INTRODUCTION

The high spatial resolution and excellent soft-tissue contrast make MR imaging an ideal tool for the detection of parenchymal and osseous lesions. The limited field of view restricting coverage to a single body region must be considered a major limitation of conventional MR imaging **(*O'Connell et al., 2002*).**

Whole-body fast MR imaging protocols have been shown to be an effective and time-efficient means of evaluating the entire skeleton for metastases and staging of head and neck cancers and lymphoma ***(Schmidt et al., 2005).***

It is possible to obtain MR images of the entire body with high quality in 30 minutes ***(Schick et al., 2005).***

Using fast MR sequences, whole-body MR imaging has been shown to be superior to bone scan in detecting lesions in the extremities, pelvis, and spine and provides additional important information about tumor morphology, tumor extension, and neurologic complications. Whole-body MR imaging is also used to detect response to therapy ***(Ballon et al., 2004)***.

MRI is ideally suited for evaluation of both diffuse and focal bone marrow disease. The bone marrow can be affected by a wide variety of pathologic processes, such as myeloproliferative diseases, osteomyelitis, and hemochromatosis, but metastatic disease is the most common cause of bone marrow disease ***(Altehoefer et al., 2008).***

MRI has some advantages over PET/CT and CT when evaluating neoplastic bone lesions. When the lesions are restricted to the bone marrow and if the trabecular bone is not significantly destroyed, CT can be negative. Also, because of tissue contrast, MRI can show smaller lesions (up to 2 mm) than CT (5 mm) and FDG PET (6 mm) ***(Schmidt et al., 2007).***

The interest in the clinical application of whole-body MRI is rapidly increasing, Furthermore, whole-body MRI may be an excellent alternative to whole-body positron emission tomography (PET)/computed tomography (CT) ***(Ohno et al., 2008)***, given its wider availability, and the lack of ionizing radiation ***(Law et al., 2009) ,*** thus gaining increasing importance and application in pediatrics ***(Darge et al.,2008).***

AIM OF THE WORK

The purpose of this study was to evaluate the diagnostic potential of a whole-body bone marrow MR protocol in the detection of bone marrow oncological diseases children.

NORMAL MAGNETIC RESONANCE IMAGING ANATOMY OF BONE MARROW

Gross Anatomy:

Bone marrow is the flexible tissue found in the interior of bones. In humans, red blood cells are produced in the heads of long bones, in a process known as hematopoiesis, on average, bone marrow constitutes 4% of the total body mass of humans; in an adult weighing 65 kilograms bone marrow accounts for approximately 2.6 kilograms. The hematopoietic compartment of bone marrow produces approximately 500 billion blood cells per day, which use the bone marrow vasculature as a conduit to the body's systemic circulation ***(Gordana et al., 2010)***.

The normal bone marrow has three primary components: osseous matrix, red marrow, and yellow marrow. The osseous components of the marrow are the trabeculae of cancellous bone **(Fig. 1)** which provide the supporting framework for the red and yellow marrow elements. The red or cellular marrow is hematopoietically active, producing RBCs, WBCs, and platelet precursors. Hematopoietically inactive yellow marrow is composed of fat cells. These two types of marrow differ in their chemical composition. Recognition of these differences is important to understanding the MRI appearance of marrow. In infants and young children, red marrow consists of approximately 40% water, 40% fat, and 20% protein. As the individual ages, the fatty elements of hematopoietic marrow increase, and by age 70 years, red marrow is composed of approximately 60% fat, 30% water, and 10% protein. Yellow marrow contains approximately 80% fat, 15% water, and 5% protein ***(Siegel, 2000).***

