

## Role of MRI in the Diagnosis of Different Bone Marrow Lesions in Pediatric Patients with Hematological Malignancies

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### ABSTRACT

**Background:** hematological malignancies are one of the major causes of childhood morbidity; leukemia is the most common of pediatric cancers whereas lymphoma is the third most common childhood malignancy, NHL accounts for approximately 7% of cancers in children younger than 20 years. In patients with hematological malignancies the diagnosis of bone marrow involvement is important to determine prognosis and treatment protocols. MR imaging is the most sensitive imaging modality in the diagnosis of bone marrow infiltration and provides excellent details and additional accurate information about the extent of bone marrow involvement. **Aim of the Work:** this study aimed to evaluate the role of MRI in the diagnosis of different bone marrow lesions in pediatric patients with hematological malignancies with a trial to highlight the role of different recent modalities in the diagnosis, staging, monitoring management and in post treatment follow up of these patients. **Patients and Methods:** this study involved 63 patients (37 males and 26 females) with mean age of 9 years (range from 1.5 years: 16 years). They are cases of bone marrow biopsy proven hematological malignancy. They were categorized into two groups, **group I:** new cases who had bone marrow infiltration, they received no previous chemotherapy, **group II:** cases under follow up who have bone infarction, with history of chemotherapy or bone marrow transplantation (BMT). The MRI examinations were performed on a superconducting 1.5 T unit. Chi-square test was used to study the association between each 2 variables or comparison between 2 independent groups as regards the categorized data. The probability error at 0.05 was considered significant, while at 0.01 and 0.001 were highly significant. **Results:** the different bone marrow lesions included in this study group of patients showed different MRI diagnostic criteria. A highly significant probability of errors was found in the relation between ADC values of bone infarction, bone marrow infiltration and red marrow. **Conclusion:** MRI provides an excellent imaging modality for the diagnosis of different bone marrow lesions in pediatric patients with hematological malignancies and can reliably differentiate between them based on the characteristic findings of each. **Keywords:** bone marrow, leukemia, lymphoma, magnetic resonance imaging.

### INTRODUCTION

Leukemia is the most common cancers of pediatric accounting for about 30% of diagnoses<sup>(1)</sup>. Lymphomas, Hodgkin's and non-Hodgkin's lymphoma, represent 3%–5% of all malignancies worldwide. By statistics, bone marrow involvement found in 5%–15% of patients with Hodgkin's lymphoma and in 20%–40% of non-Hodgkin's lymphoma patients<sup>(2)</sup>.

Bone is a substantial tissue, yet its pattern on plain X-rays may be misleading indicating inactivity. It is composed of an irregular mesh of collagen, called woven-fibered bone, which is a transient substance that either forms a marrow cavity or replaced by an osseous tissue arranged in cords, called lamellar bone<sup>(3)</sup>. In patients with hematological malignancies the diagnosis of bone marrow infiltration is crucial to determine prognosis and to identify suitable treatment protocols<sup>(2)</sup>. MR imaging is undoubtedly an extremely sensitive technique in the demonstration of bone marrow infiltration<sup>(4)</sup>.

**AIM OF THE WORK** The purpose of this study is to evaluate the role of MRI in the diagnosis of different bone marrow

lesions in pediatric patients with hematological malignancies with a trial to highlight the role of different recent modalities in the diagnosis, staging, monitoring management and in post treatment follow up of these patients.

### PATIENTS and METHODS

This study involved 63 patients (37 males and 26 females) with mean age of 9 years (range from 1.5 years: 16 years).

They are cases of bone marrow biopsy proven hematological malignancy i.e leukemia and lymphoma based on bone marrow biopsy, they were all referred to the MRI to investigate their complaint of pain either back pain or limb pain and the MRI examinations were tailored according to the patient complaint, contrast was added if patient condition permitted, sedation was used in non cooper able young patients below 7 years old, They were divided into two groups, **group I:** new cases who have bone marrow infiltration, they received no previous chemotherapy, **group II:** cases under follow up who have bone infarction, with history of chemotherapy or bone marrow transplantation (BMT) Chi-square

