Pregnancy Outcomes in Takayasu Arteritis Patients

Shiping He

Peking Union Medical College Hospital

Zhi Li

First Affiliated Hospital of Wannan Medical College

Yijun Song

Peking Union Medical College Hospital

Yunjiao Yang

Peking Union Medical College Hospital

Jing Li

Peking Union Medical College Hospital

Jiuliang Zhao

Peking Union Medical College Hospital

Yanhong Wang

Peking Union Medical College Hospital

Xinping Tian (✉ tianxp6@126.com)

Peking Union Medical College Hospital

Xiaofeng Zeng

Peking Union Medical College Hospital

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Abstract

Backgrounds

Takayasu Arteritis (TAK) is a chronic inflammatory autoimmune disease with a high prevalence in women of child-bearing age. We aim to investigate the maternal complications and pregnancy outcomes in patients with TAK and identify the related factors.

Methods

A total of 110 pregnancies in 80 TAK patients in a Chinese TAK patient cohort and 440 matched pregnancies in healthy women between 2000 to 2020 were included. The maternal complications and pregnancy outcomes between TAK patients and matched controls were compared by chi-square test. The logistic regression analysis was used to identify the risk factors of maternal complications and adverse pregnancy outcomes in patients with TAK.

Results

Maternal complications and adverse pregnancy outcomes were more frequent in pregnancies with TAK than that in healthy women ($P < 0.001$). In pregnancies with TAK, the most common maternal complication was new-onset or worsening of hypertension (18.2% [20/110]) and the most prevalent obstetrical complication was spontaneous abortion (32.7% [36/110]). Hypertension (OR 5.01, 95% CI 1.61 to 16.01), heart disease (OR 15.83, 95% CI 1.99 to 125.99), and active TAK (OR 7.54, 95% CI 1.85 to 30.72) before pregnancy were independently associated with increased maternal complications. The disease duration (OR 1.12, 95% CI 1.02 to 1.23) and active disease during pregnancy (OR 14.59, 95% CI 1.81 to 117.49) were correlated with adverse pregnancy outcomes.

Conclusion

TAK disease itself is a risk factor for adverse pregnancy outcomes. Treating the disease to a stable state before and after pregnancy, and close collaboration between rheumatologists and obstetricians are important measures to reduce maternal complications and reach favorable pregnancy outcomes.

Introduction

Takayasu arteritis (TAK) is a chronic systemic vasculitis primarily affects aorta and its major branches with unknown etiology. It can cause artery wall thickening and dilatation and lead to artery stenosis, obliteration or aneurysm formation. Inflammation and ischemia of the supplied organs of the involved arteries are common consequences of the disease, such as asymmetrical pulsation and intermittent claudication of extremities, intractable hypertension, heart valve insufficiency, and stroke in severe cases[1]. TAK, a rare disease in general, was first described by a Japan physician, with an incidence of approximately 40 per million per year in Japan[2]. It can be found in all ethnic groups, but most prevalent in Asia and Middle East area[3]. TAK affects women 5 to 12 times more than men, most of them are young women at child-bearing age[4]. Therefore, pregnancy in this special group has caused great concern. Managing the pregnancy in TAK patients remains a big challenge to both rheumatologists and obstetricians. So far, there are a few small sample studies on the pregnancy outcomes of TAK patients in the literature with contradictory results[5-21]. Some studies suggested that pregnancies in women with TAK could result in high rates of maternal hypertension (5.3% to 100%) and preeclampsia (2.7% to 75.9%)[5-21], and active TAK was associated with poor pregnancy outcomes[11, 13]. However, some studies showed that active disease was not associated with adverse pregnancy outcome[7, 8]. Furthermore, fetal outcomes in pregnancies with TAK were rarely reported and the effects of pregnancy on TAK activity were unclear. In this study, we analyzed the maternal complications and fetal outcomes as well as disease activity before and after pregnancy in Chinese TAK patients to explore the relationship between TAK and pregnancy outcomes. Meanwhile, we conducted a literature review to summary the pregnancy outcomes in patients with TAK.

