BMC Pregnancy and Childbirth

RESEARCH

Open Access

Obstetric and neonatal outcomes in women with Ankylosing spondylitis - an evaluation of a population database

Uri Amikam[1,2*], Ahmad Badeghiesh[3], Haitham Baghlaf[4], Richard Brown[1] and Michael H. Dahan[1]

Abstract

Background Ankylosing Spondylitis (AS) is a systemic chronic rheumatic disease characterized by involvement of the axial skeletal and sacroiliac joints. Although this disease is not rare amongst women of reproductive age, data regarding pregnancy outcomes have demonstrated conflicting results. We therefore aimed to compare pregnancy and perinatal outcomes between women who suffered from AS to those who did not.

Methods A retrospective cohort study using the Healthcare Cost and Utilization Project, Nationwide Inpatient Sample (HCUP-NIS). Included in the study were all pregnant women who delivered or had a maternal death in the US between 2004 and 2014. Women with an ICD-9 diagnosis of AS before or during pregnancy were compared to those without. Pregnancy, delivery, and neonatal outcomes were compared between the two groups using multivariate logistic regression models adjusting for potential confounders.

Results A total of 9,096,788 women were inclusion in the analysis. Amongst them, 383 women (3.8/100,000) had a diagnosis of AS and the rest were controls. Women with AS, compared to those without, were more likely to be older; Caucasian; from higher income quartiles; suffer from thyroid disorders, and have multiple pregnancies ($p<0.001$, all). After adjusting for confounders, patients in the AS group, compared to those without, had a higher rate of cesarean delivery (CD) (aOR 1.47, 95% CI 1.14–1.91, $p=0.003$); gestational diabetes (aOR 1.55, 95% CI 1.02–2.33, $p=0.038$); and placenta previa (aOR 3.6, 95% CI 1.6–8.12, $p=0.002$). Regarding neonatal outcomes, patients with AS, compared to those without, had a higher rate of small-for-gestational-age (SGA) neonates (aOR 2.19, 95% CI 1.22–3.93, $p=0.009$); and intrauterine fetal death (IUFD) (aOR 3.46, 95% CI 1.11–10.83, $p=0.033$).

Conclusion Women diagnosed with AS have an increased risk of obstetric complications, including CD, as well as an increased risk of SGA and IUFD.

Keywords Ankylosing spondylitis, Cesarean delivery, Obstetric complications, Small-for-gestational-age, Population-based study

*Correspondence:
Uri Amikam
uriamikam@gmail.com
[1]Department of Obstetrics and Gynecology, McGill University, 845 Rue Sherbrooke, O, Montreal, Montréal, Quebec, QC 3HA 0G4, Canada
[2]The Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[3]Department of Obstetrics and Gynecology, Rabigh Branch, King Abdulaziz University, Jeddah, Saudi Arabia
[4]Department of Obstetrics and Gynecology, University of Tabuk, Tabuk, Saudi Arabia

Background

Ankylosing spondylitis (AS) is a chronic inflammatory disease mainly involving the sacroiliac joints and spine [1]. The inflammation process causes chronic arthritis and leads to the fusion of the axial skeleton, resulting in the classical manifestation of lower back pain [2]. AS is one of the entities of spondyloarthritis, along with reactive arthritis, psoriatic arthritis, and spondylitis associated with inflammatory bowel disease [3]. Besides joint involvement, individuals with AS also have a systemic inflammatory response, which in pregnancy may have both maternal and neonatal implications that are not yet well described.

The annual incidence of AS is estimated to range from 0.0.5 to 1.4/10,000 person-years and its prevalence ranges between 0.1 and 1.4% [4]. It had previously been suggested that this disease was more prevalent in men with a 2 to 1 ratio [4, 5], whilst more recent studies have shown a more balanced incidence between sexes [6, 7]. As about 80% of patients develop the first symptoms at an age younger than 30 years, and less than 5% of patients initially present at older than 45 years [8], in women, presentation is often during the childbearing age.

Evidence shows that pregnancy does not affect the disease course [9], and the disease remains stable in the year following delivery [10].

Although AS impacts women during their reproductive years, there is conflicting data regarding pregnancy outcomes in these patients. While some studies found higher rates of preeclampsia [11] and preterm labor [11–13], others did not [14, 15]. Another limitation is that two previous large studies comprising 1642 and 2461 patients with spondylarthritis, combined all etiologies of this condition and did not examine the impact of specific diagnoses such as AS [15, 16].

Due to this conflicting data regarding the association between AS and obstetric and neonatal outcomes, our primary objective was to investigate and compare pregnancy, delivery, and neonatal outcomes in women diagnosed with AS compared to those without AS, using a large population-based cohort.

