

Dedication

I would like to dedicate this research to:

My loving and supportive parents Mr. Osman Khalifa and

Mrs. Najah El gaddal.

And to my family who have always been there for me and who've helped me through my studies.

And to Allah for paving the road for me and gracing me with everything that helped me become the person I am today and to achieve my goals in life.

And also to my teachers and supervisor, who were always supportive and helpful.

And to my friends, colleagues and everyone else in the medical profession.

Acknowledgment

I would like to Thank:

Allah for guiding me through this and helping me overcome all the difficulties and being along my side throughout all my studying years.

And to my Supervisor Dr. Selma E. Abdalla who helped me and guided me throughout the research. And to Dr. Sara Lavinia for her thorough explanation of Research methodology as a subject.

Thanks are extended to my colleagues at Omdurman Military Hospital and Rayan Specialized Laboratories staff for providing me with all the materials and information needed to conduct this research.

I would like to also thank Dr. Zeryab Imad and Mr. Tamer Imad for guiding me and sharing their expertise.

ABSTRACT

This cross-sectional case-control study aimed to investigate the effects of fasting in influencing the hematological and inflammatory response in rheumatoid arthritis patients. In this study, samples were collected from RA patients who were RF positive and anti-CCP positive during the month of Ramadan, 31 samples from the fasting group, and 31 samples from the non-fasting patients. Data was collected from patients using questionnaires and existing laboratory data. The tlcs, differential leukocyte count, ESR and hs-CRP were tested for each patient using Sysmex kx-21N device and automated ELISA, and analyzed using SPSS program for the fasting and the non-fasting groups. For the fasting RA group ESR values were significantly higher (p-value= 0.014) compared to the non-fasting RA group. Fasting RA group also obtained higher hs-CRP values (p-value= 0.00) compared to the non-fasting RA group. The absolute monocyte count revealed significantly higher values (p-value=0.013) in the fasting RA group than the non-fasting group. The tlcs, absolute neutrophil count and absolute lymphocyte count (p-value=0.942, p-value=0.451, p-value=0.877) respectively, revealed insignificant results between the fasting and non-fasting RA patients. This study concludes that fasting for 12-14 hours per day, is associated with the reduction of the inflammation progression in rheumatoid arthritis patients.

المستخلص

هدفت هذه الدراسة (المقطعية - الحالة و المجموعة الضابطة) لاستقصاء تأثير الصيام على التغير في الاستجابات الدموية و الالتهابية لدى مرضى التهاب المفاصل الروماتويدي. في هذه الدراسة ، تم جمع عينات من مرضى التهاب المفاصل الروماتويدي الذين كانوا RF و Anti-CCP إيجابيين. تم أخذ 31 عينة من مرضى الروماتويد الصيام، خلال شهر رمضان ، و 31 عينة من مرضى الروماتويد الغير صائمين. وقد تم جمع البيانات من المرضى الصيام و الغير صيام باستخدام الاستبيانات والبيانات المختبرية الموجودة. تم تحليل التعداد الكلي لكريات الدم البيضاء، و عدد الكريات البيض التفاضلية ، سُرْعَةُ تَنْقُلِ الكُرَيَاتِ الحُمْرِ و البروتين المُتَفَاعِلُ C للمجموعة الصيام و المجموعة الغير صيام باستخدام جهاز ال Sysmex kx-21n و جهاز ELISA الاتوماتي وحللت بواسطة برنامج SPSS. حصلت مجموعة مرضى الروماتويد الصيام على سُرْعَةُ تَنْقُلِ الكُرَيَاتِ الحُمْرِ أعلى بكثير قيمة ($p = 0.014$) مقارنة بمجموعة مرضى الروماتويد الغير صيام. أظهرت مجموعة مرضى الروماتويد الصيام قيم البروتين المُتَفَاعِلُ C أعلى قيمة ($p = 0.00$) مقارنة بمجموعة مرضى الروماتويد غير الصيام. كانت قيم عدد خلايا أحادية المطلقة في مجموعة الصيام أعلى بكثير (قيمة $p = 0.013$) من مجموعة مرضى الروماتويد الغير صيام. كشف التعداد الكلي لكريات الدم البيضاء ، و عدد العدلات المطلق و عدد الخلايا للمفاوية المطلقة (قيمة $p = 0.942$ ، قيمة $p = 0.451$ ، قيمة $p = 0.877$) على التوالي ، نتائج غير ذات دلالة إحصائية بين مرضى الروماتويد الصيام و الغير صيام. تلخص هذه الدراسة إلى أن الصيام لمدة تتراوح ما بين 12 الى 14 ساعة يوميًا ، له تأثير على تقليل تقدم الالتهاب في التهاب المفاصل الروماتويدي.