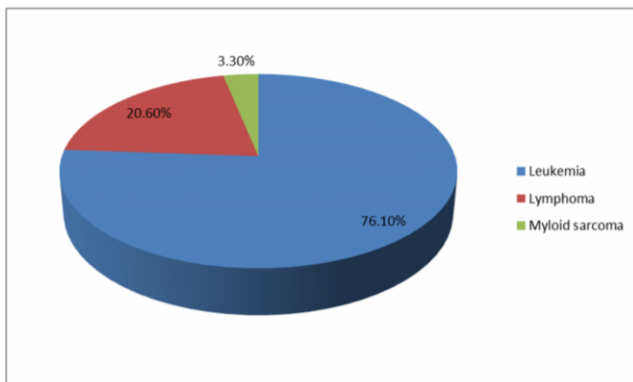
test to study the association between each 2 variables or comparison between 2 independent groups as regards the categorized data. The probability error at 0.05 was considered significant, while at 0.01 and 0.001 they were highly significant.

**The study was done after approval of ethical board of Ain Shams university and an informed written consent was taken from each participant in the study.**

**RESULTS**

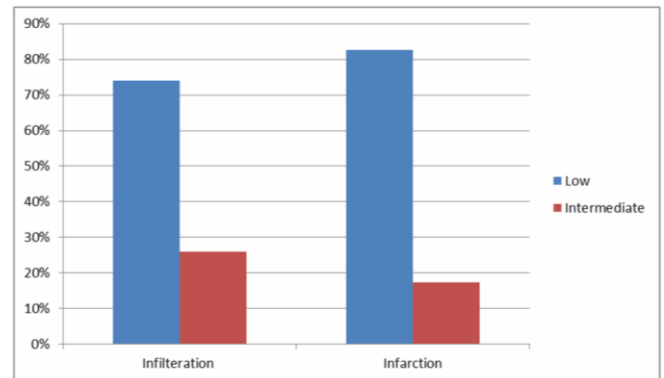
Patients were categorized into two groups, **group I:** consisted of 35 cases, they were new cases who have bone marrow infiltration, they received no previous chemotherapy, **group II:** consisted of 28 cases, they were cases under follow up who have bone infarction, with history of chemotherapy or bone marrow transplantation. This study included 63 cases, of which 26 were females representing 41% and 37 were males representing 59% with mean age of 9 years (range 1.5 years- 16 years)

We found no significant correlation between gender and hematological malignancy ( $p=0.173$ ). The study included 63 cases, 48 cases with leukemia representing 76.1%, 13 patients of lymphoma representing 20.6% and 2 patient (3.3%) with myloid sarcoma.



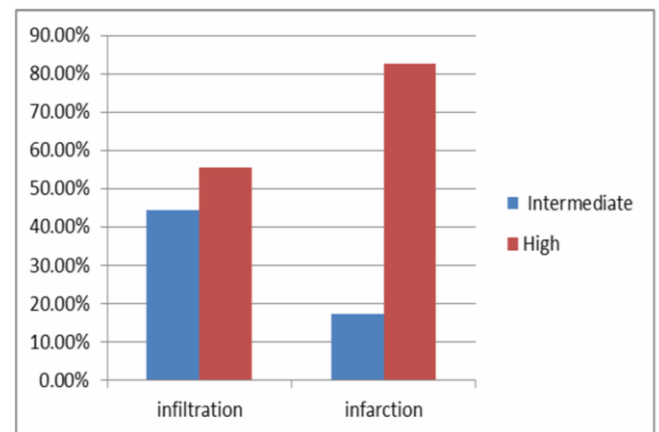
**Fig. 1: distribution of cases among different hematological malignancies**

This study included 35 patients with marrow infiltration, 26 patients of them showed low signal of their infiltrated marrow in comparison with the adjacent muscles on T1 WI representing 74% of the cases with marrow infiltration, whereas the remaining 9 patients showed intermediate signal intensity representing 26%. Regarding the 28 patients with bone infarction, 23 of them showed low signal intensity representing 82.2% and 5 showed intermediate signal intensity representing 17.8%. Using low T1 signal intensity as a sign of marrow infiltration showed 74.2% sensitivity and 65 % specificity with positive and negative predictive value of 79% and 59% respectively.

