THE ROLE OF ULTRASONOGRAPHY IN EVALUATION OF DISEASE ACTIVITY IN JUVENILE IDIOPATHIC ARTHRITIS IN EGYPT

Thesis
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بسم الله الرحمن الرحيم
(قالُواْ سُبْحانَكَ لا عِلْمَ لَنَا إلاَّ مَا
عَلَّمْتَنَا إنَّكَ أنتَ الْعَلِيمُ الْحَكِيمُ)
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ABSTRACT

Objective . The aim of this study is to evaluate capability of ultrasound to assess disease activity in juvenile idiopathic arthritis compared to clinical and laboratory evaluation.

Methods. Forty patients underwent clinical evaluation of 28 joints. Joints were assessed for swelling and tenderness. The same joints were scanned for synovial hyperplasia, joint effusion, and power Doppler (PD) signal.

Results . In total, 1120 joints were assessed both clinically and with US . On clinical examination, 182 joints (16.3 %) were swollen, 139 joints (12.4%) were tender. On US evaluation, 192 joints (17.1% of total) had synovial hyperplasia 39 joints (3.5% of total) had joint effusion and 142 joints (12.7 % of total number of examined joints) had power Doppler (PD) signal.

A total of 196 (17.5%) and 210 (18.8%) joints had clinical and US synovitis, respectively. Of the 924 clinically normal joints, 32 (3.5% of clinically normal joints) had subclinical synovitis (i.e., had synovitis on US only). Ultrasound hyperplasia was in highest correlation with clinical measurement of joint swelling, while power doppler ultrasound was in highest correlation with measurement of joints tenderness and joint effusion has the least correlation with both.

Conclusion: Study results showed ultrasound to be a reliable method in detection of synovitis and assessment of disease activity in juvenile idiopathic arthritis.

Key words:

Juvenile idiopathic arthritis, ultrasound, power doppler, synovitis, disease activity

Contents

List of Abbreviations

ACR	American College of Rheumatology
ARA	American Rheumatism Association
anti-CCP	AntiCyclic Citrullinated Peptide
ANA	AntiNuclear Antibodies
ASCT	Autologous Stem Cell Transplantation
CRP	C – reactive protein
CDAI	Clinical Disease Activity Index
DAS	Disease Activity Score
DMARDs	Disease-Modifying Antirheumatic Drugs
ESR	Erythrocyte Sedimentation Rate
EULAR	European League Against Rheumatism
ENA	Extractable Nuclear Antigens
FDA	Food and Drug Administration
FBC	Full Blood Count
gVAS	general health Visual Analog Scale
GH	Growth Hormone
Th	Helper T Cells
HLH	Hemophagocytic LymphoHistiocytosis
HLA	Human Leukocyte Antigen
IL	Interleukin
ILAR	International League of Associations for Rheumatology
IQRs	InterQuartile Ranges
JACAI	Juvenile Arthritis Child Assessment Index
JADI	Juvenile Arthritis Damage Index
JADAS	Juvenile Arthritis Disease Activity Score

JAFS	Juvenile Arthritis Functionality Scale
JAMAR	Juvenile Arthritis Multidimensional Assessment Report
JAPAI	Juvenile Arthritis Parent Assessment Index
JCA	juvenile chronic arthritis
JIA	Juvenile Idiopathic Arthritis
JRA	Juvenile Rheumatoid Arthritis
Lyp	lymphoid-specific phosphatase
MAS	Macrophage Activation Syndrome
MIF	macrophage Migration Inhibitory Factor
MRI	Magnetic Resonance Imaging
MHC	Major Histocompatibility Complex
MCP	MetaCarpoPhalangeal
MSUS	MusculoSkeletal UltraSound
NRAMP1	natural resistance associated macrophage protein 1
NSAIDs	NonSteroidal Anti-Inflammatory Drugs
n	number
PRQL	Pediatric Rheumatology Quality of Life scale
PDUS	Power Doppler Ultra Sound
PTPN22	protein tyrosine phosphatase N22
PIP	Proximal InterPhalangeal
PRF	Pulse Repetition Frequency
ROC	Receiver Operating Characteristic
RANKL	Receptor Activation of Nuclear factor-κB Ligand
Tregs	Regulatory T Cells
RA	Rheumatoid Arthritis
RF	Rheumatoid Factor
STAT3	Signal transducer and activator of transcription 3

