OP0211

PATERNAL INFLAMMATORY ARTHRITIS IS ASSOCIATED WITH A HIGHER RISK OF MISCARRIAGES: RESULTS OF A LARGE MULTICENTER STUDY (IFAME-FERTILITY)

L. F. Perez-Garcia[1], E. Röder[1], R. Goekoop[2], M. R. Kok[3], P. Kok[4], H. T. Smeele[1], I. Tchetverikov[5], A. Van der Helm - van Mil[1,6], J. H. Van der Kaap[1,7], B. Krijthe[1,8], R. Dolhain[1]. *[1]Erasmus University Medical Center, Rheumatology, Rotterdam, Netherlands*; *[2]Haga Hospital (Leyweg), Rheumatology, Den Haag, Netherlands*; *[3]Maasstad Hospital, Rheumatology, Rotterdam, Netherlands*; *[4]Reinier de Graaf Gasthuis, Rheumatology, Delft, Netherlands*; *[5]Albert Schweitzer Hospital, Rheumatology, Dordrecht, Netherlands*; *[6]Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; *[7]Adrz Medical Center, Rheumatology, Goes, Netherlands*; *[8]Franciscus Gasthuis & Vlietland, Rheumatology, Rotterdam, Netherlands*

Background: The effect of inflammatory arthritis (IA) on pregnancy outcomes has been studied mainly in women. Paternal older age, sperm DNA integrity and certain genetic defects have been associated with worse pregnancy outcomes (1). However, pregnancy outcomes of partners of men with IA have never been studied.

Objectives: To describe the pregnancy characteristics and outcomes of partners of men diagnosed with IA.

Methods: We performed a multicenter cross-sectional retrospective study conducted in eight Dutch hospitals. Men with IA (Rheumatoid Arthritis (RA), Juvenile Idiopathic Arthritis (JIA) and Spondyloarthritis (SpA)) who were over 40 years old and indicated that their family size was complete were invited to participate. Participants completed a digital questionnaire that included pregnancy-related questions and questions regarding their demographic and clinical information. To analyze the impact of IA on pregnancy outcomes, pregnancies were classified into two groups; pregnancies that occurred after diagnosis of IA and before the diagnosis of IA.

Results: In total 628 male participants diagnosed with IA were included. 408 men reported 897 singleton pregnancies that resulted in 794 live births. Regarding pregnancy characteristics, pregnancies conceived after diagnosis of IA had a higher mean paternal and maternal age at conception and a lower rate of spontaneous pregnancies (90.91 vs 96.60%, p=<0.005) (See Table 1). With regards to pregnancy outcomes, pregnancies conceived after receiving the diagnosis of IA had a lower rate of live births (86.36% and 89.22%, p=0.053) and a significant higher rate of miscarriages (12.27 vs 7.53%, p=<0.05). After correcting for maternal age and year of pregnancy, pregnancies conceived after the diagnosis of IA had a higher risk of miscarriages (OR 1.71 [CI 1.04-2.81], p<0.05). No statistically significant differences between the two groups were reported for the rates of abortions, preterm births and pregnancy complications.

Table 1. Pregnancy characteristics and outcomes.

	All pregnancies	Pregnancy after diagnosis of IA	Pregnancy before diagnosis of IA	P value
Pregnancy characteristics				
Total number of pregnancies	897	220	677	
Maternal age at conception, mean (SD)	29.00 (5.00)	30.69 (5.16)	28.45 (4.83)	**p<0.005**
Paternal age at conception, mean (SD)	31.31 (5.72)	34.27 (6.08)	30.49 (5.34)	**p<0.005**
Spontaneous pregnancy, n (%)	854 (95.21)	200 (90.91)	654 (96.60)	**p<0.005**
Pregnancy duration-months, median (IQR)	39 (38-40)	39 (38-40)	39 (38-40)	p=0.928
Pregnancy outcomes				
Live births, n (%)	794 (88.52)	190 (86.36)	604 (89.22)	p=0.053
Miscarriage, n (%)	78 (8.70)	27 (12.27)	51 (7.53)	**p<0.05**
Abortion, n (%)	25 (2.78)	3 (1.36)	22 (3.25)	p=0.128
*Medical indication	5 (20.00)	0 (0)	5 (22.73)	
*Personal reasons	20 (80.00)	3 (100.00)	17 (77.27)	
Pre-term birth	149 (16.61)	31 (14.09)	118 (17.43)	p=0.248
Pregnancy complications				
No complications during pregnancy, n (%)	754 (84.34)	184 (83.64)	570 (84.57)	p=0.741
Hypertensive disorders (hypertension, pre/eclampsia), n (%)	41 (4.57)	8 (3.64)	33 (4.87)	p=0.445
Gestational Diabetes Mellitus	11 (1.28)	2 (0.94)	9 (1.38)	p=0.619
Growth restriction	12 (1.34)	1 (0.45)	11 (1.65)	p=0.193

