence in men [10]. Manjit [5] documented maxillary sinus to be the most commonly involved sinus (86.36%) in his study. Maru and Gupta [15] also reported maxillary sinuses as the most commonly involved sinuses and the least was sphenoid sinuses. In a similar study on incidental sinus disease on PET/CT, out of 1,438 studied cases, 127 (8.8%) cases demonstrated sinus disease, with the majority being male patients (91, 71.7%). 26 patients (20.5%) demonstrated FDG-avid sinusitis and the remaining 101 (79.5%) demonstrated CT-only sinus disease [16].

Incidental PET-positive findings produce a tricky situation for clinicians, as FDG PET-CT is mostly performed in the cancer settings. The issue to address is whether the incidental finding is related to the primary disease or symbolizes a secondary tumor or an inflammatory/infectious pathology [6]. The edge of fused FDG PET-CT images in the paranasal sinuses is to obtain additional information

from CT findings and thus improve the diagnostic ability [17]. Incidentally raised FDG uptake in other head and neck areas was previously discussed in the literature. A recent study by Britt et al. [18] examined the FDG PET-CT of 293 patients with head and neck cancers. An incidental finding was documented for 35.2% of the patients, specifically in the head and neck area for 45 of them. A malignant lesion was documented for only one patient, in the parotid gland [18]. However, we found paucity of literature on incidental increased FDG uptake in the sinonasal region. A few studies analyzed the distribution of FDG uptake and SUVs in different sinonasal lesions, striving to distinguish between inflammatory, benign, and malignant lesions. In one study in the pediatric oncologic population, a total of 25 patients with paranasal sinus disease were identified [7]. Another study revealed that incidental findings with increased FDG uptake in the sinonasal spaces mimic a high risk (40%) of neoplasia and a diagnostic biopsy is needed in such cases [6]. Nonetheless, the treatment of patients with incidental sinonasal FDG uptake remains unclear.

Limitations of the study

Correlation with the medical history of sinus diseases was not made and as this was a retrospective study, correlation with any symptoms of mucosal disease could not be made.

Conclusion

From the findings of this study, it can be concluded that the frequency of incidental sinus findings of inflammatory and noninflammatory disorders is not seen uncommonly in cancer patients. It is often difficult to discriminate between inflammatory and noninflammatory sinus mucosal diseases on CT studies; however, sinusitis is a serious concern with cancer patients on chemotherapy, as these patients are already immunocompromised and very prone to develop serious infections and complications. Mucosal sinus disease should be observed, reported, and monitored and/or treated to prevent the disease from progressing and/or spreading to surrounding structures.

List of Abbreviations

FDG PET/CT:	Fluorodeoxyglucose positron emission tomography/computed tomography
GI:	Gastrointestinal
HL:	Hodgkin's Lymphoma
NHL:	Non Hodgkin's Lymphoma
SUV:	Standardize Uptake Value 5.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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None.

Consent to participate

Written consent was obtained from all the participants.

Ethical approval

Ethical approval was granted by the local Ethics Committee, reference IRB Approval # 0028 dated: 06.10.2020

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