ABBREVIATIONS

Abbreviation	
RA	Rheumatoid Arthritis
WHO	World Health Organization
IF	Intermittent Fasting
TLC	Total Leukocytes Count
Abs Neut	Absolute Neutrophil Count
Abs Mono	Absolute Monocyte Count
Abs Lymph	Absolute Lymphocytes Count
ESR	Erythrocyte Sedimentation Rate
Hs-CRP	High-sensitivity C-Reactive Protein
HLA	Human Leukocyte Antigen
RF	Rheumatoid Factor
Anti-CCP	Anti-Cyclic Citrullinated Peptides
DMARDs	Disease-Modifying Anti-Rheumatic Drugs
NsAIDs	Non-steroidal Anti-Inflammatory Drugs
CBC	Complete Blood Count
MXD	Mixed Absolute Count
WBC	White Blood Cells

RBC	Red Blood Cells
PLT	Platelets
IgM	Immunoglobulin M
IgG	Immunoglobulin G
ELISA	Enzyme linked Immuno-Sorbent Assay
PH	Potential Hydrogen
DAS-28	Disease Activity Score-28

LIST OF CONTENTS

Contents		Page
Dedication		I
Acknowledgement		II
Abstract		III
المستخلص		IV
Abbreviations		V
List of Contents		VII
List of Tables		XI
List of figures		XII
CHAPTER ONE: Introduction and Literature Review		
1.1	Introduction	2
1.2	Literature Review	4
1.2.1	Blood	4
1.2.2	Immunity	5
1.2.3	Inflammation	5
1.2.3.1	Types of Inflammation	6
1.2.4	Autoimmune disease	6
1.2.5	Rheumatoid Arthritis	7
1.2.5.1	Pathogenesis	8
1.2.5.2	Types of Rheumatoid Arthritis	9

1.2.5.3	Stages of Rheumatoid Arthritis	10
1.2.5.4	Treatment of Rheumatoid Arthritis	11
1.2.6	Fasting	11
1.2.6.1	Types of Fasting	11
1.2.7	Ramadan Fasting	12
1.2.8	Effects of fasting in Rheumatoid Arthritis pathology	12
1.2.9	Diagnosis of Rheumatoid Arthritis	13
1.2.9.1	Rheumatoid Factor	13
1.2.9.2	Anti-Cyclic Citrullinated Peptides	13
1.2.9.3	Complete Blood Count	13
1.2.9.4	Total Leukocytes Count	14
1.2.9.5	Lymphocyte Absolute Count	14
1.2.9.6	Monocyte Absolute Count	15
1.2.9.7	Neutrophils Absolute Count	16
1.2.9.8	Inflammation Markers	16
1.2.9.9	Erythrocyte Sedimentation Rate	16
1.2.9.10	High-Sensitivity CRP	17
1.3	Rationale	19
1.4	Objectives	21
1.4.1	General Objective	21
1.4.2	Specific Objectives	21

CHAPTER TWO: Materials and Method		
2.1	Study Design	23
2.2	Study Area and Duration	23
2.3	Study Population	23
2.4	Inclusion Criteria	23
2.5	Exclusion Criteria	23
2.6	Data Collection	24
2.7.1	Sample Collection	24
2.7.2	Automated Cell Analyzer (Sysmex kx-21N)	25
2.7.3	Thin Blood film	25
2.7.4	Staining method (Leishman Stain)	26
2.7.5	Differential White Blood Cell Count	27
2.7.6	ESR	27
2.7.7	IgM Rheumatoid Factor by ELISA	28
2.7.8	Anti-Citrullinated Cyclic Peptides by ELISA	28
2.7.9	High-Sensitivity C-reactive Protein	29
2.8	Data Analysis	29
2.9	Ethical Clearance	29

CHAPTER THREE: Result		
3.1	Demographic Data	31
3.2	Laboratory Data	33
CHAPTER FOUR: Discussion, Conclusion and Recommendations		
Discussion		38
Conclusion		41
Recommendation		41
References		42
Appendices		
Appendix A		46
Appendix B		47
Appendix C		48

LIST OF TABLES

Table No.	Table Title	Page No.
Table 1	Mean Age between the fasting and non-fasting RA patients	31
Table 2	Comparison of the Mean of TLC, Absolute Lymphocyte count, Absolute Monocyte count, Absolute Neutrophil count, HS-CRP, ESR between the fasting and non-fasting groups, using the Independent T test	34
Table 3	Compares the Mean of each variable among the males and females of the fasting group.	35
Table 4	Correlation of the Age with TLC, Abs Lymphocyte count, Abs Monocyte count, Abs Neutrophil count, ESR, Hs-CRP variable.	36

LIST OF FIGURES

Figure No.	Figure Title	Page No.
Figure 1	Shows gender distribution among rheumatoid arthritis patients	32
Figure 2	Shows gender distribution among the fasting and non-fasting groups	32