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ORIGINAL RESEARCH

Impact of Spondyloarthritis on Pregnancy Outcome: A Descriptive Analysis from a Specialized Center in Qatar

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Introduction: Spondyloarthritis (SpA) most commonly presents at childbearing age; thus, pregnancy is of concern. However, data on pregnancy outcomes in these patients are limited.

Purpose: This study aimed to retrospectively describe pregnancy outcomes in patients with SpA from the Middle East.

Patients and Methods: We reviewed the electronic health records of all pregnant women attending a specialized pregnancy and rheumatic disease clinic between 2016 and 2022. All pregnant patients diagnosed with axial spondyloarthritis (axSpA) and peripheral SpA were included. Data on adverse maternal and fetal outcomes were collected.

Results: Fifty-seven eligible pregnancies were identified from hospital records: 10 pregnancies ended in early miscarriage. Forty-seven pregnancies resulted in live singleton births, 25 in patients with peripheral SpA and 22 with axSpA. Human leukocyte antigen B27 was positive in 7 (15%) patients and only in women with axSpA. Twenty-nine (64%) patients received treatment throughout pregnancy. Consistent biologic disease-modifying antirheumatic drug (bDMARD) use was high, in eight (32%) patients with peripheral SpA and in nine (41%) with axSpA. A conventional synthetic disease-modifying anti-rheumatic drug (csDMARD) was used as treatment in 11 (50%) patients with peripheral SpA and two (8%) with axSpA. Twenty-two (53%) neonates were delivered by cesarean section, 19 (40%) by normal vaginal delivery and three (6%) by assisted delivery. Additionally, 44 (94%) deliveries were at term, and 42 (91%) neonates had a normal birth weight. Exploration of a subgroup showed no difference in reported outcomes between patients treated with bDMARD and those treated with csDMARD.

Conclusion: This descriptive study reports a high rate of favorable pregnancy outcomes in patients with SpA. There was no evidence to suggest a difference in pregnancy outcomes between women with axSpA and those with peripheral SpA. This study was one of the first reports from the Middle East. Further studies with larger sample size are warranted.

Keywords: axial spondyloarthritis, pregnancy, pregnancy outcomes, neonatal health, maternal health

Introduction

Spondyloarthritis (SpA) characterizes a group of chronic progressive inflammatory disorders that includes axial spondyloarthritis (axSpA), peripheral SpA, psoriatic arthritis, reactive arthritis, and enteropathic spondylitis associated with inflammatory bowel disease, with axSpA as the most common, affecting the sacroiliac joint and spine and often associated with reduced activity and quality of life.[1]

The prevalence of axSpA shows regional differences owing to genetic background. Recent estimates of axSpA prevalence per 10,000 population are 23.8 in Europe, 16.7 in Asia, 31.9 in North America, 10.2 in Latin America, and 7.4 in Africa.[2] A strong association was observed between axSpA and the human leukocyte antigen B27 (HLA-B27) genotype, which forms part of the Assessment of Spondyloarthritis International Society (ASAS) criteria for axSpA diagnosis.[3] However, HLA-B27 prevalence was further reported to show regional differences, with lower prevalence in Middle Eastern than in Western European populations, for both healthy and axSpA patient groups.[4] A recent systematic

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review has shown prevalence estimates for healthy populations to be between 0.3 and 6.8%, and in axSpA patients, estimates range from 26.2 to 91%.[4]

AxSpA most commonly presents in the second or third decade of life; hence, childbearing years and pregnancy are of particular concern. While often historically reported to be more common in men than in women, the increasing awareness of axSpA in women suggests that the prevalence could be similar to that in men.[5]

Chronic inflammatory disorders have long been shown to be associated with adverse outcomes in pregnancy.[6,7] Pregnancies in patients with SpA are similarly considered as high risk, with disease activity driving the high risks.[8] Suggested obstetric complications include preeclampsia/eclampsia, gestational diabetes, gestational hypertension, and peri-partum complications, resulting in assisted or cesarean section (CS) delivery, and fetal complications include the risk of preterm birth and low birth weight (LBW) or small for gestational age (SGA). However, evidence for adverse maternal and fetal outcomes is derived from few retrospective cohort and case–control studies and shows conflicting results.[8–15] Recent reviews and meta-analyses have suggested an increased risk of CS and preterm birth, but are not conclusive for SGA and preeclampsia.[16–18] Further, with advances in biologic disease-modifying anti-rheumatic drugs (bDMARD) that allow for better disease control, fewer adverse pregnancy outcomes are expected.[19] To our knowledge, few reports have described maternal and fetal outcomes in patients with SpA in the Middle East.