Patients And Methods

Patients

From August 2013 to December 2020, 743 patients with TAK were registered in the TAK cohort of Peking Union Medical College Hospital (PUMCH) [22]. All patients in the cohort fulfilled the 1990 ACR classification criteria of TAK[23]. A written informed consent was obtained from each patient. TAK women with at least one pregnancy after disease onset between January 2000 and December 2020 were enrolled into this study (Figure 1). Healthy Chinese women hospitalized to the Department of Obstetrics and Gynecology of PUMCH for abortion or delivery during the same period were collected as the controls. Patients with chronic obstructive pulmonary disease, asthma, hypertension, heart diseases, chronic renal insufficiency, hepatic insufficiency, endocrine diseases, and rheumatic diseases were excluded from the controls. Patients with a history of uterus surgery were also excluded. Pregnancies with assisted reproductive technology or twin- or multiple pregnancies were excluded. Therefore, 28550 healthy women at the age of pregnancy between 18 to 38 years were included and matched to pregnancies with established TAK based on propensity scores without replacement, using a 1:4 ratios with matching factor (age at pregnancy), caliper was 0.02. This study was approved by the Ethics Committee of Peking Union Medical College Hospital.

Methods

The demographic data, laboratory test results, image examinations, treatments before and after pregnancy in patients with TAK and the matched controls were collected and analyzed. We prospectively collected the data of pregnancies after registration of TAK cohort and retrospectively collected the data of pregnancies before registration and healthy women controls. Patients who are pregnant after registered in the TAK cohort of PUMCH were examined by vascular Doppler ultrasonography for all the accessible arteries (bilateral carotid artery, subclavian artery, axillary artery, celiac trunk, hepatic artery, splenic artery, renal artery and lower extremities) every 3 to 6 months during follow-up. At each visit, disease activity was assessed with the National Institutes of Health (NIH) criteria proposed by Kerr[24].

Literature search strategy

We used the terms “Takayasu arteritis”, “Takayasu”, “large vessel vasculitis”, “pregnancy”, “obstetrical complication”, “maternal complication” and “fetal outcome” in the PubMed, the Web of Science and the Cochrane Library for English-language article published from 2020 to November 2021. All articles with over 5 pregnancies with established TAK were included, while pregnancies before disease onset were excluded.

Definitions

Disease activity was assessed by the NIH criteria[24]: (1) systemic features, such as fever, musculoskeletal symptoms (other cause was excluded); (2) elevated erythrocyte sedimentation rate; (3) feature of vascular ischemia or inflammation; and (4) positive imaging results. Disease was considered to be active with new onset or worsening of two or more features.

Maternal complications were defined as the occurrence of at least one of the following events: new-onset or worsening hypertension (requiring the addition of at least one antihypertensive drug), new-onset or worsening renal artery involvement, venous thrombosis, new-onset or worsening aneurysms, new-onset or worsening heart disease, stroke, end-stage kidney disease or infection. Obstetrical complications included at least one of the following events: ectopic pregnancy, spontaneous abortion, therapeutic abortion, stillbirth, intrauterine fetal growth restriction, preterm birth, low birthweight, preeclampsia, eclampsia, or placental abruption. Spontaneous abortion referred to the cessation of embryo development and natural loss before 20 weeks of pregnancy[25]. Therapeutic abortion referred to termination of pregnancy for medical indications. All therapeutic abortion for medical indications in this study were legal abortions with the consent of the patient and the joint decision of the rheumatologists and the obstetricians who took care of the patient. Stillbirth referred to an antepartum or intrapartum fetal death occurring after 20 weeks of gestation[26]. Preterm birth was defined as a neonate born after 20 weeks but before 37 weeks of gestation. Low birthweight was defined as a newborn weighted less than 2500 grams[27]. Neonatal asphyxia referred to 5-min Apgar score less than 7. Adverse pregnancy outcome was defined as one of several maternal complications and obstetrical complications.

Statistical analysis

Data were described as means (standard deviation) or medians (interquartile range) for continuous variables and numbers with frequencies for categorical variable. Categorical variables were compared using the chi-square test. The logistic regression was used to analyze the risk factors for maternal complications and adverse pregnancy outcomes in pregnancies with TAK. Variables were entered into univariate (UV) logistic regression model. A multivariate (MV) logistic regression model was then constructed using a stepwise forward selection procedure among those candidate variables with the significance level $P < 0.10$ in the UV logistic regression analysis. A two-sided P value of < 0.05 was considered significant. Analysis was performed with the SPSS software (version 24, Chicago, IL, USA).

