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Case Series

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Role of HRCT in detection and characterization of pulmonary abnormalities in pediatric patient's undergone bone marrow transplant

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ABSTRACT

BACKGROUND & OBJECTIVE: Advancements in transplant regimens, alternative grafts, and new indications have improved bone marrow transplant activity with time. Our objective is to determine the pattern of pulmonary abnormalities using High resolution computed tomography (HRCT) chest scan and to determine the diagnostic accuracy (pulmonary abnormalities) and efficacy (in terms of radiation burden) of HRCT and X-rays after bone marrow transplant.

METHODOLOGY: It was a descriptive case series conducted at the department of Radiology, POF Hospital, Wah Cantt over a duration of 8 months (January 2021-Augest 2021). A sample size of 20 patients was calculated using the WHO calculator. Patients were recruited through non-probability consecutive sampling. Patients were undergone through HRCT and chest X-rays for diagnostic accuracy and radiation burden measurement. Data was analyzed using SPSS version 24. Fisher exact test, Receiver Operating characteristic (ROC) Curve analysis and t-test was applied for statistical analysis. p-value ≤0.05 was considered significant.

RESULTS: A total of 20 patient's undergone bone marrow transplants were included in the study. The mean age of patients was 5.25years.There were 11(55%) male and 9(45%) female in study. Pattern of pulmonary abnormalities was pleural effusion 2(10%) following nodules 1(5%), pneumonia patches 1(5%), ground glass opacities 1(5%) and septal thickening 1(5%). The diagnostic accuracy of HRCT was found to be high as compared to X-rays (88% vs 57% respectively). The mean radiation dose in HRCT and mean radiation dose in X-rays' indicate a high radiation burden in HRCT (p≤0.001).

CONCLUSION: Despite of high radiation burden in HRCT, it had high diagnostic accuracy as compared to X-rays.

KEYWORDS: High-resolution computed tomography, Pulmonary abnormalities, Diagnostic accuracy.

INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) or bone marrow transplant is an antineoplastic adoptive immunotherapy for hematological malignancies and conditions associated with bone marrow failure[1]. In the United States, an estimated 11.7 million individuals had cancer in 2007. Out of all these patients, 8% were diagnosed with hematological malignancies [2]. Bone marrow transplant offers the best chance for long-term survival among hematologic malignancies and other related disorders. An estimated 20,000 patients undergo bone marrow transplants each year in the United States[3]. In Pakistan, 9 persons/10 million populations underwent HSCT in 2016[4]. Thalassaemia is a major cause of bone marrow transplants. It is a single-gene disorder of globin chain synthesis worldwide. In Pakistan, 5% of the population is affected with thalassemia minor [5].

The early and long-term survival rate after Bone marrow transplant has been improved with the advancement in transplant regimens and alternative grafts. Literature reported that patients who survived in remission for the initial few years had the highest (80-90%) probability of survival in

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the next 10-15 years [6]. Late complication of bone marrow transplant related to pre, peri and post-transplant exposure is significantly associated with patient mortality and morbidity rate. Moreover, lifelong surveillance is mandatory to screen and prevent complications [7].

Bone marrow is used as a stem cell source through the cord or peripheral blood. An estimated 14 million volunteer donors are registered worldwide [8]. Bone marrow transplantation is a standard care treatment for patients with defined acquired and congenital disorders of the hematopoietic system. Pulmonary abnormalities after bone marrow transplant are usually diagnosed with chest radiographs or X-rays as standard initial investigation [9]. Several studies reported that the sensitivity of chest radiographs is very low for the detection of pulmonary abnormalities after bone marrow transplantation [10].

The latest technique for pulmonary abnormalities diagnosis is high-resolution computed tomography (HRCT). HRCT can detect pulmonary abnormalities with a high degree of accuracy and differentiate between several types of infections [11]. HRCT is a non-contrast computed tomography and reconstruction process. HRCT is associated with high-resolution images and high-frequency reconstruction algorithms due to the acquisition of thin slices (0.5 to 1mm) [12]. HRCT is used for early detection and exclusion of focus of infection, broad category infective causes identification, and disease pattern identification and acts as the most sensitive technique for Broncho alveolar lavage (BAL) for pneumonia detection[13]. Limited data are available on the diagnostic accuracy of HRCT in Pakistan. The present study aims to determine the pattern of pulmonary abnormalities with HRCT chest scan to determine diagnostic accuracy (pulmonary abnormalities) and efficacy (in terms of radiation burden) of HRCT and X-rays after bone marrow transplant.

METHODOLOGY

A Descriptive case series was conducted at the Department of Pediatrics, Wah Medical College POF Hospital, Wah Cant over a period of 8 months (January 2021-Augest 2021). A sample size of 22 patients (rounded off to 20) was calculated with 3%[13] pulmonary abnormalities (consolidation), 95% confidence interval and 5% significance level using the WHO calculator. Non-probability consecutive sampling was used for patient selection. Patients with age <15 years, both gender, underwent bone marrow transplants, and patients who presented with pulmonary abnormalities within 30 and 100 days following the transplant were included in the study.

