RECOMMENDATIONS

Based on the results of this study we recommend the following:

1. DAS 28-CRP should be used as disease activity index for accurate assessment of disease activity.

2. Physicians should not neglect ankles and feet involvement in RA and disease activity assessment should always involve the small joints of the feet to reflect disease activity accurately.

3. ACPA positive RA patients should be treated aggressively in the beginning of the course of the disease to avoid long-term joint destruction, bone loss and disability.

4. ACPA positive RA patients with lower BMI should be advised to eat healthy food and should be closely monitored to avoid long-term joint damage.

5. DXA scan should be performed for RA patients with:
   a. Older age.
   b. ACPA positive patients.
   c. Long disease duration.
   d. High disease activity.
   e. High radiological joint damage.
   f. High dose of Cs intake.

6. The laboratory tests for bone turnover markers should be done in conjunction with DXA.

7. More detailed longitudinal studies with a larger sample size should be performed to assess bone loss in premenopausal, postmenopausal females and males with RA.

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ANNEX I [(35)]

The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for rheumatoid arthritis

Target population (Who should be tested?): Patients who:
1) have at least 1 joint with definite clinical synovitis (swelling)
2) with the synovitis not better explained by another disease

Classification criteria for RA (score-based algorithm: add score of categories A–D;
A score of _6/10 is needed for classification of a patient as having definite RA)

	Score
A. Joint involvement	
1. 1 large joint.	0
2. 2-10 large joints	1
3. 1-3 small joints (with or without involvement of large joints)	2
4. 4-10 small joints (with or without involvement of large joints)	3
5. > 10 joints (at least 1 small joint)	5
B. Serology (at least 1 test result is needed for classification)	
1. Negative RF *and* negative ACPA	0
2. Low-positive RF *or* low-positive ACPA	2
3. High-positive RF *or* high-positive ACPA	3
C. Acute-phase reactants (at least 1 test result is needed for classification)	0
1. Normal CRP *and* normal ESR	1
2. Abnormal CRP *or* abnormal ESR	
D. Duration of symptoms	
1. <6 weeks	0
2. ≥6 weeks	1

ANNEX II [198]

Health Assessment Questionnaire

Name: Date:

In this section we are interested in learning how your illness affects your ability to function in daily life. Please feel free to add any comment on the bake of this page.

Please check the response which best describes your usual abilities Over the Past Week.

	Without Any difficulty	With Some difficulty	With much difficulty	Unable to do
DRESSING & GROOMING Are you able to:				
1. Dress yourself, including shoelaces and buttons?				
2. Shampoo your hair?				
ARISING Are you able to:				
3. Stand up from an armless straight chair?				
4. Get in and out of bed?				
EATING Are you able to:				
5. Cut your meat?				
6. Lift a full cup or glass to your mouth?				
7. Open a new milk carton?				
WALKING Are you able to:				
8. Walk outdoors on flat ground?				
9. Climb up five steps?				

Please check any AIDS OR DEVICES that you usually use for any of the above activities:

Devices used for dressing (button hook, zipper pull, etc.)	Built up or special utensils	Crutches
	Cane	Wheelchair
Special or built up chair	Walker	

Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

Dressing and grooming	Arising
Eating	Walking

Please check the response which best describes your usual abilities Over the Past Week.

	Without Any difficulty	With Some difficulty	With much difficulty	Unable to do

HYGIENE
Are you able to:

10. Wash and dry your body?

11. Take a tub bath?

12. Get on and off the toilet?

REACH
Are you able to:

13. Reach and get down a 5-pound object (such as a bag of sugar) from just above your head?

14. Bend down to pick up clothing from the floor?

GRIP
Are you able to:

15. Open car doors?

16. Open previously opened jars?

17. Turn faucets on and off?

ACTIVITIES
Are you able to:

18. Run errands and shop?

19. Get in and out of a car?

20. Do chores such as vacuuming or yard work?

Please check any AIDS OR DEVICES that you usually use for any of the above activities:

Raised toilet seat
Bathtub seat
Bathtub bar

Long-handled appliances in the bathroom
Long-handled appliances for reach

Jar opener (for jars previously opened)
Other (specify)

Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

Hygiene
Reach

Gripping and opening things
Errands and chores

ANNEX III [(36)]

Disease Activity Score Index 28 (DAS 28)

DAS28 with 4 variables:

$$DAS28 = 0.56\sqrt{(TEN28)} + 0.28\sqrt{(SW28)} + 0.70Ln(ESR) + 0.014(GH)$$

TEN28
28 joint count for tenderness

SW28
28 joint count for swelling

LnESR
Natural logarithm of Western's Erythrocyte Sedimentation Rate

GH
General health or patient's global assessment of disease activity on Visual Analogue Scale of 100mm.