Results

1. The Demographic data and clinical characteristics

The demographic data and clinical characteristics of 110 pregnancies in 80 women and 440 pregnancies of healthy women were summarized in Table 1. The major pre-pregnant complications were hypertension (31.8% [35/110]) and renal artery involvement (31.8% [35/110]). Five cases had heart disease (two moderate aortic valve insufficiency and three mild mitral regurgitation). Ten cases had renal artery intervention or surgery before pregnancy: 1 case had unilateral renal artery balloon angioplasty, 2 pregnancies in a patient had unilateral autologous kidney transplantation, 3 cases had unilateral renal artery stent implantation and 4 pregnancies in 3 patients had unilateral renal artery artificial vascular bypass grafting. Glucocorticoid (10-15 mg/d) was prescribed in 15 women with 19 (17.3% [19/110]) and immunosuppressant (azathioprine or tacrolimus) in 31 women with 40 pregnancies (36.3% [36.3/110]) during pregnancy. Twelve (10.9%) patients, 16 (14.5%) patients and 21 (19.1%) patients with active disease before pregnancy, during pregnancy or after delivery respectively. Twenty patients (18.2% [20/110]) experienced disease flares and 5 patients (4.5% [5/110]) suffered from disease deteriorations during pregnancy and/or one year postpartum. Fifteen patients (75%) experienced flare during pregnancy and the first 6 months postpartum.

2. Pregnancy outcomes

Compared with pregnancies in healthy women, we observed the higher risk of maternal complications and adverse pregnancy outcomes in pregnancies with TAK, Table 2. The most frequent maternal complication was new-onset or worsening hypertension (18.2% [20/110]) in pregnancies after disease onset, higher than controls (1.1% [5/440], $P<0.001$). In addition, new-onset or worsening hypertension were more frequently occurred in women with pre-pregnant renal artery involvement than that in women without renal artery involvement (34.5% [12/35] versus 10.7% [8/75], $\chi^2=8.95$, $P=0.003$), and more frequent in pregnancies before registration to TAK cohort of PUMCH than that in pregnancies after registration (25.0% [14/56] versus 7.4% [4/54], $\chi^2=6.22$, $P=0.019$). New-onset or worsening renal artery involvement was observed in 3 pregnancies, and two of them had severe unilateral renal artery stenosis before pregnancy. New-onset or worsening heart disease (aggravated aortic regurgitation) was observed in 3 pregnancies. Two women with TAK experienced preeclampsia, both of them were pregnant before registration to TAK cohort. Five patients with 8 pregnancies treated with renal artery intervention or surgery before pregnancy did not have maternal complications. No severe obstetrical complication such as cerebrovascular event, heart failure, pulmonary embolism and deep vein thrombosis occurred in this study.

Spontaneous abortions occurred in 36 pregnancies (32.7% [36/110]) with established TAK, higher than controls (3.7% [17/440], $P<0.001$). fetal arrest respectively As for live births, 68.2% (45/66) women with established TAK delivered by cesarean section, higher than the controls (3.8% [16/423], $P<0.001$). Cesarean section in pregnancies with TAK were performed for maternal medical indications (active TAK and intractable hypertension, 37.8% [17/45]), fetal complications (8.9% [4/45]), malposition (8.9% [4/45]), oligohydramnios (15.5% [7/45]) and other reasons (28.8% [13/45]). Three neonates were born with congenital malformation in patients with established TAK and one of them died 3 days after birth because of congenital esophageal occlusion.

3. Pregnancy outcomes of the literature review and our study

The literature review included pregnancies with established TAK from 17 different studies (Table 3). In consistent with our findings, worsening or new-onset hypertension (5.3% to 100%) was the most frequent maternal complication, and abortion (3.4% to 30.0%) was the most frequent obstetric complication. Eclampsia or pre-eclampsia affects about 13.3% (0 to 75.9%) of the pregnancies with TAK. Similarly, low birthweight and preterm birth were both more frequent in pregnancy with TAK (19.6% and 15.9% respectively).