Methods

This study is a retrospective analysis of a population-based cohort, utilizing the Healthcare Cost and Utilization Project Nationwide Inpatient Sample (HCUP-NIS) database [17]. It stands as the largest inpatient sample database in the United States of America and includes hospital inpatient stays submitted by healthcare facilities across the nation. On an annual basis, this database provides detailed information on seven million inpatient stays, encompassing a wide range of details such as patient characteristics, diagnoses, and procedures. Notably, the dataset accounts for approximately 20% of all hospital admissions in the United States, spanning across 48 states and the District of Columbia. We included in the database all women who delivered or had a maternal death between 2004 and 2014, ensuring that each pregnancy was included only once. Notably, our data included only a possibly viable pregnancy at 24 weeks or above and did not include earlier miscarriages.

The cohort was divided into two groups according to AS diagnosis – women diagnosed with AS before or during pregnancy (study group) and women without an AS diagnosis (control group). The patient's AS diagnosis was categorized based on an International Classification of Diseases 9th Revision (ICD-9) diagnosis code 720.0.

The collected data comprised a range of demographic and obstetric parameters, labor-related details, and short-term maternal and neonatal outcomes up to the point of discharge. Baseline clinical characteristics included: obesity (defined as a body mass index (BMI) greater than or equal to 30 kg/m^2); tobacco smoking during pregnancy; chronic hypertension; previous cesarean delivery (CD); pregestational diabetes mellitus (DM); thyroid disease; multiple gestations; in-vitro fertilization (IVF), and illicit drug use.

Pregnancy and delivery outcomes included: preeclampsia; eclampsia; pregnancy-induced hypertension; gestational hypertension; placenta previa; placental abruption; gestational diabetes mellitus (GDM); preterm premature rupture of membranes (PPROM); preterm delivery (<37 weeks); operative vaginal delivery; CD; placental abruption; chorioamnionitis; hysterectomy; postpartum hemorrhage (PPH); maternal infection; maternal death; need for blood transfusion; disseminated intravascular coagulation (DIC); deep vein thrombosis; pulmonary embolism and venous thromboembolism (VTE). Neonatal outcomes examined included: small-for-gestational-age (SGA) neonates; congenital anomalies and intra-uterine fetal death (IUFD).

The overall prevalence of pregnant women diagnosed with AS was ascertained and then the differences in baseline characteristics between women with a diagnosis of AS and those without were compared using the chi-squared test. Subsequently, logistic regression analyses were conducted to evaluate the unadjusted and adjusted effects of an AS diagnosis on maternal and neonatal outcomes, estimating odds ratios (OR) and 95% confidence intervals (CI). The regression models were adjusted to account for potential confounding factors, including maternal demographics, pre-existing clinical characteristics, and concurrently occurring conditions in which the chi-squared tests had shown significance. All analyses were performed using SPSS 23.0 (IBM Corporation, Chicago, USA) software.

This study exclusively utilized publicly accessible, anonymized data. As a result, in accordance with articles 2.2

and 2.4 of the Tri-Council Policy Statement (2010), institutional review board approval was not required [18].

Results

Out of the total 9,096,788 women meeting the inclusion criteria, 383 individuals were diagnosed with AS either before or during pregnancy with a calculated overall prevalence of 4.2 per 100,000. It is noteworthy that the prevalence of an AS diagnosis increased significantly across the study period ($p<0.001$) (Fig. 1).

Table 1 lists the demographic and baseline characteristics of women with and without a diagnosis of AS. Women with AS, as compared to those without, were characterized by increased maternal age (25.6% ≥35 years vs. 14.7%, $p<0.001$, respectively); were more likely of Caucasian race (80.5% vs. 52.3%, $p<0.001$); more likely to have a higher income ($p<0.001$); to have private insurance (79.1% vs. 50.6%, $p<0.001$); to have a multiple gestation (3.1% vs. 1.5%, $p=0.009$); and to suffer from thyroid disorders (8.6% vs. 2.5%, $p<0.001$). Other maternal characteristics, such as tobacco smoking during pregnancy, illicit drug use, chronic hypertension, and pregestational DM, were comparable between the two groups.

Table 2 displays the association between an AS diagnosis and pregnancy and delivery outcomes after adjusting for potential confounders, which included all demographic and baseline characteristics that differed statistically between the two groups and included age, race, medical insurance plan type, income quartiles, thyroid disorders, and multiple gestations, with the addition of GDM and placenta previa for the analysis of delivery and neonatal outcomes. Women with an AS diagnosis, compared to those without, had a higher rate of GDM (adjusted OR (aOR) 1.55, 95% CI 1.02–2.33, $p=0.038$); and placenta previa (aOR 3.6, 95% CI 1.6–8.12, $p=0.002$). They also had a higher rate of CD (aOR 1.47, 95% CI 1.14–1.91, $p=0.003$), and a lower rate of spontaneous vaginal deliveries (aOR 0.67, 95% CI 0.52–0.87, $p=0.002$). Other pregnancy and delivery outcomes, such as preeclampsia, eclampsia, placental abruption, PPROM, preterm delivery, chorioamnionitis, PPH, blood transfusion, maternal death, VTE, and DIC, were comparable between the groups ($p>0.05$ in all cases).