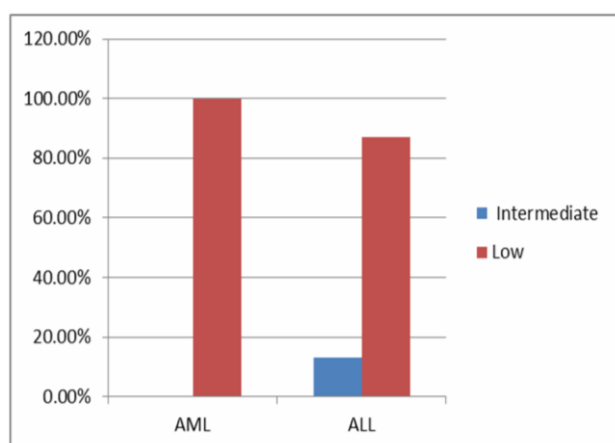


**Fig. 2: column chart showing the T1WI signal characteristics of the marrow lesions**

This study included 35 patients with marrow infiltration, 16 patients of them showed intermediate signal of their infiltrated marrow on T2 WI representing 44.4% of the cases with marrow infiltration, whereas the remaining 19 patients showed intermediate signal intensity representing 55.6%. Regarding the 28 patients with bone infarction 23 of them showed high signal intensity representing 82.7% while only 5 showed intermediate signal intensity representing 17.3%. Using high T2 signal intensity as a sign of marrow infiltration showed 54.2% sensitivity and 45 % specificity with positive and negative predictive value of 63.33% and 36% respectively.

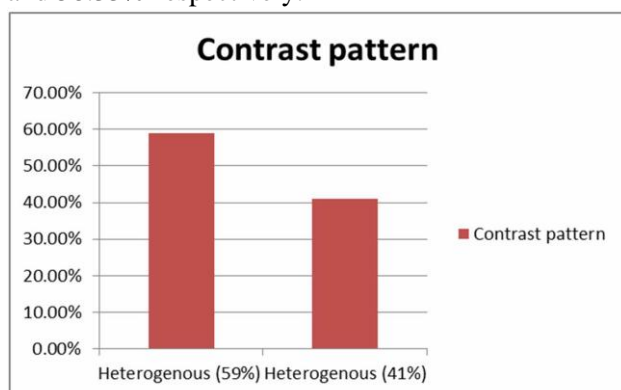


**Fig. 3: column chart showing the T2WI signal characteristics of the marrow lesions.**



**Fig 4: column chart showing T1 signal pattern of AML and ALL.**

As regards using heterogeneous contrast enhancement as a sign of marrow infiltration, it showed 58.33 % sensitivity and 100% specificity, with positive and negative predictive value of 100 % and 58.33% respectively.



**Fig 5: column chart showing contrast pattern of cases of marrow infiltration.**

The ADC of marrow infiltrative lesions ranged from  $0.36$  to  $0.59 \times 10^{-3} \text{ mm}^2/\text{s}$  with a mean value is  $0.502 \times 10^{-3} \text{ mm}^2/\text{sec}$ , while the ADC value of bone infarction ranged from  $1.22$  to  $1.97 \times 10^{-3} \text{ mm}^2/\text{s}$  with a mean value of  $1.71 \times 10^{-3} \text{ mm}^2/\text{s}$

## DISCUSSION

Hematologic malignancies are a heterogeneous group of diseases including myeloid neoplasms, lymphoid neoplasms (leukemia and lymphoma) and plasma cell disorders. Leukemia is a cancer of the blood cells that arises in bone marrow. It may be characterized as acute or chronic, depending on the maturity of the cells of origin and the disease course if untreated. Lymphoma arises in the lymphatic organs (ie, lymph nodes, spleen) and lymphatic ducts<sup>(5)</sup>.

Lymphomas are broadly divided into two major categories, Hodgkin lymphoma (HL) with a crude incidence rate of 3/100,000 and non-Hodgkin

lymphomas (NHL), which are approximately eight times more common<sup>(6)</sup>.

Leukemias are a group of diverse neoplasms which are derived from the arrested or aberrant development of a clone of normal hemopoietic cells. These immature cells proliferate progressively within the bone marrow replacing normal hemopoietic tissue and circulate within the peripheral blood becoming deposited in various organs and tissues, such as the spleen and lymph nodes<sup>(7)</sup>.