Patients who did not achieve engraftment and had evidence of pulmonary embolism were excluded from the study. Ethical approval was taken from the ethical review board (ERC=P0FH/ERC/10/20), and consent forms were taken from all participants.

Patients have undergone detailed clinical examination and laboratory investigation, including serum biochemistry, complete blood count, and ultrasonography abdomen. Patients were undergone post-bone marrow chest radiography and HRCT for suspected clinical abnormalities.

Patients with cough, dyspnea, diminished physical reserves, and frequent airway infections were considered pulmonary disease positive, while those not showing these symptoms were pulmonary disease negative. Spirometry will be used for airflow impairment. Recommended position for HRCT was prone; however, critically ill patients were positioned in a supine position.

Radiation burden was measured through radiation dose. Radiological findings were reported by an experienced radiologist. Patients who showed a neutropenic period within 3 weeks characterized by fungal infection and cytomegalovirus (CMV) pneumonia in 100 days were HRCT positive, while those not showing these signs were negative. Diagnostic accuracy and radiation burden of HRCT and X-rays were measured. Data was analyzed using SPSS version 24. Mean and standard deviation was calculated for descriptive data, while frequency and percentages were calculated for qualitative data. Fisher exact test, t-test and ROC curve analysis for diagnostic accuracy measurement were done.

RESULTS

A total of 20 patient's undergone bone marrow transplants were included in the study. The mean age of patients was 5.25 years. There were 4(20%) patients in the age group 4-7 years and 16 (80%) in >8-15 years age group. There were 11(55%) male and 9(45%) female in study. Among all the patients 20(100%), 1(5%) had chronic myelogenous leukemia, 1(5%) severe aplastic anemia, 1(5%) had acute non lymphocytic leukemia, 1(5%) had myelodysplastic syndrome and 2(10%) had thalassemia. The majority of patients showed pleural effusion 2(10%), as shown in table-I.

Among disease-positive individuals, 6(30%) were positive on HRCT, while for those who were pulmonary disease negative, 2(10%) were HRCT positive and 12(60%) were HRCT negative (p=0.001). Among all those who were pulmonary disease negative, 5(25%) were X-rays positive, and 9(45%) were X-rays negative (p=0.642), as shown in Table-II.

HRCT has 100% sensitivity, 86% specificity, 75% positive predictive value, and 100% negative predictive value, while X-rays have 50% sensitivity, 64% specificity, 38% positive predictive value and 75% negative predictive value, as shown in table-II. The accuracy of HRCT is 88%, while x-rays accuracy is 57%, as shown in Figure 3 ROC curve analysis.

Table-II shows the mean radiation dose in HRCT and the indication of high radiation burden in HRCT ($p \leq 0.001$).

Table-I: Pattern of pulmonary abnormalities.

Pattern of Pulmonary abnormalities	n(%)
Pleural effusion	2(10%)
Nodules	1(5%)
Pneumonia patches	1(5%)
Ground glass opacities	1(5%)
Septal thickening	1(5%)

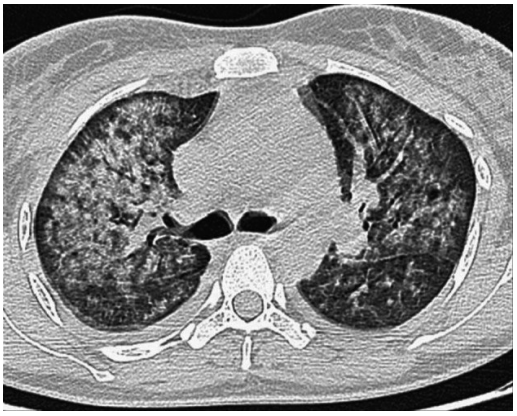


Figure-I: Bilateral diffuse ground glass opacity with air space consolidation.

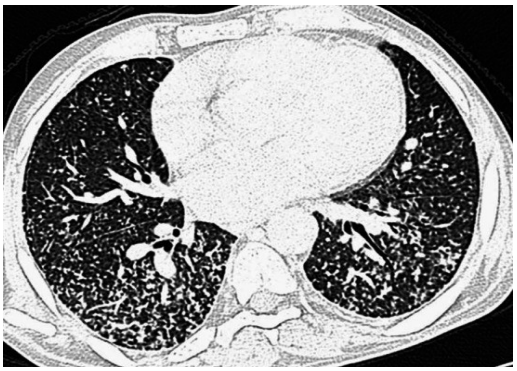
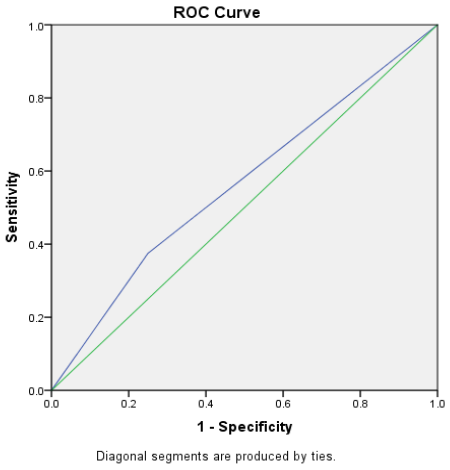


