



**POWER DOPPLER ULTRASONOGRAPHY ON
TENDONS TO ASSESS SUBCLINICAL ENTHESOPATHY
IN PATIENTS WITH PSORIASIS**

Thesis

Submitted for partial fulfillment of Masters degree in Internal medicine

Presented by

Nehal Abdel Baky Hassanen

M.B.B.CH - Ain Shams University

Supervised by

Prof. Dr. Abdel Azeem Mohamed El Hefny

Professor of Internal Medicine and Rheumatology Department

Faculty of Medicine, Ain Shams University

Assist. Prof. Dr. Maryam Ahmed Abdel-Rahman

Assistant professor of Internal Medicine and Rheumatology Department

Faculty of Medicine, Ain Shams University

Dr. Nermeen Noshay Aziz

lecturer of Internal Medicine and Rheumatology

Faculty of Medicine, Ain Shams University

Faculty of Medicine

Ain Shams University

2019



فحص الاوتار بالموجات الصوتية لتقييم التهاب الارتكاز في مرضى الصدفية

رسالة

توطئة للحصول علي درجة الماجستير في الأمراض الباطنة
مقدمة من

الطبيب/ نهال عبد الباقي حسانين
بكالوريوس الطب والجراحة- جامعة عين شمس
تحت إشراف

أد/ عبد العظيم محمد الحفني

أستاذ الأمراض الباطنة والروماتيزم
كلية الطب- جامعة عين شمس

أد/ مريم أحمد عبد الرحمن

أستاذ مساعد الأمراض الباطنة والروماتيزم
كلية الطب- جامعة عين شمس

د/ نرmin نصحي عزيز

مدرس الأمراض الباطنة والروماتيزم
كلية الطب- جامعة عين شمس
كلية الطب

جامعة عين شمس

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢



Acknowledgement

*First and foremost thanks to **ALLAH**, the Most Merciful.*

*I wish to express my deep appreciation to **Prof. Dr. Abdel Azeem Mohamed El Hefny**, Professor of Internal Medicine and Rheumatology Department, Ain Shams University, for his close supervision and guidance.*

*I wish to express my great thanks to **Assist. Prof. Dr. Maryam Ahmed Abdel-Rahman**, Assistant professor of Internal Medicine and Rheumatology Department, Ain Shams University, for her kind supervision and indispensable.*

*I wish to express my great thanks and gratitude to **Dr. Nermeen Noshay Aziz**, lecturer of Internal Medicine and Rheumatology, Ain Shams University, for her kind supervision, indispensable advice and great help in this work.*

*I wish to express my great thanks to **Dr. Safaa Abdel Salam Ali**, lecturer of Internal Medicine and Rheumatology, Ain Shams University, who did Musculoskeletal Ultrasound examination for all patients.*

Last and not least, I want to thank all my family and my colleagues for their valuable help and support.

Finally I would present my appreciation to my patients without them, this work could not have been completed.

CONTENTS

Subjects	Page
• List of Abbreviations	I
• List of tables	III
• List of Figures	IV
• Introduction	1
• Aim of the Work.....	3
• Review of literature:	
Chapter 1: Psoriasis.....	4
Chapter 2: Psoriatic Arthritis	24
Chapter 3: Musculoskeletal ultrasound	46
• Patients And Methods.....	52
• Results	58
• Discussion	67
• Summary.....	72
• Conclusion.....	73
• Recommendations	74
• References	75
• Arabic Summary.....	

LIST OF ABBREVIATIONS

APR	: Apremilast
AS	: Ankylosing Spondylitis
BB-UVB	: Broadband Ultraviolet B light
BSA	: Body Surface Area
CRP	: C- Reactive Protein
CS	: Corticosteroid
CsA	: Cyclosporine A
DLQI	: Dermatology Life Quality Index
DMARDs	: Disease-Modifying Antirheumatic Drugs
EMA	: European Medicines Agency
EMG	: Electromyography
ESR	: Erythrocyte Sedimentation Rate
FAEs	: Fumaric Acid Esters
FDA	: Food and Drug Administration
GRAPPA	: Group for Research and Assessment of Psoriasis and Psoriatic Arthritis
GUESS	: Glasgow Enthesitis Scoring System
HLA	: Human Leukocyte Antigen
IA	: Intraarticular
IFN	: Interferon
IL	: Interleukin
IL-12/23i	: Interleukin-12/23 inhibitor
IV	: Intravenous
LEF	: Leflunomide
MASES	: Maastricht Ankylosing Spondylitis Enthesitis Score
MHC	: Major Histocompatibility Complex
MICA	: MHC Class I polypeptide-related sequence A
MRI	: Magnetic Resonance Imaging
MSUS	: Musculoskeletal UltraSound
MTX	: Methotrexate