Regarding gender based susceptibility to hematological malignancies **Choi et al.**<sup>(5)</sup> found that hematologic malignancies were generally more common in males. This is in contrary to our study where we did not find significant sex predilection. This can be explained by the low sample size in the current study.

Some authors reported that leukemia is the most common hematological malignancy in pediatric age group<sup>(8,9)</sup>. This is in line with the current study where 76.1% of cases had leukemia.

As regards subtypes of leukemia we found that of the 48 leukemic patients involved in our study, 42 patients were biopsy proven ALL were representing 87.5%, similar results were detected by some authors<sup>(8,9)</sup>. They stated that ALL has the highest prevalence in pediatric age group.

We found no significant difference between AML and ALL as regards their MRI signal patterns. This is in agreement with the study of **Mulrooney et al.**<sup>(8)</sup> who stated that ALL cannot be reliably distinguished from AML by MRI

Using skeletal muscles and intervertebral discs as reference of bone marrow signal intensity has been suggested by **Silva et al.**<sup>(2)</sup> who stated that the diffuse pattern of marrow infiltration usually elicits low T1 signal in comparison to the adjacent muscles. Such conclusion has also been reached by different authors<sup>(10,11)</sup>. In the current study, we have compared the signal intensity of infiltrated bone marrow at T1 WI to that of the adjacent normal skeletal muscles or intervertebral disc, it showed 74.2% sensitivity and 65% specificity with positive and negative predictive value of 79% and 59% respectively, additionally of the 20 subjects included in our control group, 7 (35%) of them have shown low T1 signal of their normal red marrow in comparison to the adjacent muscle suggesting that T1 WI should not be used solely in the diagnosis of bone marrow infiltration.

In the present study, IV contrast was given to 12 cases with marrow infiltration. All the lesions showed contrast enhancement, however 5 (41%) of

them showed homogenous enhancement pattern whereas 7 (59%) showed heterogeneous enhancement. This agrees with results of **Ilaslan and Sundaram** <sup>(12)</sup> who stated that bone marrow infiltrates tend to enhance, although foci of absent enhancement could be seen suggestive of necrosis which results in heterogeneous pattern of enhancement. On the other hand, contrast enhanced studies were done in 7 control subjects, it revealed that normal red marrow enhances homogeneously in

100% of subjects, this agrees with results of some authors <sup>(10,13)</sup>. They stated that red marrow can enhance due to rich blood supply, high cellular density, and substantial extravascular space.

In this study, patients with bone marrow infiltration showed ADC values ranged from 0.36 to 0.59  $\times 10^{-3}$  mm<sup>2</sup>/s which agreed with the study done by **Dietrich *et al.*** <sup>(14)</sup> who found untreated patients to have ADC values of 0.45  $\pm$  0.354  $\times 10^{-3}$  mm<sup>2</sup>/s.