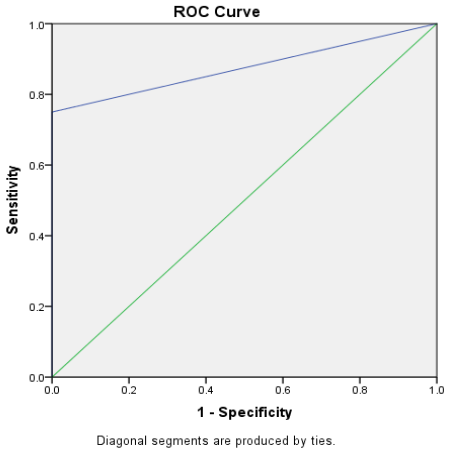
Figure-II: High-resolution computed tomography chest shows multiple small randomly distributed nodules in both lungs with a tree-in-bud appearance at places.

Table-III: Radiation burden of X-rays and HRCT.

Radiation Dose(millisievert)	Mean±SD (n=20)	p-value
X-rays	0.0064 mSv±0.00017	0.001
HRCT	0.4090 mSv±0.42899	



Receiver operating characteristics curve analysis of HRCT



Receiver operating characteristics curve analysis of X-rays

Figure-III: Receiver operating characteristics curve analysis of HRCT and X-rays.

Table-II: Association between pulmonary abnormalities and high-resolution computed tomography, X-rays.

HRCT	Pulmonary diseases			
	Positive	Negative	Total	p-value
Positive	6(30%)	2(10%)	8(40%)	0.001
Negative	0(0%)	12(60%)	12(60%)	
X-rays				
Positive	3(15%)	5(25%)	8(40%)	0.642
Negative	3(15%)	9(45%)	12(60%)	
Total	6(30%)	14(70%)	20(100%)	

DISCUSSION

HRCT is an important chest diagnostic test that plays a significant role in pulmonary abnormalities diagnosis. Tomographic patterns are usually nonspecific; however, they are useful in understanding which part of the lung is affected by diseases[14]. HRCT is also effective in showing coexisting infections like idiopathic pneumonia syndrome and bronchiolitis obliterans organizing pneumonia, leading to narrowing down differential diagnosis [15].

In the present study, a total of 20 patients who underwent bone marrow transplants were included. The pattern of pulmonary

abnormalities was pleural effusion 10%, followed by nodules in 5% of cases, pneumonia patches 5%, ground glass opacity 5% and septal thickening 5%. Boeckh et al. reported that the majority of patients undergoing hematopoietic stem cell transplantation had air space consolidation 54.8% following ground glass opacity 47.1% and nodules 38%[15,16]. Another similar study reported that lamphydenopathy 20.3% was the most common pulmonary abnormality after nodular shadow (38%) among bone marrow transplant patients[17].

In the present study, HRCT has 100% sensitivity, 86% specificity, 75% positive predictive value, 100% negative predictive value, while X-rays had 50% sensitivity, 64% specificity, 38% positive predictive value and 75% negative predictive value. The accuracy of HRCT is 88%, while that of X-rays is 57%. Zwirewich reported that HRCT had 85% sensitivity and 99.9% specificity with high diagnostic accuracy 87% in pulmonary infections diagnosis after bone marrow transplant [18]. Another similar study reported that HRCT is an effective diagnostic technique as compared to other parameters, including X-rays and ultrasound [19].

Comparison of Mean radiation dose in HRCT and x-rays indicate high radiation burden in HRCT ($p \leq 0.001$). Mayo et al. reported that the radiation dose of HRCT for chest is very high compared to routine scans [19,20]. Another similar study reported that X-rays had significantly lower radiation dose as compared to HRCT in hematopoietic stem cell transplantation patients [21].

CONCLUSION

HRCT chest is an excellent diagnostic modality for pulmonary abnormalities pattern identification among bone marrow transplant patients. HRCT has high diagnostic accuracy compared to X-rays; however, HRCT places high radiation burden on patients compared to X-rays in terms of high radiation dose. Therefore, it is recommended to restrict HRCT to limited indications and use X-rays as an initial investigation method for pulmonary abnormalities to avoid excessive radiation burden on patients.

LIMITATION: Small sample size and conduction of the study at a single center limits the generalizability of the study.

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Tahir Mehmood: Substantial contributions to the conception or design of the work
Sidra Tahir: Interpretation of data for the work
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Muhammad Arslan Farooq: Final approval of the version to be published
Shayan Gillani: Data acquisition, and data analysis for the work.

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