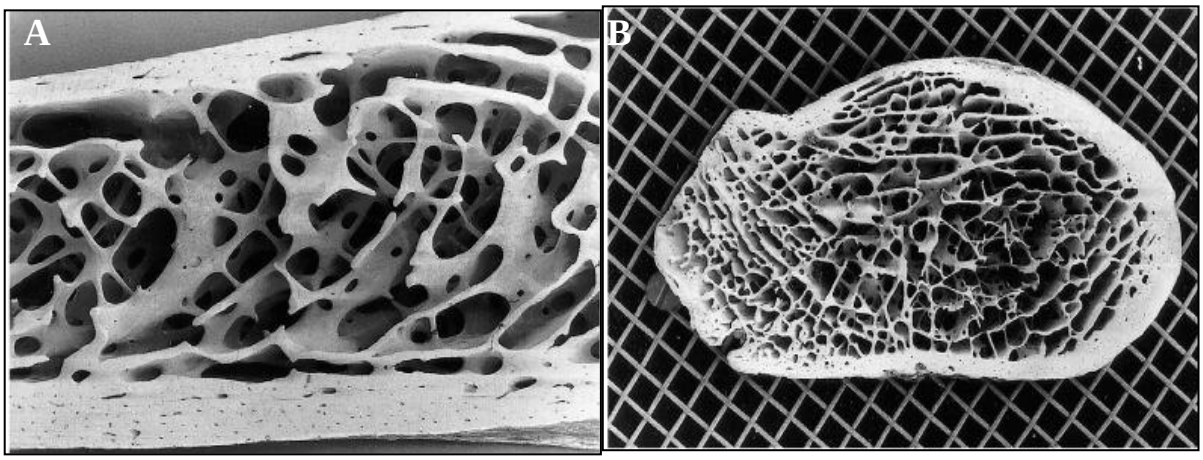

Figure (1): (a) Vertical section 2 cm below the anterosuperior border of the iliac crest. The cancellous bone consists of intersecting curved plates and struts. Osteonal (Haversian) canals can just be seen in the two cortices at this magnification **(b)** Transverse section, femoral neck (male, 45 years) viewed from the distolateral aspect towards the femoral head, showing the predominant pattern of curved intersecting plates in the cancellous bone ***(Quoted from Siegel, 2000).***

Red (hematopoietic) marrow is located within the spaces defined by the trabeculae. It is semifluid in consistency and is composed of the various hematopoietic stem cells and their progeny in assorted stages of granulocytic, erythrocytic, and megakaryocytic development. Uncommitted lymphocytes, as well as lymphoid nodules, are also present in the red marrow. The hematopoietic cellular elements are supported by reticulum cells and fat cells. The vascular system consists of centrally located nutrient arteries that send out branches that terminate in capillary beds within the bone. Postcapillary venules re-enter the marrow cavity and coalesce to form venous sinuses. Hematopoietic cell production follows the vascular arrangement, forming active hematopoietic islands between the sinusoids. Bone marrow lacks lymphatic channels. Because yellow marrow is predominantly composed of fat, it is sometimes called

fatty marrow ***(David and Miriam, 2007)***. It is too simplistic to think of red marrow as being simply made up of cells and yellow marrow as being simply made up of fat; in reality it is more complex, with relative amounts of both present in all marrow **(Fig. 2)** ***(Burdiles and Babyn, 2009).***

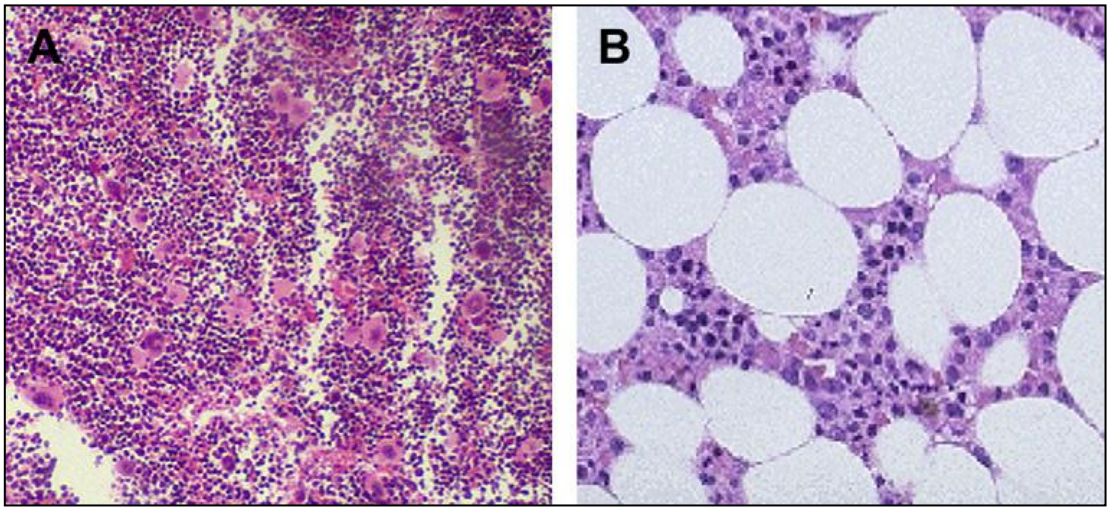

Figure (2): Histologic specimens of bone marrow demonstrating highly cellular marrow **(a)** and fatty marrow **(b)** (hematoxylin and eosin, original magnification -200) ***(Quoted from Burdiles and Babyn, 2009).***