DAS28 score	Level of disease activity
<3.2	Low
3.2– 5.1	Moderate
>5.1	High

A STUDY OF OSTEOPOROSIS IN PREMENOPAUSAL RHEUMATIOD ARTHRITIS PATIENTS

<div dir="rtl">

دراسة لهشاشة العظام فى مرضى الروماتزم المفصلى الرثياتى فى سن ما قبل انقطاع الطمث

</div>

Protocol of a thesis submitted	خطة بحث مقدمة
to the Faculty of Medicine	لكلية الطب
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requirements of the degree of	علي درجة
Doctor in Physical Medicine, Rheumatology and Rehabilitation	دكتور في الطب الطبيعى والروماتزم والتأهيل
by	من
Yousra Hisham Mohamed Moustafa Abdel-Fattah	يسرا هشام محمد مصطفى عبد الفتاح
MBBCh, Alex.	بكالوريوس الطب و الجراحة ، الأسكندرية
Master in Physical Medicine, Rheumatology and Rehabilitation	ماجستير الطب الطبيعى والروماتزم والتأهيل، الأسكندرية
Assistant lecturer	مدرس مساعد
Department of Physical Medicine, Rheumatology and Rehabilitation	قسم الطب الطبيعى والروماتزم والتأهيل
Faculty of Medicine	كلية الطب
University of Alexandria	جامعة الأسكندرية
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SUPERVISORS

المشرفون

Prof. Dr. Abdelmoneim Hussein Helal

أ.د/ عبد المنعم حسين هلال

Professor of Physical Medicine,

أستاذ الطب الطبيعى

Rheumatology and Rehabilitation

والروماتزم والتأهيل

Faculty of Medicine

كلية الطب

University of Alexandria

جامعة الأسكندرية

Prof. Dr. Dalal Mohamed Nasr

أ.د/ دلال محمد نصر القفاش

AL-Kaffash

Professor of Clinical Pathology

أستاذ الباثولوجيا الاكلينيكية

Faculty of Medicine

كلية الطب

University of Alexandria

جامعة الأسكندرية

Dr. Enas Mohamed Shahin

د/ ايناس محمد شاهين

Assisstant Professor of Physical Medicine,

أستاذ مساعد الطب الطبيعى

Rheumatology and Rehabilitation

والروماتزم والتأهيل

Faculty of Medicine

كلية الطب

University of Alexandria

جامعة الأسكندرية

CO-WORKER

المشرف المشارك

Dr. Marwa Hassan

د/ مروة حسن

Lecturer of Physical Medicine,

مدرس الطب الطبيعى

Rheumatology and Rehabilitation

والروماتزم والتأهيل

Faculty of Medicine

كلية الطب

University of Alexandria

جامعة الأسكندرية

For her knowledge in diagnosis of

لخبرتها في تشخيص الامراض

Rheumatic Diseases

الروماتزمية

CO-RESEARCHERS

Ahmed Hisham Ghoneem

Sixth grade student

Faculty of Medicine

University of Alexandria

Mobile: 01221775321

Email: a-ghoneem@hotmail.com

الباحث المساعد

احمد هشام غنيم

طالب بالسنة السادسة

كلية الطب

جامعة الأسكندرية

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by swelling, tenderness and destruction of synovial joint, leading to severe disability and premature mortality.[1-3]

Rheumatoid arthritis is not only characterized by inflammation in the synovial tissue, but also involves the bone.[4] The interaction between the inflammatory cascade and bone is characterized by a wide range of changes in the bone remodeling not only at the site of inflammation but also at skeletal sites remote from inflammation.[5]