Aim

This retrospective study aimed to describe adverse maternal and fetal outcomes in a group of patients diagnosed with SpA and categorized according to axial involvement.

Patients and Methods

Data Collection

Electronic medical records were sequentially reviewed for all patients attending the Pregnancy and Rheumatic Disease Clinic, Hamad General Hospital, Doha, Qatar, between July 1, 2016, and September 1, 2022. Patients with confirmed pregnancy and autoimmune rheumatic disease typically attend the clinic once each trimester during pregnancy and once postpartum.

The clinic was established in 2005 and has been continually run by the same expert clinician during the study time period, providing standardized clinical care. Data were de-identified, and each pregnancy was recorded as a separate event and linked using a patient identity code.

ASAS criteria were used to diagnose peripheral SpA and axSpA, with axSpA confirmed by MRI of the sacroiliac joint. Patients with confirmed spondyloarthritis prior to pregnancy were included in the present study. Peripheral and axial diseases were included, as well as radiographic and non-radiographic diseases.

Outcomes

Data on maternal and fetal outcomes, including preeclampsia/eclampsia, gestational hypertension, and gestational diabetes and gestational age at delivery, birth weight, delivery mode, delivery complications, neonatal intensive care unit (NICU) admission, and any congenital abnormalities, respectively, were collected from electronic medical records. Pregnancies with lacking data on pregnancy outcomes in hospital medical records owing to delivery outside the institution were excluded from the analysis.

Approval

This study adheres to the principles of the Declaration of Helsinki and Good Clinical Practice and is within the laws and regulations of the Ministry of Public Health, Qatar. The study was approved by the Medical Research Center at Hamad General Hospital with institutional review board approval (MRC 01–22-835). Patient consent was not required by the review board for this retrospective study. All data was anonymized.

Data Analysis

Data were analyzed using Statistical Package for Social Sciences Version 29 (SPSS Inc., Chicago, IL, USA). Descriptive statistics of mean±standard deviations for continuous data and frequency with percentages for categorical data were calculated.

Results

During the study period (July 1, 2016, to September 1, 2022), 59 pregnancies, in 28 women, were identified (Figure 1 and Supplementary Table 1). Each pregnancy was treated as a separate independent event. Two pregnancies were excluded because of incomplete pregnancy data (delivery outside the hospital and, hence, not available on electronic medical records). One pregnancy had missing birth weight data but remained in the analysis for all other outcomes.

Ten of the 57 pregnancies (18%) reported an early miscarriage (<16-week gestation). Nine miscarriages were observed in patients with peripheral SpA and one miscarriage in a patient with axSpA. Six patients who had miscarriages were on no treatment, and four miscarriages occurred in one mother who was on different treatment lines during the four pregnancies.

Descriptive Data

Forty-seven pregnancies resulted in live singleton births. Table 1 shows the maternal characteristics. Data were subdivided by maternal diagnosis into the axSpA and peripheral SpA groups for descriptive comparison (n=22 and n=25, respectively).