Bone marrow conversion:

Normal physiologic conversion of red to yellow marrow occurs during growth in a predictable and orderly fashion and is complete by 25 years of age, when the adult pattern is established **(Fig. 3)**. Although distribution of red marrow varies from person to person, it is usually symmetric in the same person ***(David and Miriam, 2007).***

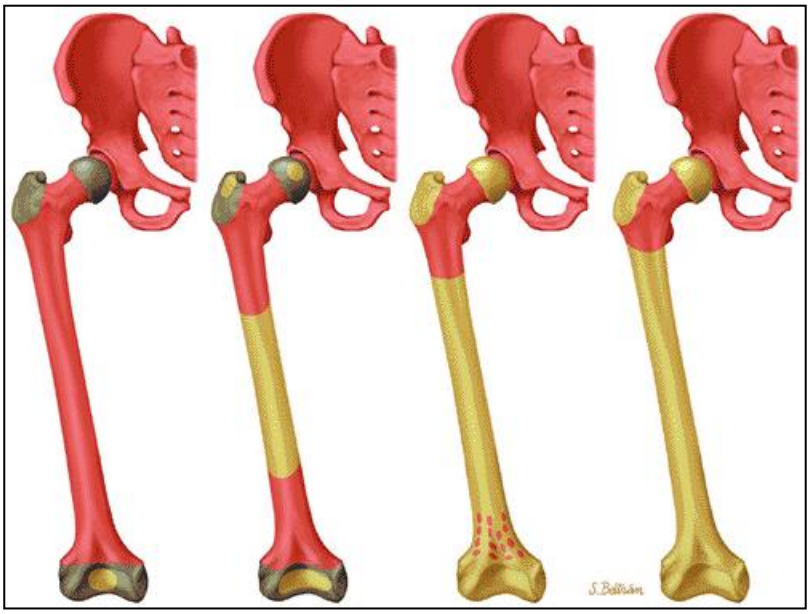

Figure (3): Bone marrow conversion from birth to adulthood. Graphic illustration demonstrating marrow distribution as a function of age with conversion of red marrow to yellow marrow ***(Quoted from David and Miriam, 2007).***

MRI appearance of normal bone marrow:

MR imaging of the normal bone marrow in children requires an understanding of the normal pattern of marrow transformation and of the signal characteristics of hematopoietic and fatty marrow ***(Foster et al., 2004)*** **(Fig. 4)**.

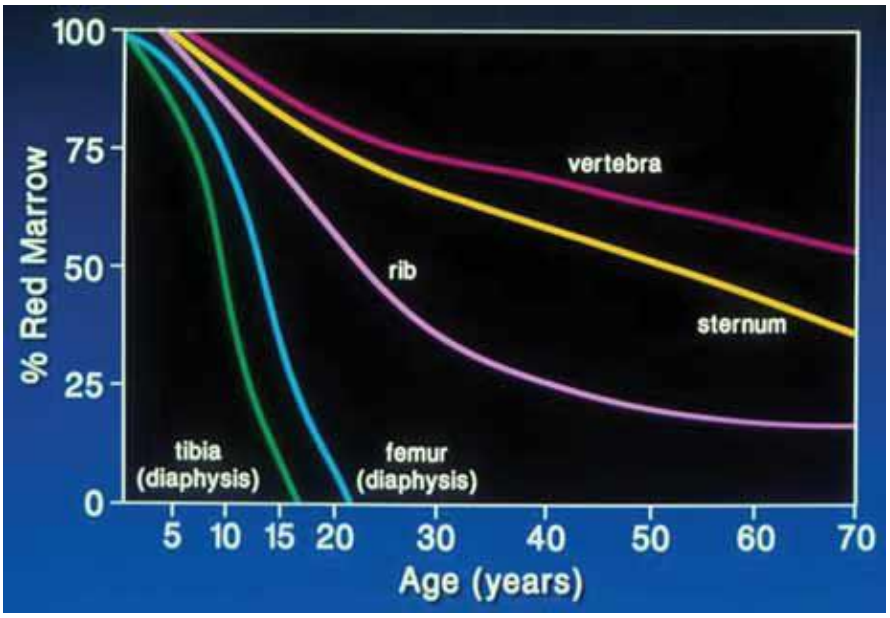

Figure (4): Normal conversion of hematopoietic marrow into fatty marrow from birth to 70 years. Diagram shows percentages of hematopoietic marrow at different anatomic sites ***(Quoted from Vogler and Murphy, 1998).***