Neonatal outcomes are presented in Table 3. Women with an AS diagnosis, compared to controls, had a higher rate of SGA neonates (aOR 2.19, 95% CI 1.22–3.93, $p=0.009$), and a higher rate of IUFD (aOR 3.46, 95% CI 1.11–10.83, $p=0.033$). There was no difference in the rate of congenital anomalies between the two groups.

Discussion

This study compared pregnancy, delivery, and neonatal outcomes between mothers with AS and those without. Our key findings were: (1) An increasing prevalence of pregnancies in women with AS across the study period; (2) That pregnant women with AS were characterized by increasing maternal age, and higher rates of Caucasian race, a higher income quartile, private medical insurance, multiple gestation pregnancies and thyroid disorders; (3) Women with AS had an increased risk for GDM, placenta previa, and CD; (4) Women with AS had higher rates of SGA neonates and IUFD compared to women without AS.

During the 11-year study period, there was a threefold rise in the prevalence of AS diagnosis among women admitted for delivery ($p<0.001$). This finding corresponds with an increase in the prevalence of AS in the general population in the US between 2006 and 2014 [19]. Similarly, a previous study examining spondyloarthritis found an increase in prevalence from 0.1% in 1997 to 0.6% in 2016 [20]. The rising prevalence of diagnosed spondyloarthritis during the study period may be attributed to

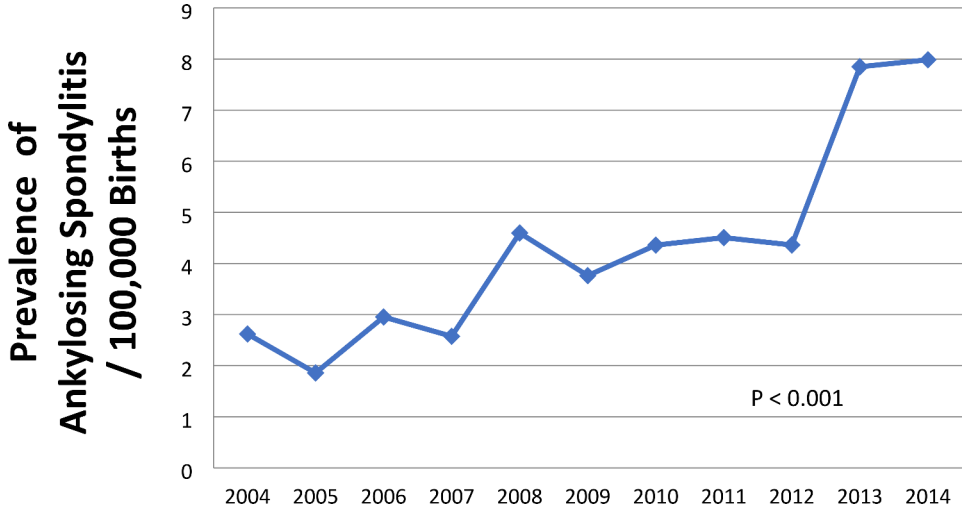

Fig. 1 Prevalence of ankylosing spondylitis in pregnant women during the study period

Table 1 Maternal characteristics

Characteristics	Ankylosing Spondylitis *N* = 383	No Ankylosing Spondylitis *N* = 9,096,405	*P*-value
Age (years)			**< 0.001**
< 25	53 (13.8%)	3,456,016 (38%)	
25–34	232 (60.6%)	4,298,758 (47.3%)	
≥ 35	98 (25.6%)	1,341,096 (14.7%)	
Race			**< 0.001**
White	248 (80.5%)	3,958,063 (52.3%)	
Black	(2.6%)	1,035,397 (13.7%)	
Hispanic	25 (8.1%)	1,756,798 (23.2%)	
Asian and Pacific	14 (4.5%)	390,363 (5.2%)	
Native American	(0.6%)	59,904 (0.8%)	
Other	11 (3.6%)	365,532 (4.8%)	
Income quartiles			**< 0.001**
Less than 39,000	44 (15.2%)	1,486,541 (27.3%)	
$39,000–47,999	57 (19.7%)	1,386767 (25.5%)	
$48,000–62,999	87 (30%)	1,355,386 (24.9%)	
$63,000 or more	102 (35.2%)	1,218,843 (22.4%)	
Plan type			**< 0.001**
Medicare	(2.3%)	56,579 (0.6%)	
Medicaid	54 (14.1%)	3,874,374 (42.7%)	
Private including HMO	303 (79.1%)	4,599,326 (50.6%)	
self-pay	(1.3%)	288,411 (3.2%)	
No charge	0	17,062 (0.2%)	
Other	12 (3.1%)	244,921 (2.7%)	
Obesity	19 (5%)	324,157 (3.6%)	0.14
Tobacco Smoking during pregnancy	20 (5.2%)	443,570 (4.9%)	0.753
Previous CD	65 (17%)	1,452,425 (16%)	0.592
Chronic hypertension	12 (3.1%)	165,218 (1.8%)	0.054
Pregestational DM	(1.3%)	86,610 (1%)	0.476
Illicit Drug use	(1.3%)	125,614 (1.4%)	0.899
Multiple gestation	12 (3.1%)	137,291 (1.5%)	**0.009**
Thyroid disease	33 (8.6%)	223,245 (2.5%)	**< 0.001**
HIV	0	2079 (0%)	0.916
IVF	(0.3%)	10,531 (0.1%)	0.705

