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MATERNAL-FETAL MEDICINE

Management and evaluation of pregnant women with Takayasu arteritis

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Abstract

Purpose To evaluate the clinical characteristics, obstetric/neonatal outcomes, and pregnancy complications of pregnant women with Takayasu arteritis (TA).

Methods We retrospectively evaluated the data of 22 pregnancies of 11 patients with TA between January 1 2000, and December 31 2017. Patient characteristics, severity of disease, obstetric outcomes, pregnancy complications, mode of delivery, and neonatal outcomes were evaluated.

Results Based on the angiographic classification, four, two, one, three, and one patient were classified into groups I, IIa, III, IV, and V, respectively. Based on Ishikawa criteria, five, two, two, and two patients were classified into groups 2a, 1, 2b, and 3, respectively. Sixteen and five pregnancies resulted in live births and spontaneous abortion, respectively. One pregnancy was terminated due to prenatally diagnosed trisomy 21. Relapse of TA was observed in five pregnancies. Mean age at diagnosis was 24.54 ± 6.23 years, and mean age at conception was 30.30 ± 4.80 years. There were two multiple pregnancies (one twin and one triplet) and 19 newborns were delivered alive. Rates of hypertensive disorders of pregnancy, preterm birth, intrauterine growth retardation, oligohydramnios, and intrauterine fetal demise were 36.4, 18.2, 13.6, 13.6, and 0%, respectively. Mean gestational age at birth was 37.25 ± 2.40 weeks and mean birthweight was 2682.10 ± 176.82 g. Median APGAR score was 8. Cesarean section rate was 50%. Regional anesthesia/analgesia was administered during 62.5% of the deliveries. Ten neonates were admitted to neonatal intensive care unit and eight neonates had neonatal respiratory complications.

Conclusion Appropriate management of pregnant women with TA within the framework of antenatal care programs and adopting a multidisciplinary approach are key to ensure successful outcomes.

Keywords Takayasu arteritis · Pregnancy · Obstetric outcomes · Antenatal care program

Introduction

Takayasu arteritis (TA) is a chronic granulomatous large-vessel vasculitis that primarily affects the aorta and its primary branches [1]. The inflammatory process associated with TA causes thickening in the walls of the affected arteries, which may lead to stenosis, occlusion, dilatation, or aneurysm formation as the disease progresses [1].

The prevalence of TA varies across different countries, with higher prevalence in Asia [2]. The highest incidence rates of the disease were reported in Japan with approximately 100–200 registered cases annually [1, 3]. In contrast, the incidence is one in three new cases per year per million population in the USA and Europe [1, 4]. Approximately, 80–90% of the cases are young women with age of onset usually between 10 and 40 years [1, 4].

Nonspecific constitutional symptoms, arthralgias, carotidynia, absent or weak peripheral pulse(s), claudication of the limbs, arterial bruits, discrepant blood pressure between arms, hypertension, angina, and neurologic symptoms may be observed in patients with TA depending on the severity of the disease [5, 6]. Laboratory findings are nonspecific, and they are commonly associated with TA-related inflammatory process. Elevated levels of acute phase reactants may be seen; however, they do not objectively reflect disease activity [7]. Proper radiologic imaging is essential for the accurate diagnosis of TA [8]. Smoothly tapered luminal narrowing or occlusion in the arterial tree of the chest, abdomen, head,

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or neck with thickening of the vessel wall is usually suggestive of TA in imaging modalities [8]. Histologic diagnosis of TA is impractical because the disease involves the large arteries. However, histologic studies indicated involvement of all arterial layers (panarteritis) by a variable inflammatory infiltrate, including acute exudative inflammation and chronic granulomatous inflammation together with hyperplasia and neovascularization [1, 9].

The diagnosis of TA is generally made with the help of clinical findings and imaging methods [1]. Different nomenclature and diagnostic criteria have been developed by Ishikawa, Sharma, American College of Rheumatology (ACR), and the International Chapel Hill Consensus Conference (CHCC) over the years [1]. Although these criteria are widely used by clinicians, optimal diagnostic criteria have not been developed yet [10]. In contrast, angiographic classification and disease severity criteria can be used for the management of TA [2, 6].

Glucocorticoids, methotrexate, leflunomide, mycophenolate mofetil, tocilizumab, azathioprine, and anti-tumor necrosis factor (TNF)-alpha agents are some treatment options for TA [2]. Angioplasty, bypass grafts, or surgical interventions may be necessitated based on the vascular complications [11]. TA is a chronic disease, and it progresses with relapses and remissions [12]. Prognosis of TA varies among the patients, and vascular involvement is usually progressive [12]. The major predictors of outcome are incidence of TA-related complications and a progressive disease course [12, 13].

TA is a relatively rare form of vasculitis that mainly affects young women of childbearing age [1, 14]. However, experience with the appropriate management of TA during pregnancy is limited [15–22]. According to previous reports, pregnancy did not affect the course of TA and even reduced disease-related symptoms [15–22]; therefore, optimal pregnancy and neonatal outcomes can be achieved with proper management protocols [15–22]. In contrast, physiologic changes of pregnancy may worsen TA-related complications and lead to poor obstetric and neonatal outcomes [15–22].

The aim of this study was to evaluate the clinical characteristics, obstetric/neonatal outcomes, and pregnancy complications of pregnant women with TA, through regular follow-up at our institution.

