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ORIGINAL ARTICLES

Pregnancy in Takayasu arteritis: a cross-sectional study and review of literature

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ABSTRACT

Objective: Takayasu arteritis (TA), a form of vasculitis affecting large-and medium-sized vessels; it mainly affects women of reproductive age. Although cardiovascular and hemodynamic changes during pregnancy represent a potential risk for TA, findings regarding risk in maternal and fetal outcomes are inconsistent. This study aimed to describe the prevalence and outcomes of pregnancies in patients with TA, along with a literature review of comparable studies on the subject matter.

Methods: This cross-sectional study was conducted between January and March 2020. We evaluated 20 women diagnosed with TA according to clinical and angiographic findings.

Results: The median age of the participants was 38 years. The median age at TA diagnosis was 26 years. Thirteen of the 20 participants reported at least one pregnancy. There were 38 pregnancies, including 26 deliveries (20 vaginal and six cesarean deliveries) and 12 abortions. The most common obstetric complication was spontaneous abortion (25%), followed by prematurity (7.9%), and eclampsia/preeclampsia (5.3%). Only one of our patients gave birth without any complications after being diagnosed with TA. In this case, the disease remained inactive throughout the pregnancy and postpartum periods.

Conclusions: The most common obstetric complication encountered was spontaneous abortion. The maternal and fetal outcome findings were similar to those of previously published studies. The literature shows that patients with stable pregestational TA generally have a good prognosis.

Keywords: Takayasu arteritis; Large vessel vasculitis; Pregnancy; Obstetric complications.

INTRODUCTION

Takayasu arteritis (TA), also known as "pulseless disease," is a chronic inflammatory disease of unknown etiology that affects large and medium-sized arteries, including the aorta and its primary branches. It is a rare disease that mainly affects women in 80%–90% of cases, with onset at the age of 10–40 years. It is highly prevalent in Asian countries, but it has already been described in different ethnic groups and in various geographic areas of the world[1].

The disease presents with transmural granulomatous inflammation that may cause stenosis, occlusion, dilatation, and/or aneurysm formation in the involved arteries. The clinical picture varies depending on the location and extent of the affected vessels, inflammatory process, and stage in which the TA is diagnosed.

During pregnancy, the maternal body undergoes circulatory changes to ensure proper oxygen and nutritional support for the fetus, as well as to protect the mother against the harmful effects of decreased venous return from uterine compression and blood loss during childbirth[2].

Although cardiovascular and hemodynamic changes during pregnancy represent a potential risk for TA- associated pregnancies, findings regarding protection or risk in maternal and fetal outcomes are inconsistent. Here, we sought to describe the prevalence and outcomes of pregnancies in TA patients along with a literature review of comparable studies on the subject matter.

MATERIAL AND METHODS

This cross-sectional descriptive study was conducted between January and March 2020. We evaluated 20 female patients diagnosed with TA who visited a public outpatient rheumatology clinic in the city of Salvador, Brazil. The inclusion criteria considered women: (i) with TA according to clinical and angiographic findings[3], (ii) who were over 18 years of age, and (iii) who agreed to participate in the study.

Epidemiologic and clinical information, including

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the number of pregnancies, deliveries, abortions, type of delivery, patient's age during pregnancy, pre-pregnancy diagnosis of systemic arterial hypertension, period of TA diagnosis (before or during pregnancy), patient-reported complications during pregnancy and childbirth, and TA treatment adopted in the gestational period, were collected.

Descriptive analysis was performed using the Statistical Package for the Social Sciences (SPSS, Chicago, IL, version 21.0). Categorical variables were expressed as frequencies and percentages, and continuous variables with normal distributions were expressed as mean ± standard deviation (SD). Variables that did not conform to a normal distribution were reported as median and interquartile range (IQR).

This study was approved by the Ethics Committee of Escola Bahiana de Medicina e Saúde Pública (CAEE: 19254619.4.0000.5544).

RESULTS

The study included 20 female patients. Table I shows the main epidemiological and clinical characteristics of the study population.

The median age of the participants was 38 years (IQR: 28-48), while the median age at diagnosis was 26 years (IQR: 21-37). According to the Numano angiographic classification[4], 60% of the sample was categorized as Type V (generalized involvement of all aortic segments). Hypertension was found to be the most commonly occurring comorbidity (80%), followed by coronary artery disease (20%), and cardiac failure (20%).

When analyzing the patients' obstetric histories, 13 out of 20 participants reported at least one pregnancy. The majority (60%) of patients were diagnosed with TA after the gestational period (Table II).