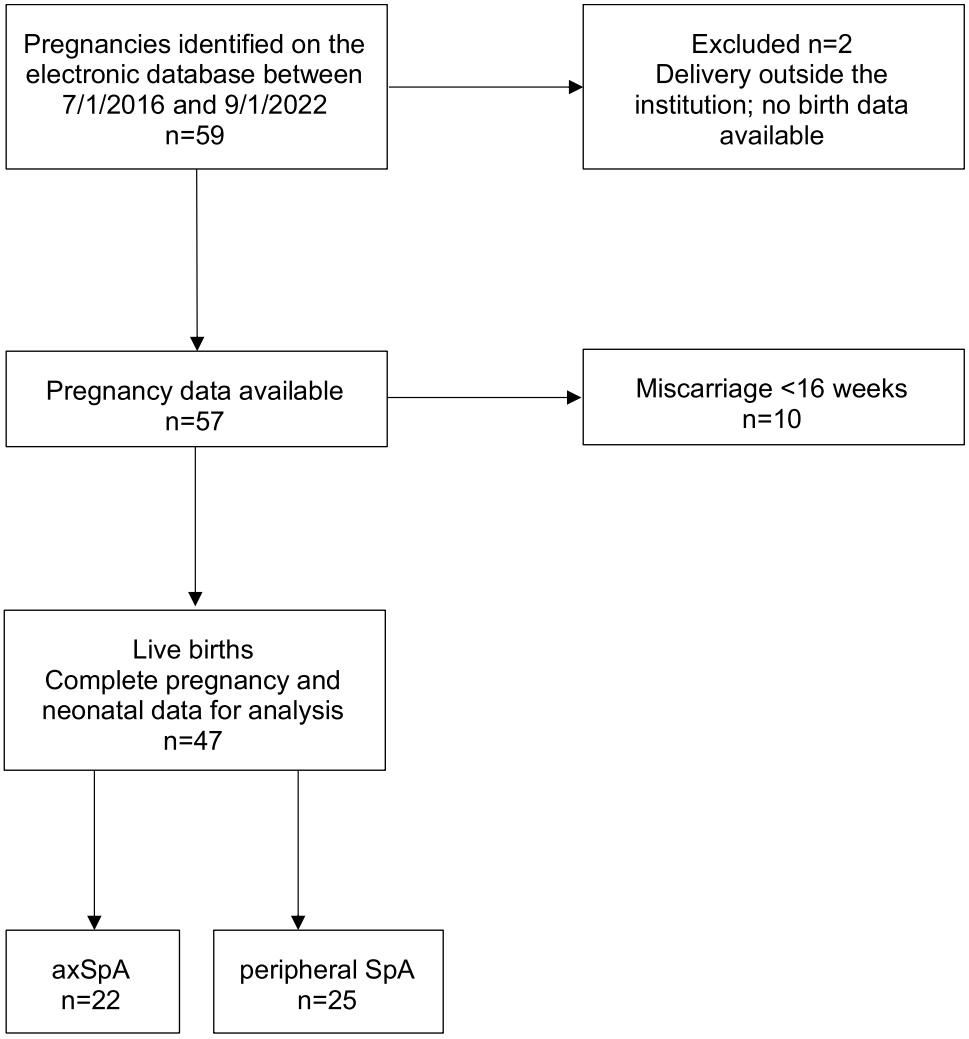

Figure 1 Flow chart showing inclusion of pregnancies in final analysis.
Abbreviations: SpA, spondyloarthritis; axSpA, axial spondyloarthritis.

Table 1 Maternal Characteristics for Pregnancies with Live Birth (n=47)

	All pregnancies n=47	Peripheral SpA n=25	axSpA n=22
Age (years) mean±SD	30.62±4.69	31.48±5.39	29.64±3.59
Maternal country of origin			
South Asia	11 (23%)	4 (16%)	7 (32%)
Southeast Asia	1 (2%)	0 (0%)	1 (5%)
Levant	3 (6%)	3 (12%)	0 (0%)
Gulf	21 (45%)	14 (56%)	7 (32%)
North Africa	11 (23%)	4 (16%)	7 (32%)
HLA-B27 positive	7 (15%)	0 (0%)	7 (32%)
Pre-existing comorbidities			
Hypertension	1 (2%)	0 (0%)	1 (5%)
Hypothyroidism	2 (4%)	2 (8%)	0 (0%)
Goiter	2 (4%)	2 (8%)	0 (0%)
Epilepsy	3 (6%)	3 (12%)	0 (0%)
Medication[a]	29 (64%)	18 (72%)	11 (50%)
NSAID	2 (4%)	0 (0%)	2 (9%)
csDMARD	13 (28%)	11 (50%)	2 (8%)
bDMARD	17 (36%)	8 (32%)	9 (41%)

Notes: [a]Some patients received more than one medication. One patient was treated with steroids alone and was regarded as not receiving any medications. NSAID treatment was discontinued in all patients at 25 weeks. bDMARD and csDMARD treatments were continued throughout pregnancy and post-delivery.