In the third trimester fetus and the newborn, the diaphyseal cortex is thick, with only a small central medullary cavitation that will eventually form the marrow cavity ***(Connolly et al., 2004).*** In the fetus, therefore, it is the bone cortex rather than the marrow that determines signal intensity (SI). This results in low SI on images obtained with all sequences of the long bones throughout the body **(Fig. 5)**. In later pregnancy and during the 1st weeks of life (***Connolly et al., 2004)***, a larger marrow space becomes evident and the SI of the shaft of the bone reflects the marrow composition ***(Vogler and Murphy, 1998).***

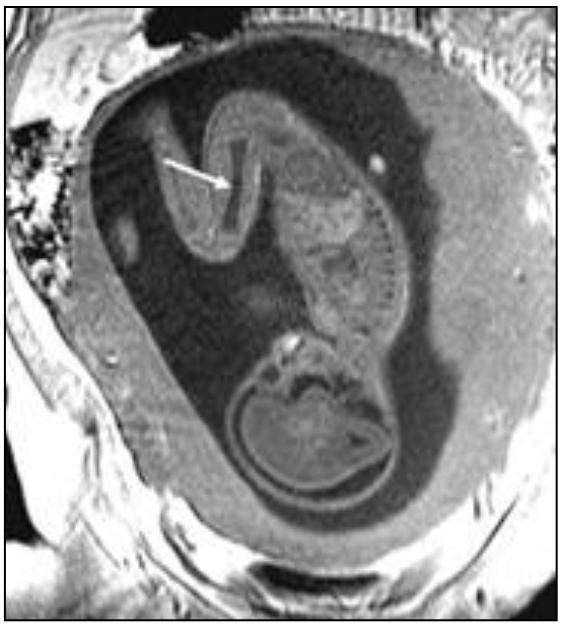

Figure (5): Sagittal T1-weighted gradient-recalled-echo MR image 24-week-old fetus with congenital diaphragmatic hernia. Femoral shaft (arrow) is of very low SI due to contribution of relatively thick cortices and little development of marrow cavity. This low SI persists in long bones into early neonatal life ***(Quoted from Connolly et al., 2004).***

At birth, hematopoietic marrow is present throughout the entire skeleton. Various regions of hematopoietic marrow then rapidly undergo conversion to fatty marrow with the transition beginning in the periphery of the skeleton in the distal phalanges of the fingers and toes and extending in a symmetric, centripetal manner into the central skeleton **(Fig.6)*(Hwang and Panicek, 2007)*.**

The cartilaginous epiphyses and apophyses lack marrow until they ossify. These centers, once ossified, initially contain hematopoietic marrow, followed by rapid conversion to fatty marrow within months of ossification. In the first decade of life, a superimposed additional sequence of marrow conversion begins in the long bones, starting in the diaphyses and progressing toward the metaphyses, particularly the distal metaphyses ***(Hwang and Panicek, 2007).***