Conclusion: This is the largest study to describe the pregnancy characteristics and outcomes of partners of men diagnosed with IA and the first to demonstrate that paternal IA is associated with a higher risk of miscarriage. Prospective studies are needed to corroborate these findings.

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OP0212

MEN DIAGNOSED WITH INFLAMMATORY ARTHRITIS BEFORE THE AGE OF 40 YEARS HAVE A LOWER FERTILITY RATE THAN THOSE DIAGNOSED AFTER THE AGE OF 40 YEARS: RESULTS OF A LARGE MULTICENTER STUDY (IFAME-FERTILITY)

L. F. Perez-Garcia[1], E. Röder[1], R. Goekoop[2], J. Hazes[1], M. R. Kok[3], P. Kok[4], H. T. Smeele[1], I. Tchetverikov[5], J. H. Van der Kaap[1,6], A. Van der Helm - van Mil[1,7], B. Krijthe[1,8], R. Dolhain[1]. *[1]Erasmus University Medical Centrum, Rheumatology, Rotterdam, Netherlands*; *[2]Haga Hospital, Rheumatology, Den Haag, Netherlands*; *[3]Maasstad Hospital, Rheumatology, Rotterdam, Netherlands*; *[4]Reinier de Graaf Gasthuis, Rheumatology, Delft, Netherlands*; *[5]Albert Schweitzer Hospital, Rheumatology, Dordrecht, Netherlands*; *[6]Adrz Medical Center, Rheumatology, Goes, Netherlands*; *[7]Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands*; *[8]Franciscus Gasthuis & Vlietland, Rheumatology, Rotterdam, Netherlands*

Background: The effect of inflammatory arthritis (IA) on fertility has been mainly studied in women. Multiple factors associated with lower fertility rate in women can also be present in male patients with IA (1). The fertility rate in men with IA, however, has never been studied.

Objectives: To describe the fertility rate (number of biological children per individual) of men with IA.

Methods: We performed a multicenter cross-sectional retrospective study conducted in eight Dutch hospitals. Men with IA (Rheumatoid Arthritis (RA), Juvenile Idiopathic Arthritis (JIA) and Spondyloarthritis (SpA)) who were over 40 years old and indicated that their family size was complete were invited to participate. Men who were still planning on having biological children were excluded. Participants completed a digital questionnaire that included fertility-related questions and questions regarding their demographic and clinical information. To analyze the impact of IA on male fertility rate, patients were divided into groups according to the age at the time of their diagnosis: age<30 years, age 31-40 years and age>41 years.

Results: In total 628 participants diagnosed with IA were included. The response rate 34.87%. Information regarding their age, age at diagnosis, clinical diagnosis and number of children is presented per group in Table 1. Regarding the total number of children per man, there was a statistically significant difference between the three groups (p=<0.005). The mean total number of children was significantly lower in men diagnosed at age<30 years (1.39 {SD 1.41}) and at age 31-40 years (1.60 {SD 1.35}) compared to those diagnosed after at age>41 years (1.88 {SD 1.14}). Compared to men from the general population of the Netherlands, the total number of children of men diagnosed at age>41 years was not statistically different (1.88 vs 1.80, respectively).

Table 1. Participants' basic demographic and clinical characteristics, including the number of biological children per men.

	All patients	IA diagnosed at age <30 years	IA diagnosed at age 31-40 years	IA diagnosed at age >41 years
Total, n (%)	628	137 (21.82)	149 (23.73)	342 (54.46)
Age, mean (SD)	57.17 (9.98)	53.01 (9.96)	52.76 (7.35)	61.06 (9.47)
Diagnosis, n (%)				
• iRA	297 (47.29)	42 (30.66)	67 (44.97)	188 (55.32)
• AJIA	10 (1.59)	10 (6.25)	0 (0)	0 (0)
• ISpA (incl. PsA)	320 (50.96)	90 (65.69)	83 (55.70)	147 (42.98)
Age at diagnosis, mean (SD)	41.29 (13.08)	26.27 (9.15)	36.99 (5.66)	49.98 (9.70)
Disease duration, mean (SD)	15.89 (11.88)	26.48 (12.57)	15.70 (8.52)	11.30 (9.87)
Number of biological children, mean (95% CI)	1.71 (1.60-1.81)	**1.39 (1.15-1.63)**[a,b]	**1.60 (1.38-1.82)**[a]	1.88 (1.75 -2.01)