Abbreviations: axSpA, axial spondyloarthritis; bDMARD, biologic disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HLA-B27, human leukocyte antigen B27; NSAID, non-steroidal anti-inflammatory drug; SD, standard deviation; SpA, spondyloarthritis.

All the patients were nonsmokers. The mean age of patients was 31.48 years and 29.64 years in peripheral SpA and axSpA patient groups, respectively. HLA-B27 was positive in seven patients (15%), all of whom had axSpA. The rate of pre-existing comorbidities was low, with a comorbidity noted in eight pregnancies (Table 1).

Treatment of SpA During Pregnancy

A high proportion (29 patients, 64% of pregnancies) received treatment: 18 patients (72%) with peripheral SpA and 11 patients (55%) with axSpA. Two patients were treated with a non-steroidal anti-inflammatory drug, which was discontinued at 25 weeks of gestation. Overall, 29 pregnancies (62%) received either a conventional synthetic disease-modifying anti-rheumatic drug (csDMARD), sulfasalazine, or a bDMARD, certolizumab; 17 of them (36%) received bDMARD throughout pregnancy and post-delivery. bDMARD was used as treatment throughout pregnancy in eight patients (32%) with peripheral SpA and nine patients (41%) with axSpA. csDMARD was used as treatment throughout pregnancy in 11 patients (50%) with peripheral SpA and in two patients (8%) with axSpA (Table 1).

Maternal Pregnancy Outcomes

Table 2 shows the maternal outcomes during pregnancy. Fifteen adverse maternal outcomes were reported: 4 in patients with peripheral SpA and 11 in patients with axSpA.

Table 2 Maternal and Fetal Outcomes for Pregnancies with Live Birth

	All Pregnancies n=47	Peripheral SpA n=25	axSpA n=22
Maternal outcomes			
Preeclampsia	3 (6%)	0 (0%)	3 (14%)
Gestational diabetes	12 (26%)	4 (16%)	8 (36%)
Gestational hypertension	0 (0%)	0 (0%)	0 (0%)
Delivery mode			
NVD	19 (40%)	12 (48%)	7 (32%)
CS (all)	25 (53%)	12 (48%)	13 (59%)
CS (elective)	22 (47%)	10 (40%)	12 (55%)
CS (emergency)	3 (6%)	2 (8%)	1 (5%)
Assisted delivery	3 (6%)	1 (4%)	2 (9%)
Indication for emergency CS/assisted delivery			
Fetal bradycardia	1 (2%)	0 (0%)	1 (5%)
Fetal distress	4 (9%)	3 (12%)	1 (5%)
Prolonged second stage	1 (2%)	0 (0%)	1 (5%)
Live births	47 (100%)	25 (100%)	22 (100%)
Gestational week			
<37	3 (6%)	2 (8%)	1 (5%)
37–41	44 (94%)	23 (92%)	21 (95%)
>41	0 (0%)	0 (0%)	0 (0%)
Birth weight (kg)[a]	3.04±0.44	3.00±0.35	3.07±0.53
<2.5	4 (9%)	2 (8%)	2 (9%)
2.5–4.0	42 (91%)	22 (92%)	20 (91%)
>4.0	0 (0%)	0 (0%)	0 (0%)
NICU admission	4 (9%)	4 (16%)	0 (0%)
Hypoxia	2 (4%)	2 (8%)	0 (0%)
Sepsis	1 (2%)	1 (4%)	0 (0%)
Distress	1 (2%)	1 (4%)	0 (0%)
Congenital abnormality	1 (2%)	1 (2%)	0 (0%)

Notes: [a]Birth weight data for n=46 owing to missing data for one pregnancy in the peripheral SpA group.
Abbreviations: axSpA, axial spondyloarthritis; CS, cesarean section; NICU, neonatal intensive care unit; NVD, normal vaginal delivery; SpA, spondyloarthritis.