Rheumatoid arthritis is accompanied by 3 types of bone involvement: periarticular osteopenia, systemic osteoporosis and bone erosions.[6] Periarticular osteopenia is one of the first radiological signs of RA, most marked in early disease and is correlated with disease activity.[4]

Systemic osteoporosis is recognized as an extra-articular complication in RA.[7] There is compelling evidence that this bone mass reduction is associated with an increased risk of fracture.[8] A study proved that osteoporosis in RA patients is often related to the use of corticosteroids,[9] but another population based study showed that cumulative disease damage was the stronger predictor of reduced bone density and that other disease and lifestyle factors have only a modest influence.[10] It was also suggested that bone mass in RA is affected by disease dependent factors, such as functional impairment and the activity of the inflammatory process itself, especially early in the course of RA.[7]

Bone erosions are radiographic hallmark of RA and reflect unfavourable prognosis. They develop within the first months of disease onset, their extent and severity reflects cumulative disease activity.[11,12]

The pathophysiological mechanisms of the 3 different types of bone involvement have previously been thought to be separate processes. A recent study has suggested that both local and systemic bone destruction are mediated by osteoclast activation.[13] The skeletal system is a target organ for RA, the relationship between focal erosions and generalized osteoporosis is complicated and modified by many aspects of RA as well as other factors.[12]

Dual energy x ray absorptiometry (DXA) is the gold standard for assessing bone density, and the World health Organisation (WHO) definition of osteoporosis is based on this. The use of DXA may be limited by the availability of equipment, cost, and reimbursement issues.[14]

AIM

The aim of this study is to assess osteoporosis in premenopausal RA patients and its correlation with other disease parameters.

SUBJECTS

Forty female patients with RA will be recruited from those attending the Outpatient Clinic of Physical Medicine, Rheumatology and Rehabilitation Department, Faculty of Medicine, Alexandria University Hospital. The diagnosis of RA will depend on the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria for RA (Annex I).[1] The patients will be selected in their premenopausal period to exclude postmenopausal and age related osteoporosis.

Patients with a history of taking treatment for osteoporosis and those with concurrent medical conditions known to affect bone metabolism (including renal or liver disease, malignancy or endocrine disorders)[15] will be excluded from the study.

Twenty age and sex matched healthy females to serve as control subjects will be included in the study.

The study will be explained to the participants and an informed consent will be given by each, after approval from the local ethical committee of Faculty of Medicine, Alexandria University.

METHODS

A. The following data will be obtained from each patient:
1. Personal data (Name, age, sex, marital status and occupation).
2. History (age of menarche, history of smoking, coffee intake, dietary habits).
3. History of present condition; (onset, disease duration, course, progression ...).
4. Medication history; [the intake of glucocorticode, non steroidal anti-inflammatory drugs (NSAIDS), Calcium, vitamin D, disease modifying antirheumatic drugs (DMARDS) and others].
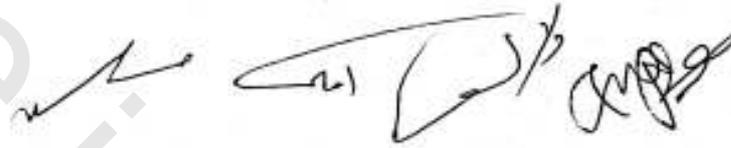
B. Then each patient will be subjected to the following:
1. Thorough clinical evaluation with stress on musculoskeletal examination.[16]
2. Disease severity assessment by Disease Assessment Severity index 28 (DAS 28)[17] (Annex II) and Health Assessment Questionnaire (HAQ).[18] (Annex III)
3. Routine laboratory investigations [hemoglobin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and Latex rheumatoid factor (RF)].[19]
4. Bone markers (β- Cross Laps,[20] Total P1NP[21] and N-MID Osteocalcin[22]).
5. Plain X-ray (PXR) hands, wrist and feet that will be assessed by Modified Sharp method.[23,24]
6. Dual X-ray absorptiometry (DXA) (radius, femur and lumbar spine).[25]

RESULTS

The results obtained will be assessed, tabulated and statistically analyzed according to established statistical methods.