Abbreviations and definitions: HMO - Health Maintenance Organization; BMI - Body Mass Index; CD – cesarean delivery; DM – diabetes mellitus; IVF – in-vitro fertilization

As per convention for use of the HCUP database, when $N < 11$, absolute case numbers cannot be reported to protect patient anonymity

advancements in classification criteria as well as technological improvements that have enhanced the accurate diagnosis of the condition. For instance, the introduction of the Assessment of Spondyloarthritis International Society classification criteria for axial spondyloarthritis in 2011 [21], includes the diagnosis of non-radiographic spondyloarthritis, supporting this hypothesis, it's noteworthy that in our cohort, the surge in prevalence was primarily observed after 2011. Therefore, the apparent increase in prevalence is more likely to reflect changes in the rates of diagnosis rather than a true increase in the actual disease prevalence.

Regarding maternal characteristics in our cohort, women with AS were more likely to be older, consistent with previous data [13, 14] that have described an older age amongst parturients with AS, and with a previous study showing a peak of AS prevalence in women between the ages of 30 to 39 years [22]. Our observation that Caucasian women had a higher rate of AS is likely attributable to the higher prevalence of the HLA-B27 subtype in this ethnic group [23], a subtype closely related to the risk of developing AS [4, 24].

Two additional noteworthy differences in maternal characteristics between the groups in our cohort include higher rates of multiple pregnancies and thyroid disorders in the AS group. The data in the literature regarding multiple pregnancies in AS is scarce since many previous studies limited the inclusion criteria to singleton pregnancies [11–13, 15, 20]. Similar to our findings, one previous study from South Korea described a higher incidence of twin pregnancy within their cohort [14]. In contrast, a smaller study of 129 patients with AS did not demonstrate such an association [25]. The higher multiple gestation rate in the AS group cannot be attributed to IVF treatment, which was comparable in both groups of our cohort. This is consistent with prior data that did not demonstrate an association between AS and infertility in women [26]. Advanced maternal age however is a recognized risk factor associated with an increased likelihood of multiple pregnancies [27] and may be a contributory factor to this observation. Previous studies have described an association between AS and thyroid disorders outside of pregnancy [28, 29], but pregnancy related data are limited and conflicting. While Keeling et al. [15] found a 6% prevalence of thyroid disorders among pregnant women with AS vs. 3.9% in controls (<0.01), two other studies did not demonstrate such a correlation [11, 25]. Whether a true association between AS and thyroid disease exists or what its etiology might be remains to be determined but until such data are available it would seem prudent to monitor thyroid function more often in these women.

Women with AS have an increased rate of GDM even after adjusting for potential confounders such as age and multiple pregnancies. This finding conflicts with previous data where no such association was observed [11, 12, 14, 25, 30]. Three of these previous studies were not powered to detect such an association, with populations of between 27 and 129 patients [12, 14, 25] nor was a meta-analysis [30] that included these three trials, with a total of 226 women. The largest trial that assessed GDM in this group was from Sweden [11] and included 1580 women, however, the incidence of GDM in the AS and control groups was only 2.1% and 2%, respectively, with