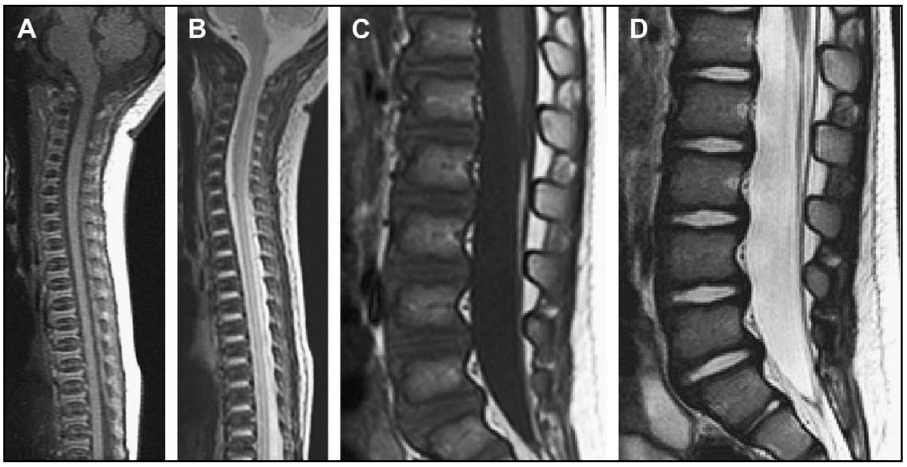

Figure (6): Normal marrow conversion in the spine. Normal appearance of the upper spine in a 1-day-old baby. Note the appearance on T1-weighted **(a)** and T2-weighted sequence **(b)**. Contrast this with the appearance in the lower spine in a 17 month old where there is increased fat present in the vertebrae especially adjacent to the basivertebral vessels on T1-weighted **(c)** and T2-weighted sequences **(d)** ***(Quoted from Hwang and Panicek, 2007).***

Persistence of significant hematopoietic marrow in the diaphyses after the first decade of life is abnormal. Prominent hematopoietic marrow in the metaphyses is normal, however, until the end of the second decade of life. Heterogeneous sharply demarcated linear areas or focal islands of red marrow can be encountered as normal variants **(Fig. 7).**

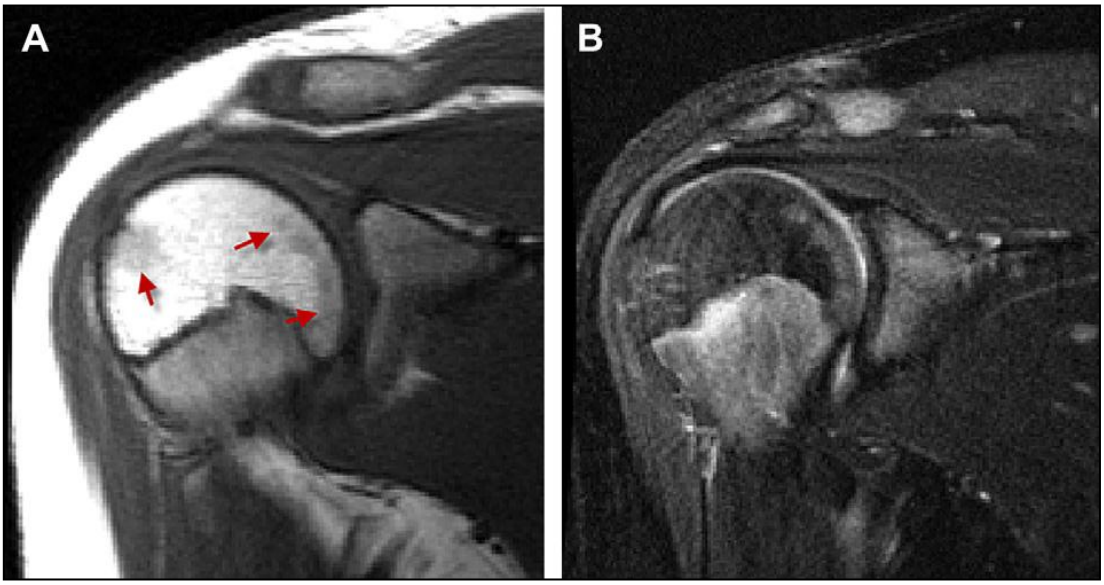

Figure (7): Foci of normal hematopoietic marrow are present within the proximal humeral epiphysis especially in the subchondral region as shown on T1-weighted (**A**, arrowheads) and T2-weighted fast spin echo sequence (**B**) ***(Quoted from Hwang and Panicek, 2007).***

Age-related changes in marrow conversion have also been addressed in the axial skeleton. In the first decade of life, the vertebral marrow is predominantly hematopoietic and shows homogeneously low signal intensity except for high signal intensity around the basivertebral vein. With aging, the amount of hematopoietic marrow in the vertebral bodies progressively decreases, but even in adults the vertebral bodies contain abundant red marrow. The decline in red marrow is accompanied by an increase in fatty marrow **(Fig.6)**. In the first decade of life, the signal intensity of the vertebral bodies is often lower than that of the adjacent disk space. In individuals older than 10 years, the signal intensity of the vertebral marrow is higher than that of the adjacent disk. The conversion of red to yellow marrow in the vertebral bodies can occur in a diffuse or focal pattern ***(Ricci et al., 1990)***.

