# PREGNANCY OUTCOME IN EGYPTIAN PATIENTS WITH RHEUMATOID ARTHRITIS

## Thesis

**Submitted for Partial Fulfillment Requirement of Master degree in internal medicine**


*Submitted by*

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***Nagham Safwat Samy***

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# LIST OF ABBREVIATIONS

| Abbreviation | | Full name |
|---|---|---|
| **11 -HSD2** | **:** | 11-hydroxysteroid dehydrogenase type 2 |
| **ACPA** | **:** | Anti citrillunated protein antibodies |
| **ACR** | **:** | American College of Rheumatology |
| **ADA** | **:** | Adalimumab |
| **ALT** | **:** | Alanine transaminase |
| **Anti Carp antibodies** | **:** | Antibodies against carbamylated proteins |
| **Anti-MCV** | **:** | Antibodies to citrullinated vimentin and mutated citrullinated vimentin |
| **ASD** | **:** | Atrial septal defect |
| **AST** | **:** | Aspartate aminotransferase |
| **axSpA** | **:** | Axial sponyloarthritis |
| **AZA** | **:** | Azathioprine |
| **BHPR** | **:** | British Health Professionals in Rheumatology |
| **BMI** | **:** | Body mass index |
| **BSR** | **:** | British Society of Rheumatology |
| **CBC** | **:** | Complete blood picture |
| **CCP** | **:** | Cyclic citrullinated peptides |
| **CDA1** | **:** | Clinical disease activity index |
| **CICs** | **:** | Circulating immune complexes |
| **CNS** | **:** | Central nervous system |
| **COX-2** | **:** | Cyclooxygenase-2 |
| **CPPD** | **:** | Calcium pyrophosphate dehydrate |
| **CRP** | **:** | C-reactive protein |
| **CS** | **:** | Cesarean section |
| **CSs** | **:** | Corticosteroids |

| Abbreviation | | Full name |
|---|---|---|
| **CVD** | **:** | Cardiovascular diseases |
| **DAS 28** | **:** | Disease Activity Score 28 |
| **DHFR** | **:** | Dihydrofolate reductase |
| **DMARDs** | **:** | Disease-modifying antirheumatic drugs |
| **EAMs** | **:** | Extra-articular manifestations |
| **EBV** | **:** | Epstein-Barr virus |
| **ELISA** | **:** | Enzyme linked immunosorbent assay |
| **ESR** | **:** | Erythrocytic sedimentation rate |
| **ETA** | **:** | Etanercept |
| **EULAR** | **:** | European League Against Rheumatism |
| **FGR** | **:** | Fetal growth restriction |
| **HCQ** | **:** | Hydroxychloroquine |
| **HLA** | **:** | Human leukocyte antigen |
| **IBD** | **:** | Inflammatory bowel disease |
| **IFN** | **:** | Interferon |
| **IFX** | **:** | Infliximab |
| **IgG** | **:** | Immunoglobin G |
| **IgM** | **:** | Immunoglobin M |
| **IL-1** | **:** | Interleukin-1 |
| **IL-1Ra** | **:** | Interleukin-1 receptor antagonist |
| **IL-2** | **:** | Interleukin-2 |
| **ILD** | **:** | Interstitial lung disease |
| **IQR** | **:** | Interquartile range |
| **JAC** | **:** | Jannus Kinase Inhibitors |
| **JIA** | **:** | Juvenile idiopathic arthritis |
| **LBW** | **:** | low birth weight |

| Abbreviation | | Full name |
|---|---|---|
| **LEF** | **:** | Leflunomide |
| **LUF** | **:** | Luteinized unruptured follicle syndrome |
| **MBDA** | **:** | Multibiomarker disease activity |
| **MCM** | **:** | Major congenital malformation |
| **MCP** | **:** | Metacarpophalangeal joint |
| **mHAQ** | **:** | Modified Health Assessment Questionnaire |
| **MRI** | **:** | Magnetic resonance imaging |
| **MTP** | **:** | Metatarso-phalangeal joint |
| **MTX** | **:** | Methotrexate |
| **NICU** | **:** | Neonatal intensive care unit |
| **NSAIDS** | **:** | Non-steroidal anti-inflammatory drugs |
| **PAG** | **:** | Pregnancy-associated globulin |
| **p-ANCA** | **:** | Positive necrotizing crescentic glomerulonephritis |
| **PG** | **:** | Prostaglandins |
| **PIP** | **:** | Proximal interphalangeal joint |
| **PlGF** | **:** | Placental growth factor |
| **RA** | **:** | Rheumatoid arthritis |
| **RF** | **:** | Rheumatoid factor |
| **RV** | **:** | Rheumatoid vasculitis |
| **SD** | **:** | Standard deviation |
| **SDAI** | **:** | Simplified Disease Activity Index |
| **sENG** | **:** | Soluble endoglin |
| **sFlt-1** | **:** | Soluble fms-like tyrosine kinase 1 |
| **SGA** | **:** | Small for gestational age |
| **SLE** | **:** | Systemic lupus erythematosus |