Table 2 Pregnancy and delivery outcomes

Outcomes	Ankylosing Spondylitis *N* = 383 (%)	No Ankylosing Spondylitis *N* = 9,096,405 (%)	Crude OR (95% CI)	Adjusted OR (95% CI)	Adjusted *p*-value
Pregnancy outcomes[a]					
Pregnancy-induced hypertension	36 (9.4%)	673,713 (7.4%)	1.3 (0.92–1.83)	1.37 (0.91–2.05)	0.136
Gestational hypertension	19 (5%)	301,588 (3.3%)	1.52 (0.96–2.41)	1.41 (0.81–2.47)	0.226
Preeclampsia	14 (3.7%)	327,376 (3.6%)	1.02 (0.6–1.73)	1.25 (0.68–2.3)	0.467
Eclampsia	0	6,944 (0.1%)	0 (0–0)	0 (0–0)	0.996
Preeclampsia and Eclampsia superimposed on hypertension	(0.8%)	47,362 (0.5%)	1.51 (0.48–4.7)	1.26 (0.31–5.1)	0.745
GDM	36 (9.4%)	523,156 (5.8%)	1.7 (1.21–2.4)	1.55 (1.02–2.33)	**0.038**
Placenta previa	(1.6%)	49,976 (0.5%)	2.88 (1.29–6.45)	3.6 (1.6–8.12)	**0.002**
Delivery outcomes[b]					
PPROM	11 (2.9%)	103,607 (1.1%)	2.57 (1.41–4.67)	2.1 (0.93–4.75)	0.074
Preterm delivery	37 (9.7%)	653,858 (7.2%)	1.38 (0.98–1.94)	1.49 (0.96–2.31)	0.072
Operative vaginal delivery	22 (5.7%)	489,379 (5.4%)	1.07 (0. 7-1.645)	1.14 (0.65–1.99)	0.653
CD	179 (46.7%)	2,939,739 (32.3%)	1.84 (1.5–2.25)	1.47 (1.14–1.91)	**0.003**
SVD	182 (47.5%)	5,667,287 (62.3%)	0.55 (0.45–0.67)	0.67 (0.52–0.87)	**0.002**
Abruptio placenta	(1%)	97,475 (1.1%)	0.97 (0.36–2.61)	1.58 (0.59–4.25)	0.366
Chorioamnionitis	(0.8%)	165,327 (1.8%)	0.43 (0.14–1.33)	0.78 (0.25–2.44)	0.672
Hysterectomy	0	7,099 (0.1%)	0 (0–0)	0 (0–0)	0.995
PPH	(2.6%)	263,955 (2.9%)	0.9 (0.48–1.68)	0.99 (0.46–2.09)	0.97
Wound complications	(0.5%)	32,731 (0.4%)	1.45 (0.36–5.83)	1.95 (0.48–7.86)	0.347
Maternal Death	0	638 (0%)	0 (0–0)	0 (0–0)	0.996
Transfusion	(1.3%)	90,362 (1%)	1.32 (0.55–3.19)	1.51 (0.56–4.11)	0.417
Others					
Maternal infection	(1%)	199,264 (2.2%)	0.47 (0.18–1.26)	0.67 (0.21–2.09)	0.49
DVT	0	3,832 (0%)	0 (0–0)	0 (0–0)	0.996
Pulmonary embolism	0	1,659 (0%)	0 (0–0)	0 (0–0)	0.996
VTE	0	5,310 (0.1%)	0 (0–0)	0 (0–0)	0.996
DIC	0	18,244 (0.2%)	0 (0–0)	0 (0–0)	0.995

a- Pregnancy Outcomes: Adjusted for age, race, insurance plan type, income quartiles, thyroid disease, and multiple gestation.

b- Delivery Outcomes: Adjusted for age, race, insurance plan type, income quartiles, thyroid disease, multiple gestation, gestational diabetes mellitus, and placenta previa.

Abbreviations and definitions: GDM – gestational diabetes mellitus; PPROM – preterm premature rupture of membranes; CD – cesarean delivery; SVD – spontaneous vaginal delivery; PPH – post-partum hemorrhage; VTE – venous thromboembolism; DIC – disseminated intravascular coagulation.

As per convention for use of the HCUP database, when $N < 11$, absolute case numbers cannot be reported to protect patient anonymity.

Table 3 Neonatal outcomes[a]

Outcomes	Ankylosing Spondylitis *N* = 383 (%)	No Ankylosing Spondylitis *N* = 9,096,405 (%)	Crude OR (95% CI)	Adjusted OR (95% CI)	Adjusted *p*-value
SGA	18 (4.7%)	198,052 (2.2%)	2.22 (1.38–3.56)	2.19 (1.22–3.93)	**0.009**
Congenital Anomalies	(1%)	38,240 (0.4%)	2.5 (0.93–6.7)	2.44 (0.91–6.57)	0.077
IUFD	(0.8%)	38,256 (0.4%)	1.87 (0.6–5.82)	3.46 (1.11–10.83)	**0.033**

a- Neonatal Outcomes: Adjusted for age, race, insurance plan type, income quartiles, thyroid disease, multiple gestation, gestational diabetes mellitus, and placenta previa

Abbreviations and definitions: SGA – small for gestational age; IUFD – intrauterine fetal death

As per convention for use of the HCUP database, when $N < 11$, absolute case numbers cannot be reported to protect patient anonymity

a different overall population incidence of GDM than that in our study. In this study, 92.7% of women in the AS group were of Nordic origin, whereas in our cohort, 19.5% of women with AS were non-Caucasian. This may explain the discrepancy in GDM rates between these two cohorts as our American population includes a substantial number of Black, Asian, and Hispanic subjects, who are more likely to demonstrate insulin resistance across different BMIs [31]. Another possible explanation for a higher rate of GDM in women with AS could be the

use of corticosteroid treatments for the control of disease symptoms or flares. In our dataset, there is no data regarding patients' medications, and therefore we cannot evaluate this possible association.