DISCUSSION

The results will be discussed in view of achievement of the aim, their significance and their comparison with previous related researches.

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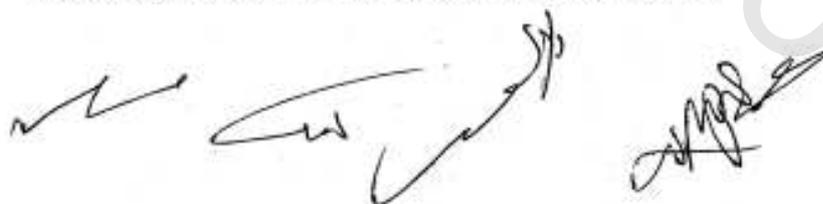
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ANNEX I[(1)]

The 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for rheumatoid arthritis

Target population (Who should be tested?): Patients who:
1) have at least 1 joint with definite clinical synovitis (swelling)
2) with the synovitis not better explained by another disease

Classification criteria for RA (score-based algorithm: add score of categories A–D;
A score of _6/10 is needed for classification of a patient as having definite RA)

	Score
A. Joint involvement	
1. 1 large joint.	0
2. 2-10 large joints	1
3. 1-3 small joints (with or without involvement of large joints)	2
4. 4-10 small joints (with or without involvement of large joints)	3
5. > 10 joints (at least 1 small joint)	5
B. Serology (at least 1 test result is needed for classification)	
1. Negative RF *and* negative ACPA	0
2. Low-positive RF *or* low-positive ACPA	2
3. High-positive RF *or* high-positive ACPA	3
C. Acute-phase reactants (at least 1 test result is needed for classification)	
1. Normal CRP *and* normal ESR	0
2. Abnormal CRP *or* abnormal ESR	1
D. Duration of symptoms	
1. <6 weeks	0
2. ≥6 weeks	1

ANNEX II[17]

Disease Activity Score Index 28 (DAS 28)

DAS28 with 4 variables:

$$DAS28 = 0.56\sqrt{(TEN28)} + 0.28\sqrt{(SW28)} + 0.70Ln(ESR) + 0.014(GH)$$

TEN28

28 joint count for tenderness

SW28

28 joint count for swelling

LnESR

Natural logarithm of Western's Erythrocyte Sedimentation Rate

GH

General health or patient's global assessment of disease activity on Visual Analogue Scale of 100mm.

DAS28 score	Level of disease activity
<3.2	Low
3.2– 5.1	Moderate
>5.1	High

ANNEX III[18]

Health Assessment Questionnaire

Name: Date:

In this section we are interested in learning how your illness affects your ability to function in daily life. Please feel free to add any comment on the bake of this page.

Please check the response which best describes your usual abilities Over The Past Week.

	Without Any difficulty	With Some difficulty	With much difficulty	Unable to do
DRESSING & GROOMING Are you able to:				
1. Dress yourself, including shoelaces and buttons?	☐	☐	☐	☐
2. Shampoo your hair?	☐	☐	☐	☐
ARISING Are you able to:				
3. Stand up from an armless straight chair?	☐	☐	☐	☐
4. Get in and out of bed?	☐	☐	☐	☐
EATING Are you able to:				
5. Cut your meat?	☐	☐	☐	☐
6. Lift a full cup or glass to your mouth?	☐	☐	☐	☐
7. Open a new milk carton?	☐	☐	☐	☐
WALKING Are you able to:				
8. Walk outdoors on flat ground?	☐	☐	☐	☐
9. Climb up five steps?	☐	☐	☐	☐

Please check any AIDS OR DEVICES that you usually use for any of the above activities:

☐ Devices used for dressing (button hook, zipper pull, etc.) ☐ Built up or special utensils ☐ Crutches
☐ Special or built up chair ☐ Cane ☐ Wheelchair
  ☐ Walker

Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

☐ Dressing and grooming ☐ Arising
☐ Eating ☐ Walking

Please check the response which best describes your usual abilities Over The Past Week.