NAPSI	: Nail Psoriasis Severity Index
NB-UVB	: Narrowband Ultraviolet B
NSAIDs	: Non Steroidal Anti Inflammatory Drugs
OA	: Osteoarthritis
PASI	: Psoriasis Area and Severity Index
PDE-4i	: Phosphodiesterase 4 Inhibitor (apremilast)
PDUS	: power Doppler ultrasound
PGA	: Physicians Global Assessment
phototx	: phototherapy
PsA	: Psoriatic Arthritis
PUVA	: Psoralen and Ultraviolet A
SpA	: Spondyloarthropathies
SSZ	: Sulfasalazine
TNF	: Tumor Necrosis Factor
vit	: vitamin

LIST OF TABLES

<i>Tab. No.</i>	<i>Subject</i>	<i>Page</i>
Table (1)	CASPAR criteria	29
Table (2)	2018 ACR guidelines for treatment of psoriatic arthritis including pharmacological therapies, non-pharmacological therapies and symptomatic treatment	35
Table (3)	TNF- α blockers	37
Table (4)	Glasgow Ultrasound enthesitis Scoring System	56
Table (5)	Clinically significant demographic data of our patients	58
Table (6)	Clinically significant descriptive data of our patients	58
Table (7)	Relevant laboratory data of 50 patients at time of study entry	59
Table (8)	PASI and GUESS scores in our patients	59
Table (9)	Abnormal U/S findings in our patients	60
Table (10)	Abnormal doppler U/S findings in our patients	60
Table (11)	Correlation between total GUESS and other parameters	61
Table (12)	Correlation between GUESS& other parameters	63
Table (13)	Correlation between PASI score and other parameters	65
Table (14)	Correlation between PASI score and other parameters	66

LIST OF FIGURES

<i>Fig. No.</i>	<i>Subject</i>	<i>Page</i>
Fig. (1)	Psoriasis vulgaris	7
Fig. (2)	Guttate psoriasis	8
Fig. (3)	Inverse psoriasis	8
Fig. (4)	Pustular psoriasis	9
Fig. (5)	Erythrodermic psoriasis	9
Fig. (6)	Nail manifestations seen in nail psoriasis.	11
Fig. (7)	Psoriasis treatment algorithm	17
Fig. (8)	GRAPPA treatment schema for active psoriatic arthritis (PsA).	39
Fig. (9)	Ultrasonography appearances of enteritis	50
Fig. (10)	Sex distribution	59
Fig. (11)	Correlation between GUESS & metatarsal squeeze test	62
Fig. (12)	Correlation between GUESS & age	64
Fig. (13)	Correlation between GUESS and age of disease onset	64

Abstract

Background: Psoriatic arthritis is a long-term condition that affects some people who have psoriasis. In severe cases, there's a risk of the joints becoming permanently damaged or deformed. Diagnosis of psoriasis-associated enthesopathy helps early detection and treatment of psoriatic arthropathy before joint damage becomes established.

Objective: to detect the presence of asymptomatic enthesal abnormalities in psoriatic patients in an attempt for preclinical detection of psoriatic arthritis before full joint affection becomes established.

Methods: A cross-sectional study included 50 with psoriasis without evidence of arthropathy collected from Ain Shams University hospitals. All the patients were subjected to the following: Full history, clinical examination, routine laboratory investigations and power doppler US on both lower limb entheses.

Results: The present study proved that 48 patients out of 50 with psoriasis showed enthesal abnormalities at least in one site of lower limbs detected by MSUS and this was assessed using glasgow ultrasound enthesopathy scoring system (GUESS).

Conclusion: MSUS is useful in the detection of early findings of psoriatic arthropathy especially the presence of enthesitis even in asymptomatic patients.