4. Factors associated with maternal complications and adverse pregnancy outcomes

Risk factors of maternal complications in pregnancies after TAK onset was analyzed by logistic regression analysis (Table 4). Hypertension (OR 5.01, 95.0% CI 1.61 to 16.01, $P=0.006$), heart disease (OR 15.8, 95.0% CI 1.99 to 125.99, $P=0.009$) and active TAK (OR 7.54, 95.0% CI 1.85 to 30.72, $P=0.005$) before pregnancy were independently correlated with maternal complications in pregnancies with disease.

Table 5 showed the univariate and multivariate analyses results of associated factor for adverse pregnancy outcomes pregnancies with established TAK. Multivariate analyses showed that disease duration (OR 1.12, 95.0% CI 1.02 to 1.23, $P=0.024$) and (OR 14.59, 95.0% CI 1.81 to 117.49, $P=0.012$) was independently correlated with adverse pregnancy outcomes.

Discussion

TAK is a chronic systemic inflammatory autoimmune disease with a high prevalence in women of child-bearing age. Understanding factors related to maternal complications and adverse pregnancy outcomes are critical for pre-pregnant management of TAK patients. However, because of the rarity of the disease and the scarce of studies about the pregnancy outcomes in this group of patients, we have very limited understanding of the factors associated with disease activity after pregnancy and pregnancy outcomes.

There is inconsistency in maternal complications and fetal outcomes reported in different studies[5-21]. Nonetheless, the most common maternal complications in patients with TAK is hypertension with an overall incidence of 5.3% to 100%[5-21]. In consistent with the past reports, new-onset or worsening hypertension is the most frequent maternal complication in our study, with the incidence of 18.2% (20/110). However, only two preeclampsia developed in TAK patients, while the rate of pre-eclampsia or eclampsia was 0 to 75.9% in previous studies[5-21]. Patients pregnant after registered in the TAK cohort were followed up by the rheumatologists and the obstetricians every 3 to 6 months, and none of them experienced eclampsia or preeclampsia. This may be due to the blood pressure as well as the disease was well-controlled before and after pregnancy in our patients. Comarmond et al reviewed 505 pregnancies in 373 TAK patients in a meta-analysis and found that miscarriage and therapeutic abortions occurred in 12% and 7% patients respectively[28]. In our study, 36 spontaneous abortions (32.7% [36/110]) and 8 therapeutic abortions (7.3% [8/110]) occurred in pregnancies with TAK. However, the spontaneous abortions rate is about 4.3 to 10% in general population in China[25, 29]. This high rate of spontaneous abortions in patients with TAK might attribute to active disease immediately before pregnancy, but the details were still unknown. Other factors associated with miscarriage in women with TAK need further research.

In this study, much more pregnancies were terminated by cesarean section in women with established TAK than matched healthy controls in PUMCH during the same period (68.2% versus 3.8%, $P<0.001$). Uncontrolled blood pressure and active TAK were the main reasons for medical indicated cesarean section, but many patients were operated because their obstetricians concerned about the unfavorable outcomes that might happen. We found that hypertension (OR 5.01, 95.0% CI 1.61 to 16.01) and active TAK (OR 7.54, 95.0% CI 1.85 to 30.72) before pregnancy were correlated with

maternal complications. Therefore, tight control of hypertension and control the disease to remission before pregnancy are critical to reduce maternal complications and achieve satisfactory pregnancy outcome.

Singh et al found that TAK women with renal artery involvement were at high risk of vascular complications that could negatively affect fetal and maternal outcomes[15]. Consistent with previous studies, we found that pre-pregnant renal artery involvement increased the risk of hypertension during pregnancy ($\chi^2=8.95$, $P=0.003$). Therefore, treatment of renal artery stenosis prior to pregnancy is important to reduce the risk of adverse pregnancy outcomes.

We found that heart disease before pregnancy (OR 15.83, 95.0% CI 1.99 to 125.99) was independently associated with maternal complications in pregnancies with TAK and also carried the highest risks for maternal complications. This highlighted that intensive management and monitoring of women with heart disease is essential before conception and throughout pregnancy. It is noteworthy that heart diseases in this group of patients included aortic valve insufficiency and mitral regurgitation, which may be related to hypertension or the disease itself. However, no heart failure, aortic dissection, aortic aneurysm, and coronary heart disease occurred during pregnancy. Further studies are needed to explore other heart involvements related to pregnancy in TAK.