SDAI	Simplified Disease Activity Index
SD	Standard Deviation
SJC	Swollen Joints Count
SoJIA	Systemic onset Juvenile Idiopathic Arthritis
TJC	Tender Joints Count
TNF	Tumor Necrosis Factor
TNFAIP3	Tumor necrosis factor, alpha-induced protein 3
US	UltraSonography
VAS	Visual Analogue Scale
WISP 3	WNT1 inducible signaling pathway 3

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INTRODUCTION

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children worldwide (**Manners PJ, Bower C, 2002**). It is a chronic inflammatory disease that affects about 1 of every 1,000 children worldwide (**Ravelli A, Martini A, 2007**).

Synovitis has a central role in the development of cartilage damage and bony erosion in JIA, and moreover therapeutic decisions are primarily influenced by the presence of synovitis on clinical examination. However, studies have shown that current techniques of clinical examination may underestimate significant joint inflammation (**Kane D, et al, 2004**) .

Underrecognition of synovitis may lead to delayed diagnosis and treatment of joint disease. The issue of subclinical synovitis may be particularly relevant in JIA. In the current ILAR classification of JIA; oligoarthritis and polyarthritis are defined on a basis of the number of affected joints (</= 4 or > 4 , respectively) (**Petty RE. et al , 2004**) .

Therefore, the presence of subclinical disease in some joints may alter patient classification or affect the identification of patients requiring more aggressive or specific treatment .

US is increasingly used by clinicians for the evaluation of joint disease. It has been shown to be sensitive in the detection of synovitis and bone erosion in both small and large joints (**Grassi W, 2003**)

US has several advantages over other imaging methods, including noninvasiveness, rapidity of performance , relatively low cost , ability to scan multiple joints at one time , repeatability, safety, and high patient

acceptability. Another advantage of US is that it is the only imaging technique that can be coupled with the conventional clinical approach to the patient in the standard rheumatology setting .

Implementation of US in adult rheumatology clinical practice has been reported to have a significant effect on clinical decision making (**Karim Z, et al, 2001**) .

AIM OF THE WORK

The purpose of the this study is to compare clinical evaluation and US evaluation of synovitis, And to study the capability of US to assess disease activity and determine subclinical joint inflammation in children with JIA .

JUVENILE IDIOPATHIC ARTHRITIS

Definition and historical review:

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children worldwide with a range of clinical presentations and outcomes (**Ravelli A and Martini A, 2007**).

It is comprised of a heterogeneous group of several disease subtypes that are characterized by the onset of arthritis prior to the age of 16 years with symptoms that persist for more than 6 weeks (**Kim KH and Kim DS, 2010**).

The First detailed description of juvenile arthritis was made by Cornil in1864. By the end of the 19th century at least 38 case reports of arthritis in children had been published and reviewed by Diamant-Berger. He recognized differing subtypes of disease and attempted to classify at least three different patterns (i.e., acute, slow, and partial forms) of childhood arthritis. In1897. **(Lisabith V, et al, 2004)**.

the pinnacle of description of childhood arthritis occurred, when George Frederic Still reported on 22 children with chronic arthritis and commented that childhood arthritis was more than one disease and mostly different from chronic arthritis as described in adults. Since these first publications, different names have been used

for the description of childhood arthritic diseases and different classification systems have been developed (K**irsten M, 2010**).

American Rheumatism Association (ARA) criteria for the classification of juvenile rheumatoid arthritis (JRA) were made in 1972 and revised in 1977 (**Brewer EJ, et al. 1977**).

European League Against Rheumatism (EULAR) criteria for juvenile chronic arthritis (JCA) were made in 1978. International League of Associations for Rheumatology (ILAR) criteria for juvenile idiopathic arthritis (JIA) were made in Santiago in 1994, then revised in Durban, 1997, then had a second revision in Edmonton, 2001, last revision was in 2004 (**Stabile A, et al , 2006**)