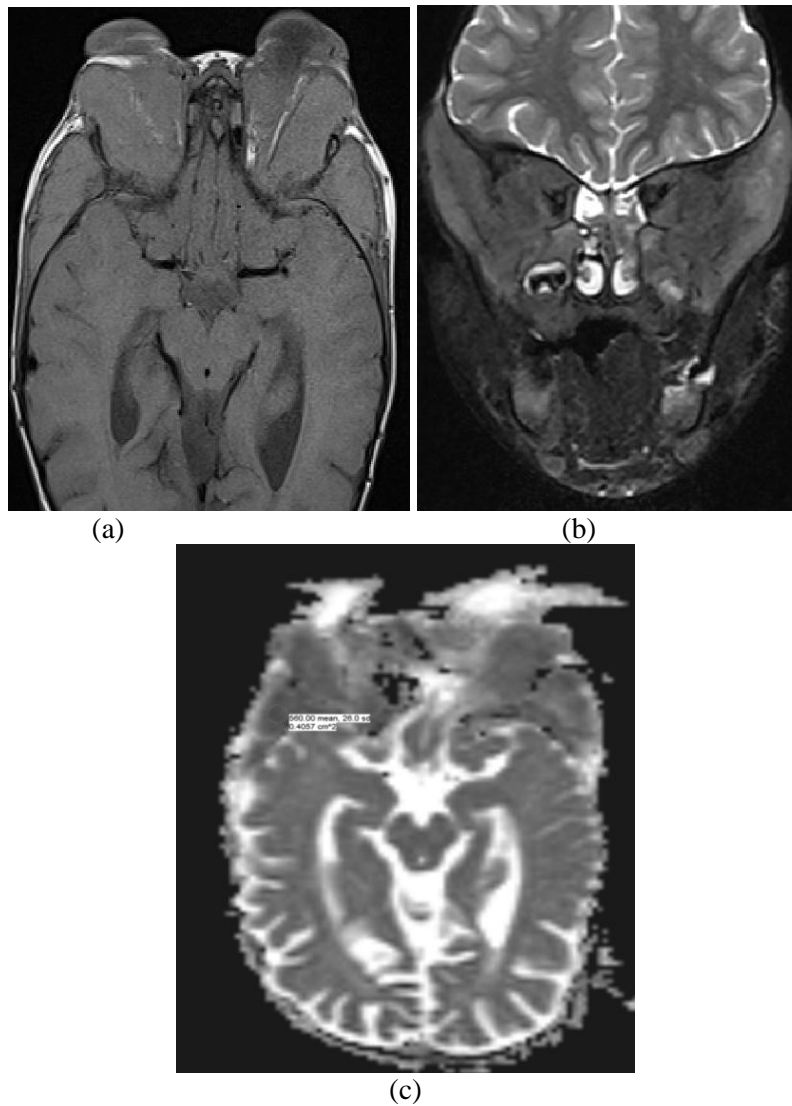


Fig 1: axial T1 WI elicit intermediate SI(a), coronal STIR elicit intermediate SI(b), ADC =560  $\times 10^{-3}$  mm<sup>2</sup>/sec(c). Images show bilateral rather symmetrical abnormal marrow SI of both temporal bones.