A total of 38 pregnancies, including 26 deliveries (20 vaginal deliveries and six cesarean sections) and 12 abortions, were reported. The mean number of pregnancies in 13 patients was 2.92. Eight patients (61.53%) had more than two pregnancies. The number of deliveries ranged from zero to five, the majority of which were normal.

It should be noted that only one patient had a history of contraceptive use and from those who were nulligravida. Three patients had a desire to have children, but had doubts about the outcome of pregnancy as they had TA and stated that they had never discussed the issue with their physicians. The remaining four patients received medical advice contraindicating pregnancy. None of the patients were diagnosed with systemic hypertension before pregnancy.

Table III describes various complications that occur during pregnancy, childbirth, and puerperium. Of the 38 pregnancies, there were nine spontaneous abortions,

TABLE I. Characteristics of the patients with Takayasu Arteritis (TA) in Salvador, Brazil

Variables	TA Patients (n=20)	
	Median	Interquartile range
Age (years)	38	(28.3 – 48.5)
Age at Diagnosis (years)	26	(21.3 – 39.0)
Angiography Classification	**n**	**%**
I	4	20
IIa	1	5
IIb	1	5
III	1	5
IV	1	5
V	12	60
Arterial hypertension	16	80
Renovascular hypertension	9	45
Chronic kidney disease*	1	5
Chronic coronary syndrome	4	20
Acute Miocardial Infarction	2	10
Stroke	1	5
Cardiac Failure	4	20.0

*Chronic kidney disease: glomerular filtration rate <60 mL/min/1.73 m(2) for 3 months or more. Angiography classification: Type I: branches from the aortic arch; Type IIa: ascending aorta, aortic arch and it's branches; Type IIb: ascending aorta, aortic arch, thoracic descending aorta; Type III: thoracic descending aorta, abdominal aorta and/or renal arteries; Type IV: abdominal aorta and/or renal arteries; Type V: combined features of type IIb and IV.

that accounted for the most common complications, followed by premature births. One patient experienced cardiac arrest during cesarean delivery due to anesthetic complications but was adequately resuscitated. No deaths were observed during our study.

Only one patient became pregnant after being diagnosed with TA. This patient was diagnosed with TA at age 23 due to systemic symptoms, arterial hypertension, and a finding of saccular aneurysms in the aortic isthmus originating from the brachiocephalic artery trunk and occlusion of the left subclavian artery (Type IIb). Due to a strong PPD reactor and suspicious pulmonary image, she used a concomitant treatment regimen for tuberculosis and high-dose prednisone.

Three months after starting drug therapy, she was submitted to a bypass surgery with a Y Dacron tube placement from the ascendant aorta to the right brachiocephalic trunk and left common carotid. She used

TABLE II. Obstetric data from patients with Takayasu Arteritis (TA) in Salvador, Brazil

Variables	Patients N (%)	Median (interquartile range)
Term childbirth deliveries:		
0:	8/20 (40%)	1 (0 – 2)
1:	5/20 (25%)	
>2:	7/20 (35%)	
Abortions:		
0:	15/20 (75%)	0 (0 – 0,75)
1:	3/20 (15%)	
>2:	2/20 (10%)	
Deliveries:		
Normal:	20	
Cesarean:	06	

N: Number of pregnancies

TABLE III. Complication rates for pregnancies in patients with Takayasu Arteritis in Salvador, Brazil

Variables	Pregnancy (N)	%
Spontaneous abortion	9	25%
Eclampsia / Preeclampsia	2	5.3%
Preterm birth	3	7.9%
Cardiorespiratory arrest	1	2.6%
Postpartum hemorrhage	2	5.3%
Placenta previa	1	2.6%

N: Number of pregnancies

prednisone low-dose and Methotrexate for two years which was replaced by azathioprine due to gastrointestinal intolerance. At the age of 26, she became pregnant; at this time, she had an angiotomography exam without signs of activity and low inflammatory tests (CRP and ESR). The assistant rheumatologist and obstetrician team chose to wean off the medications despite not being formally contraindicated during pregnancy. There were no complications during pregnancy, the delivery was by cesarean section, and the patient remains under follow-up at the outpatient clinic after two years with clinical and radiological stability and remains without immunosuppressants.

DISCUSSION

TA is a rare condition that generally affects women of childbearing age. Therefore, it is important to identify the impacts of overlapping physiological processes of adaptation on an ongoing inflammatory process in the vasculature due to TA[2,6].