An age-related pattern of red to yellow marrow conversion also occurs in the pelvis. Pelvic marrow is predominantly hematopoietic in the first two decades of life ***(Dawson et al., 1992)***. Red to yellow conversion begins in the acetabulum superiorly and medially. By the third decade, these areas usually contain mainly fatty marrow.

In the event of increased functional demand for hematopoiesis, yellow marrow may reconvert to red marrow. Conditions triggering reconversion include chronic anemias, such as sickle cell disease and thalassemia; stress; endurance running; obesity; extensive marrow replacement from marrow proliferative or replacement disorders; and chemotherapy with marrow stimulating agents, such as granulocyte colony–stimulating factor (G-CSF) **(Figs. 8&9)** ***(Hwang and Panicek, 2007)***.

The extent of reconversion depends on the severity and duration of the stimulus. The reconversion process proceeds in the reverse order from initial conversion (ie, from central to peripheral skeleton), and in the long bones from the metaphyses to the diaphyses ***(Resnick et al., 2007).***

In clinical practice, prominent red marrow can be observed in some areas including in the epiphyses, most commonly in the distal femur, proximal tibia, and proximal humerus. This is often interpreted as evidence of marrow reconversion, but the lack of sequential studies does not allow documentation of reconversion. A better term for this finding may be an ‘‘extended hematopoietic marrow pattern ***(Resnick et al., 2007)***.

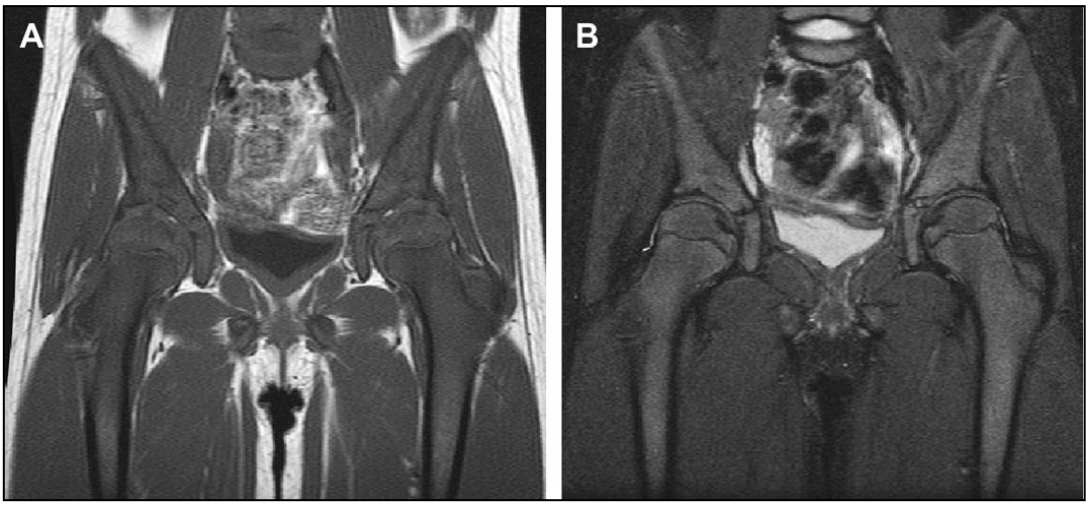

Figure (8): Bone marrow reconversion. A 10-year-old girl with known sickle cell disease showing extensive low signal intensity on T1-weighted imaging with hematopoietic marrow within the pelvis and proximal femora **(A)** and slight increased signal on fast inversion recovery sequences **(B).** Note the complete replacement of expected fatty marrow within the proximal femoral epiphysis ***(Quoted from Hwang and Panicek, 2007).***