Keywords: subclinical enthesopathy, psoriatic arthritis, musculoskeletal ultrasound

INTRODUCTION

Psoriasis is an inflammatory skin disease characterized by itchy, erythematous, scaly lesions, papules and sometimes pustules (*Boehncke and Schön, 2015*).

About 11% of those diagnosed with psoriasis have also been diagnosed with psoriatic arthropathy (PsA). However, about 30% of people with psoriasis will eventually develop PsA. While joint affection is the main distinguishing feature between PsA and psoriasis, a well known extra-articular feature of PsA is tendinopathy and enthesopathy (*Ritchlin et al., 2017*).

PsA shows significant clinical variability with potential involvement of both the peripheral and the axial skeleton. In addition to arthritis, inflammatory changes include other tissues resulting in enthesitis and dactylitis which are the hallmarks of PsA (*Coates et al., 2012*).

MSUS is a rapidly evolving technique that helps determining the joint structure involved in the inflammatory process and is one of the radiological methods recommended to reveal synovitis at any joint and has the potential to be used not only to detect joint synovitis, but also to examine the surrounding soft tissues in order to determine the presence of tenosynovitis, dactylitis and/or enthesitis (*Ruta and Alva, 2016*).

MSUS has been known to be a reliable tool in detecting enthesitis and is more accurate than clinical examination, conventional radiography, and even MRI,

especially during the early stages of inflammatory process in enthesitis (*Ozçakar et al., 2005*).

Furthermore, occult enthesitis detected using MSUS, especially with a power Doppler signal, has a predictive value for the occurrence of joint changes in patients with psoriasis (*El Miedany et al., 2015*).

Psoriatic patients without joint involvement of young and middle aged groups are more susceptible for synovitis, enthesitis and tenosynovitis which may detect occult joint involvement predicting the clinical onset of PsA in these age groups therefore regular US examination is of benefit to patients with PsA, and more attention should be paid to young and middle aged non-PsA psoriatic patients (*Tang et al., 2018*).

AIM OF THE WORK

In the present study we tried to detect the presence of asymptomatic enthesal abnormalities in psoriatic patients in an attempt for preclinical detection of psoriatic arthritis before full joint affection becomes established.

PSORIASIS

Definition:

Psoriasis is a phenotypically heterogeneous immune mediated skin disease that often follows a relapsing and remitting course. It is characterized by well-demarcated, scaly, erythematous lesions that often detected at sites of trauma (extensor surfaces of elbows and knees), however it may involve any part of the body. It is common, complex trait that is associated with many associations including arthritis, diabetes mellitus, hypertension, obesity, cardiovascular disease, reduced quality of life and depression (*Mahil et al., 2015*).

Epidemiology:

Psoriasis is documented to affect 1-3 % of the world's population. This estimate, however, is built up on population based studies based on geographic/ethnic groups. The prevalence of psoriasis is actually variable and has been documented to range from 0.05 to 3.7 % depending on ethnicity and geographic location with most research suggesting a higher rate of psoriasis in white compared to other ethnic groups (*Kaufman and Alexis 2018*).

Environmental factors induce inflammatory activity in people having genetic susceptibility. Many alterations could be triggered by environmental risk factors such as diet, microbial infections (from bacteria, fungus and virus), chemical irritants or UV radiation exposure and bad habits (such as smoking and drinking alcohol) (*Zeng et al., 2017*).

A total of 36 genes are found to account for 22% of psoriasis heritability, and more than 16 genetic loci have confirmed association with psoriasis susceptibility. HLA-Cw6 on chromosome 6 is considered to be the risk variant in the PSOR1 (MIM 177900) susceptibility locus that carries the greatest risk of early onset of psoriasis. The known susceptibility genes which are involved in this immune mediated process are IL-23/Th17 axis of psoriasis immunopathogenesis (*Coates et al., 2016*) (A).