We have identified a significantly higher rate of placenta previa in the AS group. Previous data on this is lacking, with only two previous studies examining this association. In one study [25] placental abruptions and placenta previa were combined with no overall association with AS whilst the other study included only 12 patients and was therefore underpowered to evaluate this. The total number of cases of placenta previa in our cohort was small (less than 11 cases) and therefore this possible association would require further evaluation in a much larger population cohort.

Women with AS had a higher rate of CD than controls, after adjusting for potential confounders such as age, GDM, and multiple pregnancies. This finding is consistent with those observed in two meta-analyses [26, 30], which found an OR for CD of 1.7–1.83 in AS patients. A previous study aimed to evaluate factors related to the higher incidence of CD amongst AS women [32]. This study found a CD rate of 50.8%, with older maternal age, a longer disease duration, presence of preeclampsia, and AS requiring medications (such as tumor necrosis factor inhibitor (TNFi), disease-modifying antirheumatic drugs (DMARD), or corticosteroids) being factors associated with a higher risk for CD. Although a meta-analysis [30] found both emergency CD and elective CD to be more frequent in women with AS compared to controls, the prevalence of elective CD (OR 2.26) was particularly increased compared to emergency CD (OR 1.29). In the HCUP database, indications for CD are not available, and we cannot determine the reasons for this higher incidence of CD.

The rates of both SGA and IUFD were higher in the AS group compared to controls, while the rate of congenital anomalies was comparable. A previous meta-analysis also found a higher rate of SGA in AS patients compared to controls, with an OR of 2.05 (95% CI 1.09–3.89) [26], while another meta-analysis showed an increased trend of SGA neonates which did not reach statistical significance (OR 1.66, 95% CI 0.93–2.95). This could reflect factors related to disease activity or pharmacotherapy with for example both corticosteroids and TNFi being associated with SGA [33, 34]. For IUFD the data are scarce. A Swedish study [13] reported only one case of IUFD amongst 388 women with AS. Another study from Denmark [20] examined perinatal mortality and reported six cases of IUFD amongst 590 gestations in patients with AS but did not find a difference compared to non-AS controls. Given the small number of IUFD cases in our cohort (less than 11), it is hard to draw definitive conclusions regarding this finding, and again this will likely only be determined by much larger population studies.

Our study has several strengths. First, we examined only patients with AS, excluding other causes of spondyloarthritis that may individually have different prognoses. Second, we examined a range of pregnancy and delivery complications, providing detailed insights that can enable physicians to offer more precise counseling to pregnant women diagnosed with AS. This encompasses a heightened understanding of overall obstetric outcomes, along with perinatal prognoses. Additionally, this is one of the largest cohorts to address this topic. Lastly, due to our reliance on a population-based cohort, the outcomes of our study are applicable to the broader American population.

Notably, only deliveries at more than 24 weeks of gestation were included in our study. This was in order to focus on evaluating pregnancy and delivery outcomes in pregnancies that reached fetal viability, thereby excluding first and early second-trimester miscarriages and abortions. As a result, this study's findings are applicable only to patients who reached 24 weeks of gestation and beyond.

Our study has several limitations. First due to the nature of the dataset used, there was no information on disease severity and pharmacotherapy in the AS group, all of which may potentially influence perinatal complications. Additional maternal characteristics that may also impact upon outcomes, such as autoimmune disorders, cardiovascular disease, and thrombophilia, were also not reported in our cohort. Furthermore, data on the obstetrical history of women in this cohort was unavailable due to coding restrictions and the need to protect patient anonymity. This limitation could introduce bias to our results. For instance, if women with AS had a higher rate of nulliparity, it might account for the observed lower rate of SVD in this group. Additionally, due to the anonymized nature of the study, we could not detect if a patient had more than one delivery during the study period. This may affect our results if, for example, the women in the AS group with GDM had more than one delivery during the study period, since a previous pregnancy with GDM is a risk factor for GDM recurrence in a subsequent pregnancy [35]. Notably, our cohort was restricted to the period before 2015, which reflects a limitation due to changes in coding within HCUP that prevent later data from being analyzed in a comparable fashion. Therefore, some potential updates in the obstetric and rheumatologic management of parturients with AS, such as the use of biologic treatments during pregnancy, which became more common during the 2010s [36], may not be reflected in the study.

In conclusion, women diagnosed with ankylosing spondylitis demonstrate a heightened occurrence of obstetrical complications, such as GDM and CD, along with an elevated risk of delivering SGA neonates. These results underscore the significance of thorough patient counseling, multidisciplinary care, and vigilant obstetric monitoring for individuals with AS throughout the course of their pregnancies.