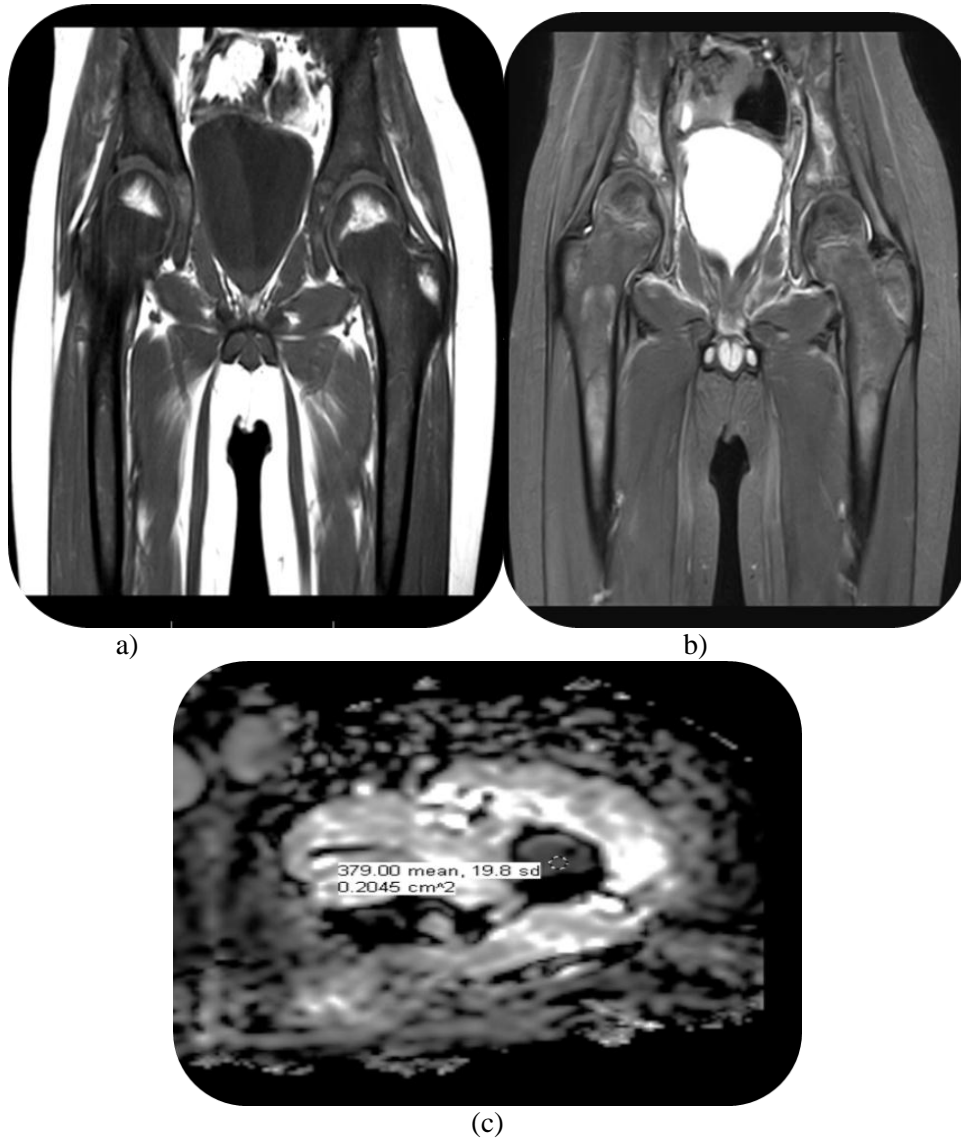


Fig 2: diffused abnormal marrow SI is seen at the both iliac bones as well as both femoral diaphysis.  
Fig. A coronal T1 WI elicit abnormal low SI lower than that of the adjacent normal skeletal muscles.  
Fig. B coronal STIR they elicit abnormal patchy bright signal  
Fig. E ADC values of the left femur is  $0.379 \times 10^{-3} \text{ mm}^2/\text{sec}$

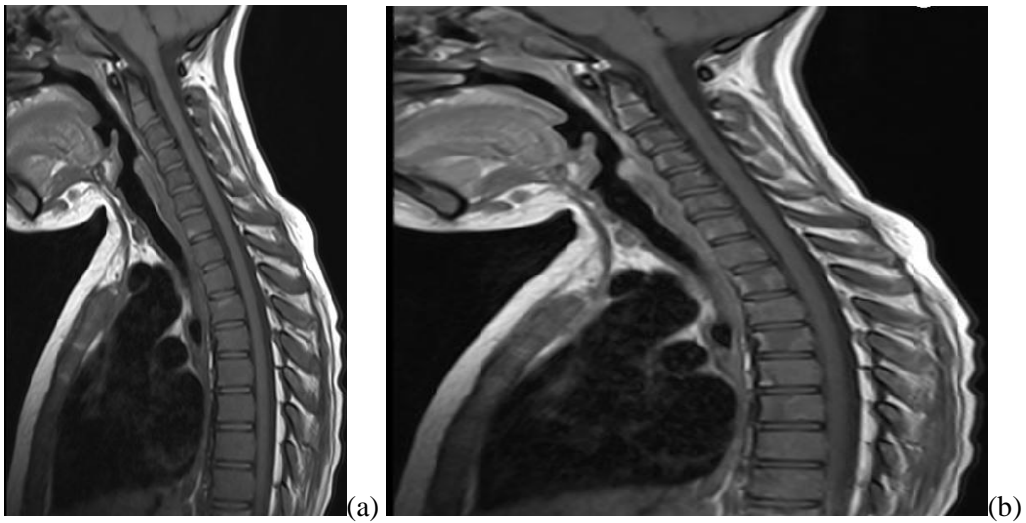


Fig. 3: a) sagittal T1 WI of the cervical and upper dorsal vertebrae elicit heterogeneous SI, b) sagittal post contrast T1 WI of the cervical and upper dorsal vertebrae show heterogeneous postcontrast enhancement.

## CONCLUSION

Patients with hematological malignancy can show infiltrative marrow lesions, bone infarcts or normal red marrow reconversion. Conventional MRI sequences including T1 and T2 WI are not reliable to discriminate between different marrow lesions. Contrast enhanced studies as well as ADC value have additive role in differentiating between different marrow lesions. However, despite several imaging techniques, several encountered diagnostic dilemma can be solved simply by being acquainted with patient's history and age matched pattern of bone marrow conversion and reconversion. Last but not least, MRI has the ability to provide broader assessment of bone marrow status which had rendered MRI to become a key player regarding bone marrow involvement in cases of hematological malignancies overcoming bone marrow biopsy in several aspects.

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