Fetal Outcomes

The majority, 44 pregnancies (94%) were term and only three (6%) were pre-term deliveries. CS was the most common delivery method (25 deliveries, 53%), with normal vaginal delivery accounting for 19 deliveries (40%). Assisted delivery was required in three (6%) cases. CS was performed on 12 patients (48%) with peripheral SpA and 13 patients (59%) with axSpA.

Birth weight was normal in 42 neonates (91%). The remaining four neonates were categorized as LBW, with two of them being delivered pre-term. Four neonates (9%) required admission to the NICU. One neonate was born with a congenital abnormality; however, no further data were available on this case.

To further explore the effects of treatment on pregnancy outcomes, we analyzed data from a subgroup of patients treated with bDMARD and csDMARD (Table 3). There were no suggestions of differences in the rate of adverse maternal and fetal outcomes (CS rate, gestational age at delivery, birth weight, NICU admission, or congenital abnormalities) between patients receiving bDMARD or csDMARD treatment.

Table 3 Maternal and Fetal Outcomes for Pregnancies with a Live Birth: Sub-Group Analysis of Patients Treated with bDMARD or csDMARD During Pregnancy

	bDMARD[a] n=17	csDMARD n=12
Maternal outcomes		
Preeclampsia	2 (12%)	0
Gestational diabetes	7 (41%)	2 (17%)
Gestational hypertension	0	0
Delivery mode		
NVD	4 (24%)	4 (33%)
CS (all)	11 (65%)	7 (58%)
CS (elective)	11 (65%)	5 (42%)
CS (emergency)	0	2 (17%)
Assisted delivery	2 (12%)	1 (8%)
Live births	16 (100%)	12 (100%)
Gestational week		
<37	3 (18%)	0
37–41	14 (82%)	12 (100%)
>41	0	0
Birth weight (kg)		
<2.5	2 (12%)	1 (8%)
2.5–4.0	14 (82%)	11 (92%)
>4.0	0	0
NICU admission	3 (18%)	1 (8%)
Hypoxia	2 (12%)	0
Sepsis	1 (6%)	0
Distress	0	1 (8%)
Congenital abnormality	1 (6%)	0

Notes: [a]One patient received combination therapy with bDMARD and csDMARD. For this analysis, these patients were included in the bDMARD group.
Abbreviations: CS, cesarean section; bDMARD, biologic disease-modifying anti-rheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; NICU, neonatal intensive care unit; NVD, normal vaginal delivery.

Discussion

In this study, we describe the maternal and fetal pregnancy outcomes in patients with axSpA and peripheral SpA. We showed low rates of adverse maternal or fetal pregnancy outcomes in patients with axSpA and peripheral SpA. To the best of our knowledge, few studies in the Middle East have reported on pregnancy outcomes in patients with SpA.

Two case–control studies have investigated pregnancy outcomes in patients with axSpA, with conflicting results.[9,15] A small case–control study by Timur et al has shown no differences in route of delivery, birth weight, and NICU admission between patients with axSpA (n=20) and matched controls (n=40).[15] Conversely, a larger study by Jakobsson et al showed increased risk of emergency CS, SGA, and preterm delivery in patients with axSpA (n=308) than in healthy controls (n=1082).[9] In our study, we did not compare to healthy controls. However, the overall rate of adverse maternal and fetal outcomes was low.

A study of the Danish National Birth Register[10] has found an increase in preterm birth and elective/emergency CS and no increase in SGA or preeclampsia when comparing pregnancies between patients with SpA and those without SpA. A similar study by Keeling et al analyzed data from the Alberta Pregnancy-Birth Cohort and found no increase in preterm birth or SGA, CS rate, or hypertensive disorders in patients with SpA compared with women with no inflammatory arthritis.[20] In contrast, a recent meta-analysis has described a statistically significant increase in the rate of CS in

axSpA.[18] Nevertheless, there were non-significant trends towards increased prevalence of preeclampsia, IUGR and LBW, SGA, NICU admissions, and congenital abnormalities with axSpA.[18]

Rate of Cesarean Section in Spondyloarthritis

In this study, we report a high CS rate in patients with peripheral SpA and those with axSpA, explained by a high rate of elective CS. It is important to note that elective CS in our study population was primarily due to patient choice. This reported CS rate is high in comparison with that reported by Jakobsson et al (showing a CS rate of 28.9% in cases and 16.4% in controls),[9] Morin et al (24.2% in cases and 17.5% in controls);[19] and Keeling et al (29.1% in patients with SpA).[20] Conversely, Timur et al have shown a similar high CS rate (55% in patients with axSpA).[15]