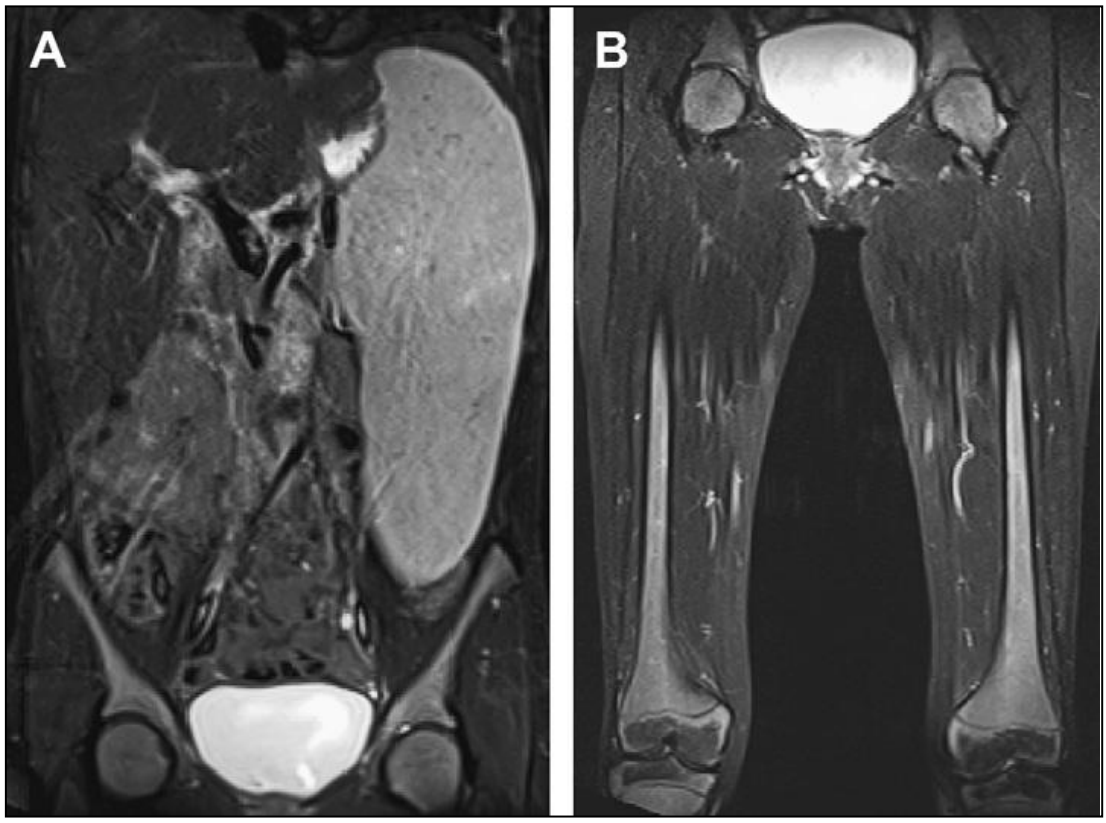

Figure (9): Child with hypercellular marrow and abnormal marrow appearance. This is caused by peripheral destruction and consumption of red blood cells. Note the marked splenomegaly **(A)** and diffuse increased signal greater than adjacent muscles within the pelvis and femoral shafts and distal epiphysis from hypercellular marrow on coronal short-tau inversion recovery (STIR) images **(A, B)** ***(Quoted from Hwang and Panicek, 2007).***

MR imaging, particularly T1-weighted imaging easily depicts marrow conversion, as the signal characteristics of fatty and hematopoietic marrow are different ***(Darge et al., 2008).***

MRI reflects the overall concentrations of fat and water in the marrow rather than its histologic makeup. MR imaging will detect all fat in the marrow, including the 40% fat that is present in hematopoietic marrow. Therefore, the transformation will appear to proceed faster on MR imaging than on histologic studies ***(Darge et al., 2008).***

Tables (1) summarize the signal intensity of bone marrow on different sequences. On water sensitive images (i.e. STIR), hematopoietic marrow is of higher signal intensity than fatty marrow, having a signal intensity that is in between muscle and cerebrospinal fluid, and which decreases with age **(Fig.10)** ***(Meyer et al., 2005).***

Table (1): MRI characteristics of red and yellow marrow, (fig.11)

MRI	Red marrow	Yellow marrow
T1-weighted	Intermediate	High
T2-weighted SE	Intermediate	Intermediate/high
STIR, T2-fat saturated	Moderately high	Low
Gradient-echo	Low	Intermediate
Contrast enhancement	Moderate enhancement	No enhancement

(Quoted from Vande Berg et al., 2005)

Marrow enhancement after intravenous administration of gadolinium contrast agents can be seen especially in infants and young children with highly vascular normal hematopoietic marrow. The degree of enhancement depends on the type of marrow present. Greater enhancement is visible with hematopoietic marrow than fatty marrow where enhancement is not visually evident. Normal marrow enhancement decreases with advancing age, paralleling an increasing proportion of marrow fat, and its decreasing vascularity ***(Babyn et al., 1998)***.

A delay in scanning after gadolinium injection reduces the degree of enhancement obtained.