The mean number of pregnancies was 1.9 per patient, similar to that reported previously in other studies. The lowest mean value has been found to be only 1.3 pregnancies per patient, whereas another study reported a value of 2.5[5,6]. The majority of our patients experienced pregnancy in the third decade of life, as in a study from India, in which 75% of the 16 patients became pregnant between the ages of 20 and 30 years[7].

Twelve patients in the present study were diagnosed with TA after their first pregnancy. This result is consistent with the data obtained by another study that evaluated 110 pregnancies in 58 patients, and observed that the majority (66.6%) of women were pregnant before diagnosis[7].

TA is rare and difficult to identify, often leading to delayed diagnosis. Early diagnosis of TA is difficult because early stage symptoms are non-specific, and the patient can be asymptomatic. Additionally, the disease progresses slowly, with late onset of complications. Thus, it is one of the main reasons why these patients become mothers before a TA diagnosis[8]. In this scenario, it is also necessary to consider the voluntary delay of pregnancy or fear of maternal-fetal complications as essential factors that reduce the incidence of pregnancies after diagnosis[9].

Only one of our patients gave birth without complications after being diagnosed with TA. As previously mentioned, in this case, the physician's option was to suspend the immunosuppressive treatment during the gestational period. This conduct may be questioned because although the impression of stable disease, the real assessment of disease activity in TA is very complex, and there is no consensus on how long immunosuppressant drugs should be used.

Various studies have found a low frequency of TA disease activity in pregnant patients. It has been postulated that a possible polarization of cytokines via T lymphocytes might assist maternal-fetal communication and influence this process. It has been suggested that pregnancy does not exacerbate disease activity, nor does vasculitis itself have any influence on the pregnancy of patients[8, 10].

In contrast, a French study concluded that TA increased the risk of complications during pregnancy by 13 times[5]. A study with the largest number of pregnancies that evaluated 96 TA patients and 240 pregnancies reported that 40% of the patients encountered com-

plications such as preeclampsia (21%) and high blood pressure (15%)[6].

The most common obstetric complication encountered in our sample was spontaneous abortion (23.68%), while eclampsia and preeclampsia were detected in only two (5.26%) pregnancies. We also observed a low frequency of premature deliveries, as reported in a previous study[11].

The prevalence of abortion varies widely, with the lowest rate at 3% and the highest at 30%[9]. In addition to having a common occurrence in the first trimester, even in healthy women, an important point to be explored regarding abortion is the common positivity of antiphospholipid antibodies (aPL) in TA. A study revealed that 41% (9/22) of patients with TA had persistently positive aPL or a concurrent diagnosis of antiphospholipid syndrome[12]. Antiphospholipid antibodies were not investigated in the present study.

Decisions about delivery in TA patients are made based on the severity and extent of vascular disease and the overall state of maternal health. Cesarean section is recommended for patients with diseases with angiography classifications IIb and III, which are considered more complex. For patients with less complicated conditions (classified as I and IIa), vaginal childbirth may be considered with epidural analgesia and close follow-up of blood pressure[13]. Our study was associated with a predominance of vaginal deliveries. However, this decision had no relationship with the disease status of patients, as only one patient was pregnant after the diagnosis of TA.

Another relevant point in our study was the observation that 7 (35%) of the women with TA had concerns about pregnancy, and four of them had also received medical recommendations contraindicating pregnancy. Another study found that one-third of 58 patients had been advised by their physician to ideally plan their pregnancy during low activity states of the disease, despite the fact that assessment of disease activity is difficult in TA[14].

Gestational prognosis may vary according to the angiographic profile of the disease, especially if hypertension and pre-eclampsia are present. If the patient has only supra-aortic vessel involvement and no systemic arterial hypertension, the risk of obstetric complications is lower. However, stenosis of the abdominal aorta and/or renal arteries can potentially lead to significantly greater complications.

Severe aortic valvular disease and aortic aneurysm are risk factors for maternal morbidity and fatality; therefore, patients with these conditions should be discouraged from conceiving. In case of unexpected pregnancy, therapeutic abortion should be considered[15].

Limitations of our study include the relatively small sample size, a consequence of TA being a rare disease. Furthermore, there is the possibility of a memory bias, as the patients were asked about facts from the past.

In conclusion, pregnancy in patients with TA has become a significant concern due to several reasons. The disease mainly affects women of childbearing age, and it remains unclear whether pregnancy could exacerbate the vascular process. The maternal and fetal outcomes of our sample were similar to those of previously published studies. Existing literature shows that patients with stable pregestational TA generally have a good prognosis.

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