The rate of preterm delivery in our study was low and of a similar rate to that previously reported in axSpA.[21] Literature is conflicting in this area, but review data suggest an overall increased risk of preterm delivery[17] or a non-significant trend.[18] Further, birth weight is influenced by gestation and potentially affected by a high elective CS rate. We were not able to calculate SGA since data on the sex of the neonates were not collected; thus, unadjusted birth weight data were used. However, in addition to a low rate of preterm delivery, our study found a low incidence of LBW in this population. Only two neonates who were delivered at term were classified as LBW.

Consideration of Treatment with bDMARD

Recently, consistent treatment with bDMARD throughout pregnancy, for maternal and fetal outcomes, has been highlighted in the literature,[19,22,23] with bDMARD use not being associated with adverse outcomes.[22] A Swedish cohort study has shown decreased rates of elective CS, preeclampsia, preterm delivery, and infant infection in patients with axSpA. It inversely showed an increased use of bDMARD indicating that treatment with bDMARD and good disease control may reduce pregnancy complications in these women.[19]

Critically, we did not find any suggestions of increased adverse maternal or fetal outcomes in patients treated with bDMARD compared to patients treated with csDMARD during pregnancy.

The use of bDMARD has increased in recent years. In contrast to other studies, we report a high rate (36%) of consistent treatment with bDMARD throughout pregnancy; Meissner et al and Pons et al showed bDMARD usage of 27.5% and 8%, respectively.[22,24] Owing to this change in the treatment of SpA, Morin et al have further suggested that older study results are not directly comparable with the more recent results,[19] further supporting the need for up-to-date studies on outcomes in patients with SpA.

The miscarriage rate in the present study was 18%. We were unable to draw any further relevant conclusions because of repeated miscarriages in the same woman, potentially skewing our results. A similar analysis has shown a miscarriage rate of 7.5% in patients with axSpA.[22] This outcome is an important consideration for future studies to fully understand whether this risk is related to the disease, the treatment of the disease, or unrelated causes.

Strengths of the Study

This study is one of the few to report on pregnancy outcomes of patients with SpA in the Middle East. Due to potential differences in the disease presentation and severity in different areas of the world, local data are important to guide clinical practice. Moreover, the importance of HLA-B27 during pregnancy is not well established. Our results show that 32% of the patients with axSpA were positive for HLA-B27, which is lower than that reported in European patients.[4]

The high rate and consistent use of bDMARD throughout pregnancy make the data from this study both reliable and clinically relevant.

Limitations of the Study

The major limitations of this study were the lack of a healthy control group, the relatively small sample size and the lack of disease activity measures. The small sample size, combined with the small expected differences between patients with axSpA and those with peripheral SpA, did not allow us to statistically compare these patient groups.

Our population included 47 pregnancies in 26 patients, and we report that the number of births varied considerably between one and seven births per woman, resulting in the sample size being insufficient to allow adjustment for within-person effects.

Conclusions

In this retrospective study, we demonstrate a high rate of favorable pregnancy outcomes in a sample of patients from the Middle East. Despite the high rate of bDMARD use in this population, the study size was not sufficiently large to draw conclusions, however, there was no evidence of adverse pregnancy outcomes. The study reports a high rate of CS, attributed to maternal choice. Larger, up-to-date studies that allow for multivariate analysis of treatment effects and disease activity measures during pregnancy are warranted.

Abbreviations

ASAS, Assessment of Spondyloarthritis International Society; axSpA, axial spondyloarthritis; CS, cesarean section; bDMARD, biologic disease-modifying anti-rheumatic drug; csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; HLA-B27, human leukocyte antigen B27; NICU, neonatal intensive care unit; NSAID, non-steroidal anti-inflammatory drug; NVD, normal vaginal delivery; SD, standard deviation; SpA, spondyloarthritis.

Data Sharing Statement

The data sets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Disclosure

The authors report there are no competing interests to declare.

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