Abbreviations

AS	Ankylosing spondylitis
HCUP-NIS	Healthcare Cost and Utilization Project, Nationwide Inpatient Sample
ICD-9	International Classification of Diseases 9th Revision
BMI	Body mass index
CD	Cesarean delivery
DM	Diabetes mellitus
IVF	In-vitro fertilization
GDM	Gestational diabetes mellitus
PPROM	Preterm premature rupture of membranes
PPH	postpartum hemorrhage
DIC	Disseminated intravascular coagulation
VTE	Venous thromboembolism
SGA	Small-for-gestational-age
IUFD	Intra-uterine fetal death
OR	Odds ratio
CI	Confidence intervals
TNFi	Tumor necrosis factor inhibitor
DMARD	Disease-modifying antirheumatic drugs

Acknowledgements
Not applicable.

Author contributions
UA and MD: Drafting the manuscript; AB and HB: performed the data acquisition and coding and performed the data analysis; RB: Manuscript editing and interpretation of data; All authors drafted the manuscript for scientific content and approved the final submitted manuscript.

Funding
There has been no funding for this research.

Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This study exclusively utilized publicly accessible, anonymized data. As a result, per articles 2.2 and 2.4 of the Tri-Council Policy Statement (2010), institutional review board approval was not required [18].

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 18 December 2023 / Accepted: 16 September 2024
Published online: 03 October 2024

References

1. Mokbel A, Lawson DO, Farrokhyar F. Pregnancy outcomes in women with ankylosing spondylitis: a scoping literature and methodological review. Clin Rheumatol. 2021;40(9):3465–80.
2. Ritchlin C, Adamopoulos IE. Axial spondyloarthritis: new advances in diagnosis and management. BMJ. 2021;372:m4447.
3. Sieper J, Rudwaleit M, Baraliakos X, Brandt J, Braun J, Burgos-Vargas R, et al. The Assessment of SpondyloArthritis international society (ASAS) handbook: a guide to assess spondyloarthritis. Ann Rheum Dis. 2009;68(Suppl 2):ii1–44.
4. Braun J, Sieper J. Ankylosing spondylitis. Lancet. 2007;369(9570):1379–90.
5. Kennedy LG, Will R, Calin A. Sex ratio in the spondyloarthropathies and its relationship to phenotypic expression, mode of inheritance and age at onset. J Rheumatol. 1993;20(11):1900–4.
6. Nelson DA, Kaplan RM, Kurina LM, Weisman MH. Incidence of Ankylosing Spondylitis among Male and Female United States Army Personnel. Arthritis Care Res (Hoboken). 2023;75(2):332–9.
7. Rusman T, van Vollenhoven RF, van der Horst-Bruinsma IE. Gender differences in Axial Spondyloarthritis: women are not so lucky. Curr Rheumatol Rep. 2018;20(6):35.
8. Feldtkeller E, Khan MA, van der Heijde D, van der Linden S, Braun J. Age at disease onset and diagnosis delay in HLA-B27 negative vs. positive patients with ankylosing spondylitis. Rheumatol Int. 2003;23(2):61–6.
9. Lui NL, Haroon N, Carty A, Shen H, Cook RJ, Shanmugarajah S, et al. Effect of pregnancy on ankylosing spondylitis: a case-control study. J Rheumatol. 2011;38(11):2442–4.
10. Ursin K, Lydersen S, Skomsvoll JF, Wallenius M. Disease activity during and after pregnancy in women with axial spondyloarthritis: a prospective multicentre study. Rheumatology (Oxford). 2018;57(6):1064–71.
11. Morin M, Frisell T, Stephansson O, Hellgren K. Temporal trends in adverse pregnancy outcomes in axial spondyloarthritis in Sweden: a cohort study. Lancet Rheumatol. 2023;5(3):e121–9.
12. Zbinden A, van den Brandt S, Ostensen M, Villiger PM, Forger F. Risk for adverse pregnancy outcome in axial spondyloarthritis and rheumatoid arthritis: disease activity matters. Rheumatology (Oxford). 2018;57(7):1235–42.
13. Jakobsson GL, Stephansson O, Askling J, Jacobsson LT. Pregnancy outcomes in patients with ankylosing spondylitis: a nationwide register study. Ann Rheum Dis. 2016;75(10):1838–42.
14. Park EH, Lee JS, Kim YJ, Lee SM, Jun JK, Lee EB, et al. Pregnancy outcomes in Korean women with ankylosing spondylitis. Korean J Intern Med. 2021;36(3):721–30.
15. Keeling SO, Bowker SL, Savu A, Kaul P. A Population-level analysis of the Differing effects of Rheumatoid Arthritis and Spondyloarthritis on Peripartum outcomes. J Rheumatol. 2020;47(2):197–203.
16. Skomsvoll JF, Ostensen M, Baste V, Irgens LM. Number of births, interpregnancy interval, and subsequent pregnancy rate after a diagnosis of inflammatory rheumatic disease in Norwegian women. J Rheumatol. 2001;28(10):2310–4.
17. Steiner C, Elixhauser A, Schnaier J. The healthcare cost and utilization project: an overview. Eff Clin Pract. 2002;5(3):143–51.
18. Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research. Council, Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans. 2018.
19. Curtis JR, Winthrop K, Bohn RL, Suruki R, Siegel S, Stark JL, et al. The Annual Diagnostic prevalence of Ankylosing spondylitis and Axial Spondyloarthritis in the United States using Medicare and MarketScan databases. ACR Open Rheumatol. 2021;3(11):743–52.
20. Mork S, Voss A, Moller S, Bliddal M. Spondyloarthritis and outcomes in pregnancy and labor: a Nationwide Register-based Cohort Study. Arthritis Care Res (Hoboken). 2021;73(2):282–8.
21. Rudwaleit M, van der Heijde D, Landewé R, Akkoc N, Brandt J, Chou CT, et al. The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. Ann Rheum Dis. 2011;70(1):25–31.
22. Park JS, Hong JY, Park YS, Han K, Suh SW. Trends in the prevalence and incidence of ankylosing spondylitis in South Korea, 2010–2015 and estimated differences according to income status. Sci Rep. 2018;8(1):7694.
23. Reveille JD, Hirsch R, Dillon CF, Carroll MD, Weisman MH. The prevalence of HLA-B27 in the US: data from the US National Health and Nutrition Examination Survey, 2009. Arthritis Rheum. 2012;64(5):1407–11.
24. Braun J, Sieper J. Fifty years after the discovery of the association of HLA B27 with ankylosing spondylitis. RMD Open. 2023;9(3):e003102.
25. Smith CJF, Bandoli G, Kavanaugh A, Chambers CD. Birth outcomes and disease activity during pregnancy in a prospective cohort of Women with Psoriatic Arthritis and Ankylosing Spondylitis. Arthritis Care Res (Hoboken). 2020;72(7):1029–37.