| Abbreviation | | Full name |
|---|---|---|
| **SPSS** | **:** | Statistical package for Social Science |
| **SS** | **:** | Sjogrens syndrome |
| **SSZ** | **:** | Sulfasalazine |
| **STNFRs** | **:** | Soluble tumor necrosis factor-alpha receptors |
| **T2DM** | **:** | Type 2 diabetes mellitus |
| **Th1** | **:** | T helper cell 1 |
| **TH2** | **:** | T helper cell 2 |
| **TNF-a** | **:** | Tumor necrosis factor-a |
| **TNFI** | **:** | Tumor necrosis factor inhibitors |
| **TTP** | **:** | Time to pregnancy |
| **US** | **:** | Ultrasound |
| **VSD** | **:** | Ventricular septal defect |

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# INTRODUCTION

Rheumatoid arthritis (RA) is considered a chronic immune-mediated inflammatory disease which can cause significant disability, morbidity, and mortality. RA affects women three times more often than men, commonly in their childbearing years ***(Kieran et al., 2018).***

Rheumatoid arthritis may adversely influence pregnancy through several mechanisms. The inflammatory process of RA may affect the placenta, leading to adverse birth outcomes for example low birth weight. RA disease activity may thus necessitate drug treatment to ensure a successful pregnancy outcome. At the same time, exposure to anti-inflammatory, immunosuppressive or biological drugs in utero may adversely affect pregnancy outcome. In recent years, RA treatment regimens have included earlier and more aggressive use of disease modifying drugs. In addition, lifestyle factors such as smoking is a risk factor for RA which can lead to preterm birth and small for gestational age (SGA) infants ***(Norgaard et al., 2010).***

Also, fertility is compromised in women with rheumatoid arthritis (RA). Most of them have fewer children than they intended to have and they are more often nulliparous ***(Jenny et al., 2017).***

Because in most women with RA antirheumatic treatment has to be adjusted before trying to conceive, a longer the time to pregnancy can result in a prolonged period with less controlled disease and consequently an increased risk for permanent damage to the joints . Female causes include anovulation, endometriosis, and unilateral or bilateral tubal occlusion. In 8–28% of subfertile couples, no specific cause is found during fertility assessments. They are referred to as couples with unexplained subfertility ***(Jenny et al., 2017).***

# AIM OF THE WORK

The aim of this study was to assess pregnancy outcomes in women diagnosed with RA compared with reference women from the general population with focus on mode of delivery, small for gestational age, preterm birth, perinatal death and congenital malformations.

# REVIEW OF LITERATURE

## Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a systemic chronic inflammatory disease, which affects mainly synovial joints, reducing life expectancy and quality of life. Although joint involvement is the most common feature of the disease with the typical symmetric tenderness and swelling of {metacarpophalangeal (MCP) joints, proximal interphalangeal (PIP) joints, wrists and metatarso-phalangeal (MTP) joints}, extra-articular manifestations, which reflect systemic involvement are common and include manifestations on the heart, skin, renal, eye, lung, gastrointestinal and nervous systems ***(Xhaferi and Lamaj, 2015).***

## Epidemiology

RA affects 0.5% to 1% of the population worldwide, with women 2 to 3 times as likely as men to be affected with the disease. Studies in industrialized countries show annual incidences between 5 and 50 per 100 000 with results varying based on case identification methods and geographical differences. RA is common in northern Europe and North America. Age at onset is usually between 30 and 70 . Evidence suggests that RA incidence may decline with disease onset shifting towards older age groups ***(Kerola et al., 2015).***