Abundant expression of chemerin in psoriatic skin induces the infiltration of plasmacytoid dendritic cells to the dermis and epidermis; these release IFN- α , leading to the activation and maturation of myeloid dendritic cells. These cells migrate to lymph nodes where they act as antigen presenting cells and release co-stimulatory signals and cytokines [IL-6, IL-12, IL-15, IL-17, IL-21, IL-23, IL-27, IL-31, IL-32, IL-33, IL-35, IL-36, IL-37, IL-38, IL-39, IL-40, IL-41, IL-42, IL-43, IL-44, IL-45, IL-46, IL-47, IL-48, IL-49, IL-50, IL-51, IL-52, IL-53, IL-54, IL-55, IL-56, IL-57, IL-58, IL-59, IL-60, IL-61, IL-62, IL-63, IL-64, IL-65, IL-66, IL-67, IL-68, IL-69, IL-70, IL-71, IL-72, IL-73, IL-74, IL-75, IL-76, IL-77, IL-78, IL-79, IL-80, IL-81, IL-82, IL-83, IL-84, IL-85, IL-86, IL-87, IL-88, IL-89, IL-90, IL-91, IL-92, IL-93, IL-94, IL-95, IL-96, IL-97, IL-98, IL-99, IL-100, IL-101, IL-102, IL-103, IL-104, IL-105, IL-106, IL-107, IL-108, IL-109, IL-110, IL-111, IL-112, IL-113, IL-114, IL-115, IL-116, IL-117, IL-118, IL-119, IL-120, IL-121, IL-122, IL-123, IL-124, IL-125, IL-126, IL-127, IL-128, IL-129, IL-130, IL-131, IL-132, IL-133, IL-134, IL-135, IL-136, IL-137, IL-138, IL-139, IL-140, IL-141, IL-142, IL-143, IL-144, IL-145, IL-146, IL-147, IL-148, IL-149, IL-150, IL-151, IL-152, IL-153, IL-154, IL-155, IL-156, IL-157, IL-158, IL-159, IL-160, IL-161, IL-162, IL-163, IL-164, IL-165, IL-166, IL-167, IL-168, IL-169, IL-170, IL-171, IL-172, IL-173, IL-174, IL-175, IL-176, IL-177, IL-178, IL-179, IL-180, IL-181, IL-182, IL-183, IL-184, IL-185, IL-186, IL-187, IL-188, IL-189, IL-190, IL-191, IL-192, IL-193, IL-194, IL-195, IL-196, IL-197, IL-198, IL-199, IL-200, IL-201, IL-202, IL-203, IL-204, IL-205, IL-206, IL-207, IL-208, IL-209, IL-210, IL-211, IL-212, IL-213, IL-214, IL-215, IL-216, IL-217, IL-218, IL-219, IL-220, IL-221, IL-222, IL-223, IL-224, IL-225, IL-226, IL-227, IL-228, IL-229, IL-230, IL-231, IL-232, IL-233, IL-234, IL-235, IL-236, IL-237, IL-238, IL-239, IL-240, IL-241, IL-242, IL-243, IL-244, IL-245, IL-246, IL-247, IL-248, IL-249, IL-250, IL-251, IL-252, IL-253, IL-254, IL-255, IL-256, IL-257, IL-258, IL-259, IL-260, IL-261, IL-262, IL-263, IL-264, IL-265, IL-266, IL-267, IL-268, IL-269, IL-270, IL-271, IL-272, IL-273, IL-274, IL-275, IL-276, IL-277, IL-278, IL-279, IL-280, IL-281, IL-282, IL-283, IL-284, IL-285, IL-286, IL-287, IL-288, IL-289, IL-290, IL-291, IL-292, IL-293, IL-294, IL-295, IL-296, IL-297, IL-298, IL-299, IL-300, IL-301, IL-302, IL-303, IL-304, IL-305, IL-306, IL-307, IL-308, IL-309, IL-310, IL-311, IL-312, IL-313, IL-314, IL-315, IL-316, IL-317, IL-318, IL-319, IL-320, IL-321, IL-322, IL-323, IL-324, IL-325, IL-326, IL-327, IL-328, IL-329, IL-330, IL-331, IL-332, IL-333, IL-334, IL-335, IL-336, IL-337, IL-338, IL-339, IL-340, IL-341, IL-342, IL-343, IL-344, IL-345, IL-346, IL-347, IL-348, IL-349, IL-350, IL-351, IL-352, IL-353, IL-354, IL-355, IL-356, IL-357, IL-358, IL-359, IL-360, IL-361, IL-362, IL-363, IL-364, IL-365, IL-366, IL-367, IL-368, IL-369, IL-370, IL-371, IL-372, IL-373, IL-374, IL-375, IL-376, IL-377, IL-378, IL-379, IL-380, IL-381, IL-382, IL-383, IL-384, IL-385, IL-386, IL-387, IL-388, IL-389, IL-390, IL-391, IL-392, IL-393, IL-394, IL-395, IL-396, IL-397, IL-398, IL-399, IL-400, IL-401, IL-402, IL-403, IL-404, IL-405, IL-406, IL-407, IL-408, IL-409, IL-410, IL-411, IL-412, IL-413, IL-414, IL-415, IL-416, IL-417, IL-418, IL-419, IL-420, IL-421, IL-422, IL-423, IL-424, IL-425, IL-426, IL-427, IL-428, IL-429, IL-430, IL-431, IL-432, IL-433, IL-434, IL-435, IL-436, IL-437, IL-438, IL-439, IL-440, IL-441, IL-442, IL-443, IL-444, IL-445, IL-446, IL-447, IL-448, IL-449, IL-450, IL-451, IL-452, IL-453, IL-454, IL-455, IL-456, IL-457, IL-458, IL-459, IL-460, IL-461, IL-462, IL-463, IL-464, IL-465, IL-466, IL-467, IL-468, IL-469, IL-470, IL-471, IL-472, IL-473, IL-474, IL-475, IL-476, IL-477, IL-478, IL-479, IL-480, IL-481, IL-482, IL-483, IL-484, IL-485, IL-486, IL-487, IL-488, IL-489, IL-490, IL-491, IL-492, IL-493, IL-494, IL-495, IL-496, IL-497, IL-498, IL-499, IL-500, IL-501, IL-502, IL-503, IL-504, IL-505, IL-506, IL-507, IL-508, IL-509, IL-510, IL-511, IL-512, IL-513, IL-514, IL-515, IL-516, IL-517, IL-518, IL-519, IL-520, IL-521, IL-522, IL-523, IL-524, IL-525, IL-526, IL-527, IL-528, IL-529, IL-530, IL-531, IL-532, IL-533, IL-534, IL-535, IL-536, IL-537, IL-538, IL-539, IL-540, IL-541, IL-542, IL-543, IL-544, IL-545, IL-546, IL-547, IL-548, IL-549, IL-550, IL-551, IL-552, IL-553, IL-554, IL-555, IL-556, IL-557, IL-558, IL-559, IL-560, IL-561, IL-562, IL-563, IL-564, IL-565, IL-566, IL-567, IL-568, IL-569, IL-570, IL-571, IL-572, IL-573, IL-574, IL-575, IL-576, IL-577, IL-578, IL-579, IL-580, IL-581, IL-582, IL-583, IL-584, IL-585, IL-586, IL-587, IL-588, IL-589, IL-590, IL-591, IL-592, IL-593, IL-594, IL-595, IL-596, IL-597, IL-598, IL-599, IL-600, IL-601, IL-602, IL-603, IL-604, IL-605, IL-606, IL-607, IL-608, IL-609, IL-610, IL-611, IL-612, IL-613, IL-614, IL-615, IL-616, IL-617, IL-618, IL-619, IL-620, IL-621, IL-622, IL-623, IL-624, IL-625, IL-626, IL-627, IL-628, IL-629, IL-630, IL-631, IL-632, IL-633, IL-634, IL-635, IL-636, IL-637, IL-638, IL-639, IL-640, IL-641, IL-642, IL-643, IL-644, IL-645, IL-646, IL-647, IL-648, IL-649, IL-650, IL-651, IL-652, IL-653, IL-654, IL-655, IL-656, IL-657, IL-658, IL-659, IL-660, IL-661, IL-662, IL-663, IL-664, IL-665, IL-666, IL-667, IL-668, IL-669, IL-670, IL-671, IL-672, IL-673, IL-674, IL-675, IL-676, IL-677, IL-678, IL-679, IL-680, IL-681, IL-682, IL-683, IL-684, IL-685, IL-686, IL-687, IL-688, IL-689, IL-690, IL-691, IL-692, IL-693, IL-694, IL-695, IL-696, IL-697, IL-698, IL-699, IL-700, IL-701, IL-702, IL-703, IL-704, IL-705,