[a] p< 0.05 compared to those diagnosed age >41 years[b] p< 0.05 compared to those diagnosed age >31-40 years

Conclusion: This is the largest study ever conducted to evaluate the impact of IA on male fertility. We demonstrated that men diagnosed with IA before and during their reproductive years have a lower fertility rate than those men diagnosed with IA after their reproductive years. Multiple mechanisms (biological and non-biological) can be responsible for this association. More research is needed to identify the causes of these lower fertility rates in men with IA.

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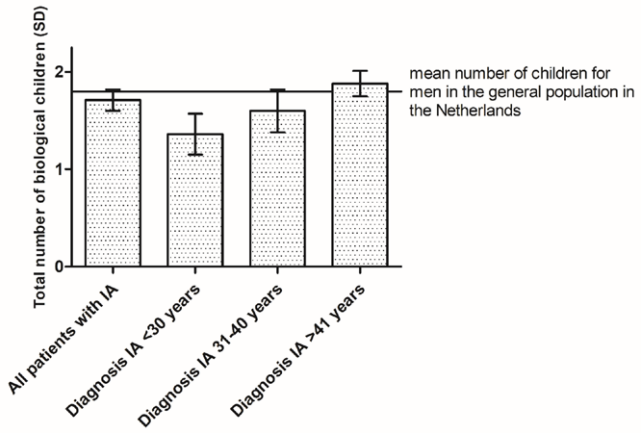

Figure 1. Total number of biological children (mean and SD) per group.

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OP0213 SEX DIFFERENCES IN MULTIMORBIDITY BETWEEN PATIENTS WITH RHEUMATOID ARTHRITIS AND COMPARATORS IN A LARGE NATIONWIDE US STUDY

H. J. Dykhoff[1], E. Myasoedova[2,3], M. Peterson[2], J. M. Davis III[2], V. Kronzer[2], C. Coffey[2], T. Gunderson[3], C. S. Crowson[2,3]. [1]*Mayo Clinic, Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Rochester, United States of America*; [2]*Mayo Clinic, Division of Rheumatology, Rochester, United States of America*; [3]*Mayo Clinic, Department of Quantitative Health Sciences, Rochester, United States of America*

Background: Patients with rheumatoid arthritis (RA) have an increased burden of multimorbidity. Although many comorbidities vary by sex, sex differences in multimorbidity among individuals with RA have not been examined.

Objectives: We aimed to compare multimorbidity between women and men with RA and comparators without RA.

Methods: We used a large longitudinal, real-world data warehouse with de-identified administrative claims for commercial and Medicare Advantage enrollees, to identify cases of RA and matched controls. Cases were defined as patients aged ≥18 years with ≥2 diagnoses of RA in January 1, 2010 - June 30, 2019 and ≥1 prescription fill for methotrexate in the year after the first RA diagnosis. Controls were persons without RA matched 1:1 to RA cases on age, sex, census region, calendar year of index date (corresponding to the date of second diagnosis code for RA), and length of prior medical/pharmacy coverage. Race was classified as non-Hispanic White (White), non-Hispanic Black (Black), Asian, Hispanic, or other/unknown, based on self-report or derived rule sets. Multimorbidity (2 or more comorbidities) was defined using 25 chronic comorbidities from a combination of the Charlson and Elixhauser Comorbidity Indices assessed during the year prior to index date. Rheumatic comorbidities were not included. Logistic regression models were used to estimate odds ratios (OR) with 95% confidence intervals (CI).