	Without Any difficulty	With Some difficulty	With much difficulty	Unable to do
HYGIENE Are you able to:				
10. Wash and dry your body?	☐	☐	☐	☐
11. Take a tub bath?	☐	☐	☐	☐
12. Get on and off the toilet?	☐	☐	☐	☐
REACH Are you able to:				
13. Reach and get down a 5-pound object (such as a bag of sugar) from just above your head?	☐	☐	☐	☐
14. Bend down to pick up clothing from the floor?	☐	☐	☐	☐
GRIP Are you able to:				
15. Open car doors?	☐	☐	☐	☐
16. Open previously opened jars?	☐	☐	☐	☐
17. Turn faucets on and off?	☐	☐	☐	☐
ACTIVITIES Are you able to:				
18. Run errands and shop?	☐	☐	☐	☐
19. Get in and out of a car?	☐	☐	☐	☐
20. Do chores such as vacuuming or yard work?	☐	☐	☐	☐

Please check any AIDS OR DEVICES that you usually use for any of the above activities:

☐ Raised toilet seat ☐ Long-handled appliances in the bathroom ☐ Jar opener (for jars previously opened)
☐ Bathtub seat
☐ Bathtub bar ☐ Long-handled appliances for reach ☐ Other (specify)

Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

☐ Hygiene ☐ Gripping and opening things
☐ Reach ☐ Errands and chores

الملخص العربى

الروماتيزم المفصلى الرثيانى هو التهاب المفاصل المزمن الأكثر انتشارا ويتميز بالتورم والتألم بالمس وتلف المفاصل الزلالية. على الرغم من أنه يعتبر "مرض المفاصل" يرتبط الروماتيزم المفصلى الرثيانى بمشاركة مظاهر إضافية غير مفصلية بما في ذلك الألم العضلي الليفى الثانوي والتهاب الأوعية الدموية الروماتيزمي. هناك أيضا أمراض هامة مصاحبة للمرض، بما في ذلك الأورام اللمفاوية غير الهودجكن ومرض نقص تروية القلب وهشاشة العظام.

هشاشة العظام هي مرض العظام الأكثر شيوعا وتمثل مشكلة كبيرة للصحة العامة. تتميز بانخفاض كتلة العظام وتدهور النسيج العظمي وتعطيل عمارة العظام و قوتها وخطر في زيادة نسبة حدوث الكسور.

يزيد انتشار هشاشة العظام في مرضي الروماتيزم المفصلى الرثيانى ضعفين بالمقارنة مع السكان عموما. هناك انخفاض في كثافة المعادن في العظام بالإضافة إلى زيادة في نسبة حدوث الكسور بالورك والعمود الفقري في مرضى الروماتيزم المفصلى الرثيانى مقارنة بالمرضى بدون الروماتيزم المفصلى الرثيانى.

كان الهدف من هذه الدراسة تقييم هشاشة العظام في مرضى الروماتيزم المفصلى الرثيانى فى سن ما قبل انقطاع الطمث وعلاقته مع معالم المرض الأخرى.

اشتملت هذه الدراسة على ثلاثة وأربعين مريضا بالروماتيزم المفصلى الرثيانى (٣١ مريض بأجسام مضادة ضد بروتين السترولين موجبة و ١٢ مريض بأجسام مضادة ضد بروتين السترولين سالبة) حققوا معايير التصنيف للكلية الأمريكية للروماتيزم/ والعصبة الأوروبية ضد الروماتيزم للعام ٢٠١٠ لتشخيص الروماتيزم المفصلى الرثيانى .

تم الحصول على تاريخ مفصل من كل مريض يليها تقييم سريري شامل مع التركيز على فحص العضلات والعظام وتقييم نشاط المرض والقدرة الوظيفية. تم قياس علامات دوران العظام بما في ذلك مستوي مصل الدم لإجمالي البروكولاغين نوع I للأمين الطرفي البروببتيدي والبيتا كروسلاب وأوستيوكالسين لتقييم دوران العظام. كما تم تقييم إشعاعي لليدين والقدمين لتقييم تقرحات وضيق مساحة المفاصل بواسطة نتيجة شارب المعدلة وتم كذلك قياس كثافة المعادن في العظام في العمود الفقري و عظم الورك والساعد بواسطة قياس امتصاص طاقة أشعة اكس المزدوجة.

تم ضم ثلاثين فرد من الأصحاء بسن وجنس مطابق للمرضى كمجموعة ضابطة.