26. Hamroun S, Hamroun A, Bigna JJ, Allado E, Forger F, Molto A. Fertility and pregnancy outcomes in women with spondyloarthritis: a systematic review and meta-analysis. Rheumatology (Oxford). 2022;61(4):1314–27.
27. Practice Bulletin No. 169: Multifetal Gestations: Twin, Triplet, and Higher-Order Multifetal Pregnancies. Obstet Gynecol. 2016;128(4):e131-46.
28. Emmungil H, Erdogan M, Kalfa M, Karabulut G, Kocanaogulları H, Inal V, et al. Autoimmune thyroid disease in ankylosing spondylitis. Clin Rheumatol. 2014;33(7):955–61.
29. Peluso R, Lupoli GA, Del Puente A, Iervolino S, Bruner V, Lupoli R, et al. Prevalence of thyroid autoimmunity in patients with spondyloarthropathies. J Rheumatol. 2011;38(7):1371–7.
30. Maguire S, O'Dwyer T, Mockler D, O'Shea F, Wilson F. Pregnancy in axial spondyloarthropathy: a systematic review & meta-analysis. Semin Arthritis Rheum. 2020;50(6):1269–79.
31. Kodama K, Tojjar D, Yamada S, Toda K, Patel CJ, Butte AJ. Ethnic differences in the relationship between insulin sensitivity and insulin response: a systematic review and meta-analysis. Diabetes Care. 2013;36(6):1789–96.
32. Lee JS, Oh JS, Kim YJ, Hong S, Lee CK, Yoo B, et al. Reasons for the high cesarean delivery rate among women with Ankylosing spondylitis: using the Korean National Health Insurance Database. J Rheumatol. 2020;47(5):668–73.
33. Bröms G, Kieler H, Ekbom A, Gissler M, Hellgren K, Lahesmaa-Korpinen AM, et al. Anti-TNF treatment during pregnancy and birth outcomes: a population-based study from Denmark, Finland, and Sweden. Pharmacoepidemiol Drug Saf. 2020;29(3):316–27.
34. Bandoli G, Palmsten K, Forbess Smith CJ, Chambers CD. A review of systemic corticosteroid use in pregnancy and the risk of select pregnancy and birth outcomes. Rheum Dis Clin North Am. 2017;43(3):489–502.
35. Getahun D, Fassett MJ, Jacobsen SJ. Gestational diabetes: risk of recurrence in subsequent pregnancies. Am J Obstet Gynecol. 2010;203(5):e4671–6.
36. Flint J, Panchal S, Hurrell A, et al. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding-part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids. Rheumatology (Oxford). 2016;55(9):1693–7.

Publisher's note