The interaction between TAK disease activity and pregnancy is inconclusive. In a French retrospective study[7], no correlation was found between disease activity and obstetrical complications. In 102 pregnancies in Indian TAK patients, Gupta et al concluded that TAK disease activity assessed by Indian Takayasu Arteritis clinical score (ITAS) could not predict pregnancy outcome[8]. Comarmond et al found active disease according to NIH criteria was an independent risk factor for obstetrical and maternal complications in a study of 98 pregnancies in 52 patients with TAK[13]. In addition, this study suggested that active TAK before pregnancy was correlated with maternal complications (OR 7.54, 95.0% CI 1.85 to 30.72), and active TAK during pregnancy negatively affect pregnancy outcome (OR 14.59, 95.0% CI 1.81 to 117.49). This might suggest that control the disease to remission before and during pregnancy could reduce adverse pregnancy outcomes.

There is controversy about the impact of pregnancy on TAK disease activity. Some studies showed that pregnancy was not the risk factor to cause TAK disease flare[14, 30]. On the contrast, Tanacan et al[10] reported 5 patients experienced relapses during pregnancy in 11 TAK patients, suggesting that pregnancy increased the risk of disease flare. In our study, 20 patients (18.2% [20/110]) had disease flares and 5 patients (4.5% [5/110]) suffered from disease deteriorations during pregnancy and/or one year postpartum. Nevertheless, there is limited evidence supporting that pregnancy increases the risk of TAK relapse. More studies are needed to better assess the relation between pregnancy and TAK.

There are some limitations in our study. First, although this study is the largest study thus far in the literature according to our knowledge, the sample size of this study is not large enough to clarify many controversies such as the mutual effect of pregnancy with TAK. In addition, some data were collected retrospectively. Another limitation is that a few of patients in this study missed data for disease activity assessment immediately before pregnancy and immediately after delivery. This compromised the ability of this study to reveal the impact of pregnancy on disease activity.

Conclusion

In general, pregnancies in patients with TAK should be considered as high risk pregnancy and should be closely monitored by rheumatologists and obstetricians. The main complications were new-onset or worsening hypertension for mothers and spontaneous abortion for obstetric complications. Hypertension, heart valve disease and active disease before pregnancy are risk factors for maternal complications, while long disease duration and active disease during pregnancy are risk factors for adverse pregnancy outcomes. Pregnancy may negatively affect TAK disease activity. Controlling the disease to remission before pregnancy, and closely monitoring disease activity during pregnancy are essential to improve the pregnancy outcome of TAK patients.

Abbreviations

TAK: Takayasu arteritis

PUMCH: The Peking Union Medical College Hospital

NIH: The National Institutes of Health

IQR: Interquartile rang

SD: Standard deviation

BMI: Body mass index

NA: not applicable

IUGR: intrauterine growth restriction

UV: Univariate

MV: multivariate

OR: Odd ratio

CI: Confidence interval

Declarations

Availability of data and materials

The raw data used during the current study are available from the corresponding author on reasonable request.

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Disclosure statement

The authors have declared no conflicts of interest.

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Contributors

SH, ZL, YS did the study design and compiled the manuscript. SH and ZL independently searched the literature. SH, ZL, YS, JL, JZ participated in data collection and verified the underlying data. SH, YY, YW carried out data analysis. XT and XZ supervised the study. All authors read and approved the final manuscript.

Patients and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patients consent for publication

Not required.

Ethics approval

This study was approved by Peking Union Medical College Hospital (JS-2038).