اظهر مرضى المجموعة الموجبة نشاط مرض وعجز أعلي من مرضى المجموعة السالبة. كما أظهر أيضا مرضى المجموعة الموجبة ارتفاع معدل دوران العظام بواسطة مصل دم البيتا كروسلاب بالمقارنة بالمجموعة الضابطة. تم العثور على تلف بالمفاصل أكثر شدة كما هو موضح بنتيجة شارب المعدلة في مرضى المجموعة الموجبة عن المجموعة السلبية.

يتسم مرضى المجموعة الموجبة أيضا بارتفاع معدل فقدان العظام كما هو موضح بانخفاض ملحوظ في قياس كثافة المعادن في عظم الورك و الساعد بالمقارنة بالمجموعة الضابطة وتتسم بارتفاع معدل فقدان العظام في العمود الفقري بالمقارنة بمرضى المجموعة السالبة والمجموعة الضابطة. يتسم مرضى المجموعة السالبة بارتفاع معدل فقدان العظام في عظمه الورك فقط بالمقارنة بالمجموعة الضابطة.

هناك علاقة ذات دلالة إحصائية بين دوران العظام وكل من عمر المرضى ونشاط المرض في مرضى المجموعة الموجبة. هناك علاقة ذات دلالة إحصائية بين تلف المفاصل ومدة المرض ومؤشر كتلة الجسم والجرعة التراكمية للكورتيكوستيرويد وفقدان العظام في عظم الورك والساعد في مرضى المجموعة الموجبة فقط.

كانت هناك علاقة ذات دلالة إحصائية بين فقدان العظام في العمود الفقري ونشاط المرض والعجز والجرعة التراكمية للكورتيكوستيرويد وفقدان العظام في عظم الورك والساعد في مرضى المجموعة الموجبة.

لجنة الإشراف

أ.د/ عبد المنعم حسين هلال   ....
أستاذ الطب الطبيعي والروماتيزم والتأهيل
كلية الطب
جامعة الإسكندرية

أ.د / دلال محمد نصر الدين القفاش   ....
أستاذ الباثولوجيا الاكلينيكية
كلية الطب
جامعة الإسكندرية

أ. د/ ايناس محمد شاهين   ....
أستاذ الطب الطبيعي و الروماتيزم والتأهيل
كلية الطب
جامعة الإسكندرية

أ.م. د / مروة محمد حسن   ....
أستاذ مساعد الطب الطبيعي و الروماتيزم والتأهيل
كلية الطب
جامعة الإسكندرية

دراسة لهشاشة العظام فى مرضى الروماتيزم المفصلى الرثيانى فى سن ما قبل انقطاع الطمث

مقدمة من

يسرا هشام محمد مصطفى عبد الفتاح

(بكالوريوس طب و جراحه ٢٠٠٥ – ماجستير ٢٠١٠)

كليه الطب ـ جامعة الإسكندرية

للحصول على درجة

الدكتوراه

فى

الطب الطبيعي والروماتيزم والتأهيل

موافقون	لجنة المناقشة والحكم على الرسالة
....	**أ.د/ عبد المنعم حسين هلال** أستاذ الطب الطبيعي والروماتيزم والتأهيل كلية الطب جامعة الإسكندرية
....	**أ.د/ أميرة حسن الجربى** أستاذ الباطنه والروماتيزم كلية الطب جامعة الإسكندرية
....	**أ.د/ محمد محمود الوقد** أستاذ الروماتيزم كلية الطب جامعة القاهرة

دراسة لهشاشة العظام فى مرضى الروماتيزم المفصلى الرثيانى فى سن ما قبل انقطاع الطمث

رسالة علمية

مقدمة إلى كلية الطب– جامعة الإسكندرية
إستيفاء للدراسات المقررة للحصول على درجة

الدكتوراه

فى

الطب الطبيعي والروماتيزم والتأهيل

مقدمة من

يسرا هشام محمد مصطفى عبد الفتاح

(بكالوريوس طب و جراحه ٢٠٠٥ – ماجستير ٢٠١٠)
كليه الطب ـ جامعة الإسكندرية

٢٠١٥