Results: The study included 16,363 cases with RA and 16,363 matched non-RA comparators (mean age 58.2 years, 70.7% female for both cohorts). In both cohorts, women were slightly younger (mean age 57.5 vs. 59.8 years). Among RA patients, women were more racially/ethnically diverse than men, with 72% of women (78% men) being White, 12% (10%) Hispanic, 11% (7%) Black, 3% (3%) Asian, and 3% (3%) other/unknown. Racial/ethnic diversity was similar among non-RA women and men with 74% women (75% men) being White, 9% (9%) Hispanic, 10% (8%) Black, 4% (4%) Asian, and 3% (4%) other/unknown. Patients with RA had more multimorbidity than non-RA subjects (51.3% vs 44.8%). Observed rates of multimorbidity were similar in women and men with RA (51.6% vs 50.5%, p=0.18), but among non-RA patients, women had lower observed rates of multimorbidity than men (43.7% vs 47.4%, p<0.0001). However, following adjustment for age, race/ethnicity, and geographic region, multimorbidity among RA patients was greater in women versus men (OR: 1.19; 95% CI: 1.11-1.28) and similar among non-RA women and men (OR: 0.97 for females; 95% CI: 0.90-1.05). Examination of individual comorbidities showed that women with RA had more depression, hypothyroidism, diabetes mellitus, and chronic pulmonary disease compared to men with RA and women without RA.

Conclusion: This large nationwide study showed increased occurrence of multimorbidity in women with RA compared to men with RA, while women and men without RA had similar levels of multimorbidity following adjustment for age, race/ethnicity, and geographic region. The underlying mechanisms for these sex differences require further investigation.

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OP0214 IMPACT OF A MULTI-MORBIDITY SCREENING AND PREVENTION PROGRAM IN CHRONIC INFLAMMATORY RHEUMATIC DISEASES ON THE ONE-YEAR HOSPITALIZATION RATE BASED ON AN ANALYSIS OF THE FRENCH NATIONAL HEALTH DATABASE

G. Decarriere[1], J. Pastor[2], D. Demoulin[2], G. Mouterde[1], C. Lukas[1], B. Combe[1], G. Mercier[2], J. Morel[1], C. Daien[1]. [1]*CHU, Rheumatology, Montpellier, France*; [2]*CHU, Medical Information, Montpellier, France*

Background: A screening program for multimorbidities started in 2014 at the Montpellier University Hospital for primary prevention in patients with chronic inflammatory rheumatic diseases (IRD).

Objectives: The objective of this work was to assess the impact of this program on morbidity by comparing the hospitalization rate of those patients in the year following the screening to the one of patients with IRD who did not benefit from this program.

Methods: Patients with IRD who benefit from the screening program in 2015, 2016 and 2017 were identified in the French national health database PMSI and matched to 3 controls living in the same area on age, sex, type of IRD, use of intravenous (IV) biologic (b) DMARDs and index date. The exclusion criteria were subjects in secondary prevention identified as history of myocardial infarction in the previous 5 years or use of antiplatelet therapy. The primary outcome was the rate of all-cause hospitalization in the following year. The secondary endpoints were hospitalizations for another reason than IRD ("non-IRD") including those for cardiovascular [CV] events and major fractures. Hospitalization rates were compared between the two groups in the year after screening (or index date) and also between the year preceding screening and the year after for each group. Univariate and multivariate odds ratios (CI95%) were calculated, taking into account the medical history (hypertension, diabetes, heart failure, CV disease, COPD, major fractures in the 5 years preceding the index date) and hospitalizations in the previous year.

Results: 486 patients were identified and matched with 1458 controls. 67.08% had rheumatoid arthritis and 21.81% spondyloarthritis; 7% of them had IV bDMARDs. Unscreened patients had more hypertension (19% vs 10.1%), diabetes (9% vs 4.9%), heart failure (2.3% vs 0.4%) and "non-IRD" hospitalizations (78.5% vs 72.2%) in the 5 years preceding the index date. In the year following the index date, the percentages of "all causes" and "non-IRD" hospitalizations were significantly higher in non-screened than in screened patients (n = 1944, 64.8% versus 51%, Chi2 test, p <0.001; and 47.1% versus 37.9%, p <0.001 respectively). 17 (1.17%) cardiovascular events occurred in non-screened versus 2 (0.41%) in screened patients (n = 1944, Chi2 test, p = 0.14). There was no difference in the occurrence of CV events or major fractures between the 2 groups. In multivariate analysis, screening was associated with a 49% (0.51 [0.41-0.64]) reduction in "all causes" hospitalization and a 27% (0, 73 [0.58-0.91]) decrease in "non-IRD" hospitalization, with no difference for CV or fracture cardiological events. The risk factors associated with "non-IRD" hospitalization were: history of "non-IRD" hospitalization in the previous year (2.26 [1.63-3.13]), IV bDMARDs (1.69 [1, 14-2.53]) and age> 70 years (1.44 [1.02-2.03] vs <50 years). Hospitalization in the previous year for "all causes" or "non-IRD" was associated with