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Tables

Table 1. Demographic and clinical characteristics in women with TAK and healthy women

Variables	Pregnancies with TAK (n=110)	Matched controls (n=440)
Age at pregnancy, median (IQR), years	27.5 (24, 30)	27.5 (24, 30)
BMI, mean (SD), kg/m ²	22.3 ± 3.67	21.7 ± 2.85
Age at TAK onset, median (IQR), years	22 (19, 25)	NA
Age at TAK diagnosis, median (IQR), years	25 (22, 27)	NA
Numano classification, n (%)		
Type I	21 (19.1)	NA
Type IIa	7 (6.4)	NA
Type IIb	12 (10.9)	NA
Type III	0 (0.0)	NA
Type IV	2 (1.8)	NA
Type V	68 (61.8)	NA
Complications before pregnancy, n (%)		
Hypertension	35 (31.8)	0
Renal artery involvement	35 (31.8)	0
Heart disease	5 (4.5)	0
Vascular intervention or surgery	18 (16.4)	0
Renal artery intervention or surgery	10 (9.1)	0
Active TAK before pregnancy	12 (10.9)	NA
Glucocorticoid (10-15 mg/d) during pregnancy, n (%)	19 (17.3)	0
Immunosuppressant during pregnancy, n (%)	40 (36.3)	0
Active TAK during pregnancy, n (%)	16 (14.5)	NA
Active TAK after delivery, n (%)	21 (19.1)	NA

TAK, Takayasu arteritis; IQR, interquartile rang; SD, standard deviation; BMI, body mass index; NA, not applicable

Table 2. Maternal and fetal outcomes in women with TAK and healthy women

Variables	Pregnancies with TAK (n=110)	Matched controls (n=440)	<i>p</i>
Maternal complications, n (%)	21 (19.1)	6 (1.4)	<0.001
New-onset or worsening hypertension	20 (18.2)	5 (1.1)	<0.001
New-onset hypertension	7 (6.4)	5 (1.1)	0.003
Worsening hypertension	13 (11.8)	0	<0.001
New-onset or worsening renal artery involvement	3 (2.7)	0	0.008
New-onset or worsening heart disease	3 (2.7)	0	0.008
Obstetric complications/fetal outcomes, n (%)			
Eclampsia/preeclampsia	2 (1.8)	2 (0.5)	0.185
Spontaneous abortions	36 (32.7)	17 (3.7)	<0.001
Therapeutic abortions	8 (7.3)	0	<0.001
Stillbirths	0	0	
Live births	66 (60.0)	423 (96.1)	<0.001
Cesarean section	45 (68.2)	16 (3.8)	<0.001
Preterm birth	7 (10.6)	8 (1.9)	<0.001
Low birthweight	7 (10.6)	1 (0.2)	<0.001
Neonatal asphyxia	1 (1.5)	1 (0.2)	0.252
Congenital malformation	3 (4.5)	1 (0.2)	0.009
Neonatal death	1 (1.5)	0	0.135
Adverse pregnancy outcomes, n (%)	68 (61.8)	32 (7.3)	<0.001

TAK, Takayasu arteritis

Table 3. Summary pregnancies outcomes in patients with TAK in previous studies

Study	Patients, n	Pregnancies, n	Mean or median maternal age, year	Relapse or disease activity, n (%)	Worsened hypertension	or new-onset hypertension, n (%)	Eclampsia	or preeclampsia, n (%)	Maternal mortality, n (%)
Gönenli, et al. 2021[5]	40	75	28.3	8 (10.6)	12 (16.0)	4 (5.3)		3 (4.0)	0
Pyo, 2020[6]	7	12	32.0±12.0	0	7 (58.3)	0		1 (8.3)	0
Abisror, et al. 2020[7]	33	43	30.3	NA	11 (26.0)	4 (9.0)		3 (7.0)	0
Gupta, et al. 2020[8]	26	38	30.0 (27.0, 33.5)	15 (39.5)		15 (39.5)		0	0
David, et al. 2020[9]	16	22	23.5 (22.0, 25.5)	NA	7 (31.8)			2 (9.1)	0
Tanacan, et al. 2019[10]	11	22	30.3±3.8	5 (22.7)		8 (36.4)		0	0
Kirshenbaum and Simchen 2018[11]	6	20	29.3±3.0	2 (10.0)	2 (10.0)	6 (30.0)		1 (5.0)	0
Gudbrandsson, et al. 2017[12]	23	37	29.4±4.9	10 (58.8)		NA	1 (2.7)	1 (2.7)	0
Comarmond, et al. 2015[13]	52	98	27	39 (39.8)	11 ((11.2)	15 (15.3)		24 (24.5)	0
Assad, et al. 2015[14]	NA	38	25.1 (5.2)	NA		12 (31.5)		0	0
Singh, et al. 2015[15]	12	18	NA	NA		12 (66.7)		2 (11.1)	0
Alpay-Kanitez, et al. 2015[16]	17	21	24.5±6.6	4 (40.0)	3 (14.3)			2 (9.5)	0
Tanaka, et al. 2014[17]	20	27	30 (22, 35)	NA		NA		4 (14.8)	0
Hidaka, et al. 2012[18]	10	26	29.3±5.2	NA		2 (7.7)		0	
Mandal, et al. 2012[19]	17	29	NA	NA		29 (100)	2 (6.9)	22 (75.9)	1 (3.4)
Suri, et al. 2010[20]	15	37	27.6±4.7	NA		10 (27.0)	0	22 (59.5)	1 (2.7)
Sharma, et al. 2000[21]	12	24	23.6±3.6	NA		11 (91.7)	0	4 (33.3)	0
Current study	80	110	27.5 (24.0, 30.0)	16 (14.5)	13 (11.8)	7 (6.4)		2 (1.8)	0
Total	NA	697	NA	99 (24.6)	192 (30.9)		91 (13.3)		2 (0.3)

Continued table

Study	Spontaneous abortion	or induced abortions, n (%)	Still births, n (%)	Live births, n (%)	Caesarean section	Preterm birth, n (%)	Low birthweight, n (%)	IUGR, n (%)	Neonatal death, n (%)
Gönenli, et al. 2021[5]		8 (10.7)	1 (1.3)	66 (88.0)	NA	3 (4.5)	NA	4 (6.1)	0
Pyo, 2020[6]	2 (16.7)	1 (8.3)	0	9 (75)	8 (88.9)	1 (11.1)	2 (22.2)	1 (11.1)	0
Abisror, et al. 2020[7]		NA	NA	43 (100)	20 (47.0)	9 (21)	NA	6 (14.0)	1 (2.3)
Gupta, et al. 2020[8]	10 (26.3)	6 (15.8)	2 (5.3)	20 (52.6)	NA	2 (10.0)	6 (20.0)	NA	1 (5.0)
David, et al. 2020[9]	6 (27.3)	NA	0	16 (72.7)	10 (62.5)	4 (25.0)	NA	5 (31.3)	0
Tanacan, et al. 2019[10]	5 (22.7)	1 (4.5)	0	16 (72.7)	8 (50.0)	4 (25.0)	3 (15.8)	3 (15.8)	0
Kirshenbaum and Simchen 2018[11]	6 (30.0)	1 (5.0)	0	13 (61.5)	7 (53.8)	4 (30.8)	4 (30.8)	3 (23.1)	0
Gudbrandsson, et al. 2017[12]	6 (16.2)	6 (16.2)	0	25 (67.6)	8 (32.0)	4 (16.7)	3 (12.5)	NA	0
Comarmond, et al. 2015[13]	9 (9.2)	3 (3.1)	2 (2.0)	84 (85.7)	16 (19.0)	8 (9.5)	NA	5 (6.0)	1 (1.2)
Assad, et al. 2015[14]		3 (7.8)	0	35 (92.1)	24 (68.5)	16 (45.7)	12 (34.2)	NA	0
Singh, et al. 2015[15]		5 (27.8)	0	13 (72.2)	3 (23.7)	1 (7.7)	NA	6 (46.2)	1 (7.7)
Alpay-Kanitez, et al. 2015[16]		1 (4.8)	0	20 (95.2)	9 (45.0)	2 (10.0)	NA	1 (5.0)	0
Tanaka, et al. 2014[17]		NA	NA	27 (100)	9 (33.3)	3 (11.1)	3 (11.1)	NA	0
Hidaka, et al. 2012[18]	5 (19.2)	3 (11.5)	0	18 (69.2)	2 (11.1)	2 (11.1)	NA	2 (11.1)	0
Mandal, et al. 2012[19]	1 (3.4)		2 (6.9)	26 (89.7)	9 (34.6)	5 (19.2)	NA	15 (57.8)	0
Suri, et al. 2010[20]		7 (18.9)	5 (13.5)	25 (67.6)	7 (28.0)	7 (28.0)	NA	6 (24.0)	0
Sharma, et al. 2000[21]		2 (8.3)	5 (20.8)	17 (70.8)	1 (5.9)	4 (23.5)	5 (29.4)	5 (29.4)	0
Current study	36 (32.7)	8 (7.3)	0	66 (60.0)	45 (68.2)	7 (10.6)	7 (10.6)	NA	1 (1.5)
Total	141 (22.5)		24 (3.8)	496 (79.1)	186 (40.8)	86 (15.9)	45 (19.6)	62 (15.3)	5 (1.5)

NA, not applicable; IUGR: intrauterine growth restriction

Table 4. Univariate and multivariate logistic regression analyses for factors predictive of maternal complications in pregnancies with TAK

Factors	UV		MV	
	<i>OR</i> (95% <i>CI</i>)	<i>P</i>	<i>OR</i> (95% <i>CI</i>)	<i>P</i>
Age at pregnancy, years	0.99 (0.87, 1.11)	0.812		
BMI, kg/m ²	1.06 (0.93, 1.20)	0.386		
Age at TAK onset, years	1.06 (0.96, 1.18)	0.269		
Disease duration, years	0.98 (0.88, 1.08)	0.645		
TAK Numano classification				
Type I- IIb	0.48 (0.16, 1.44)	0.190		
Type IV-V	2.07 (0.70, 6.17)	0.190		
Hypertension before pregnancy	3.83 (1.43, 10.26)	0.010	5.01 (1.61, 16.01)	0.006
Renal artery involvement before pregnancy	2.98 (1.12, 7.91)	0.028		
Heart disease before pregnancy	7.25 (1.13, 46.56)	0.037	15.83 (1.99, 125.99)	0.009
Vascular intervention or surgery	1.26 (0.37, 4.31)	0.712		
Active TAK before pregnancy	8.40 (2.34, 30.2)	0.001	7.54 (1.85, 30.72)	0.005
Glucocorticoid during pregnancy	0.45 (0.10, 2.10)	0.307		
Immunosuppresants during pregnancy	1.79 (0.68, 4.68)	0.237		

UV, univariate; MV multivariate; *OR*, odd ratio; *CI*, confidence interval; TAK, Takayasu arteritis; BMI, body mass index

Table 5. Univariate and multivariate logistic regression analyses for factors predictive of adverse pregnancy outcomes in pregnancies with TAK

Factors	UV		MV	
	<i>OR</i> (95% <i>CI</i>)	<i>P</i>	<i>OR</i> (95% <i>CI</i>)	<i>P</i>
Age at pregnancy, years	1.06 (0.96, 1.17)	0.282		
BMI, kg/m ²	1.00 (0.90, 1.11)	0.982		
Age at TAK onset, years	0.98 (0.90, 1.06)	0.568		
Disease duration, years	1.09 (1.00, 1.19)	0.057	1.12 (1.02, 1.23)	0.024
TAK Numano classification				
Type I- IIb	0.89 (0.40, 1.97)	0.767		
Type IV-V	1.13 (0.51, 2.50)	0.767		
Hypertension before pregnancy	2.80 (1.13, 6.96)	0.027		
Renal artery involvement before pregnancy	2.80 (1.13, 6.96)	0.027		
Heart disease before pregnancy	2.56 (0.28, 23.74)	0.407		
Vascular intervention or surgery	1.75 (0.58, 5.32)	0.325		
Active TAK before pregnancy	3.45 (0.72, 16.59)	0.120		
Active TAK during pregnancy	11.60 (1.47, 91.49)	0.020	14.59 (1.81, 117.49)	0.012
Glucocorticoid during pregnancy	1.07 (0.39, 2.98)	0.895		
Immunosuppresants during pregnancy	0.75 (0.77, 4.00)	0.184		

UV, univariate; MV multivariate; *OR*, odd ratio; *CI*, confidence interval; TAK, Takayasu arteritis; BMI, body mass index

Figures

Figure 1

Flow chart showing the pregnancies and patients included into the study, TAK cases (A) and controls (B). TAK, Takayasu arteritis; PUMCH, Peking Union Medical College Hospital