Materials and methods

We retrospectively evaluated the data of 22 pregnancies of 11 patients with TA who were followed at the Division of Perinatology, Hacettepe University, between January 1, 2000 and December 31, 2017. The necessary data were withdrawn from the electronic database of the Division of Perinatology, Hacettepe University. Written informed consents were obtained from all participants, and the study protocol was approved by Hacettepe University Ethics Committee (GO 18/68). Patient characteristics, severity of the disease, obstetric outcomes, pregnancy complications, mode of delivery, and neonatal outcomes were evaluated.

All patients were diagnosed with TA before conception based on the criteria defined by the American College of Rheumatology (ACR) [2]. TA was diagnosed if at least three of the following six criteria were present: (1) age at disease onset ≤ 40 years, (2) claudication of the extremities, (3) decreased pulsation of one or both brachial arteries, (4) difference of at least 10 mmHg in the systolic blood pressure between the arms, (5) bruit over one or both subclavian arteries or the abdominal aorta, (6) arteriographic narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities, not due to arteriosclerosis, fibromuscular dysplasia, or other causes [2]. Radiological imaging procedures were performed before or between pregnancies to evaluate the arterial involvement and disease severity. In all patients, TA was classified angiographically based on the classification suggested by Moriwaki et al. [6]. This classification consists of five groups based on the arterial involvement site: type I, branches of the aortic arch; type IIa, ascending aorta, aortic arch, and branches of the aortic arch; type IIb, ascending aorta, aortic arch and its branches, and thoracic descending aorta; type III, thoracic descending aorta, abdominal aorta, and/or renal arteries; type IV, abdominal aorta and/or renal arteries, and type V, features of types IIb and IV (diffuse involvement). Furthermore, involvement of the coronary or pulmonary arteries was designated as C (+) or P (+), respectively [6]. Necessary pre-pregnancy arrangements were made for medications by perinatologists and rheumatologists. In addition, severity of the disease was assessed by using the Ishikawa severity criteria [2]. Group 1 was defined as absence of disease-related complications; group 2a was defined as the presence of mild retinopathy, mild or moderate secondary hypertension, aortic/arterial aneurism, or aortic regurgitation; group 2b was defined as the presence of severe retinopathy or secondary hypertension; and group 3 was defined as the presence of two or more complications of group II [2, 14].

The patients were registered in a special antenatal care program provided by a multidisciplinary team (rheumatologists, cardiologists, and perinatologists) during their pregnancies. Necessary laboratory tests, such as complete blood count, clinical urine test, blood sugar, liver function tests, C-reactive protein, erythrocyte sedimentation, and complement components 3 and 4 were performed during the course of follow-up. Low-molecular-weight heparin (LMWH) (enoxaparin 2000 Anti-Xa IU/0.2 mL), oral prednisone (4 mg methylprednisolone), and aspirin (100 mg ASA) were added to the treatment protocol as soon as a pregnancy was

confirmed. Addition of necessary drugs and required dose changes were implemented based on the recommendations of rheumatologists during pregnancy. Pregnancy follow-up consisted of serial ultrasonography to evaluate fetal growth, aneuploidy screening (combined or triple test), fetal anatomy scanning at the 20th to 24th gestational weeks, oral glucose challenge test, and non-stress test weekly (after the 28th gestational week).

The mean patient age at the diagnosis of TA, mean age at conception, mean gestational age at spontaneous abortion, mean gestational age at birth, mean birthweight, and median 5th-minute APGAR score were calculated. Arterial involvement site, angiographic classification of the disease, and Ishikawa Severity Classification were evaluated for all patients. Pregnancy complications, pregnancy outcome, relapse of TA during pregnancy, medications during pregnancy, onset of labor, mode of delivery, cesarean section (CS) indications, methods of anesthesia, neonatal complications, and additional maternal diseases were reported for all pregnancies. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS® version 22.0; IBM, Armonk, NY, USA).

Results

This study consisted of 22 pregnancies of 11 patients with TA. Age at diagnosis, arterial involvement site, angiographic classification, and Ishikawa Severity Criteria of the patients before their pregnancies are shown in Table 1. Based on the angiographic classification of TA, four patients were classified as group I, two patients were classified as group IIa, one patient was classified as group III, three patients were classified as group IV, and one patient was classified as group V. Seven patients had supradiaphragmatic arterial involvement, and three patients had isolated infradiaphragmatic disease (one of them had bilateral renal artery involvement together with abdominal aorta involvement), and one patient had both supra- and infradiaphragmatic disease. Pulmonary artery involvement was observed in four patients. Based on the Ishikawa criteria, five, two, two, and two patients were classified into groups 2a, 1, 2b, and 3, respectively.

Of 22 pregnancies, one patient had four pregnancies, three patients had three pregnancies, two patients had two pregnancies, and the remaining five patients had one pregnancy. Sixteen and five pregnancies resulted in live births (16/22, 72.7%) and spontaneous abortion (5/22, 22.7%), respectively. Relapse of TA was observed in five pregnancies (22.7%). Two of the exacerbations occurred in the first trimester, and both resulted in a miscarriage. The remaining three relapses occurred in the last trimester, and two resulted in oligohydramnios with intrauterine growth retardation (IUGR), and prelabor CS was performed to prevent perinatal morbidity. Preeclampsia occurred in one of these pregnancies with IUGR, and both neonates were admitted to the neonatal intensive care unit (NICU). In contrast, one of the patients with third trimester relapse responded well to pulse high-dose corticosteroid therapy and delivered vaginally at term without any complication. One pregnancy was terminated due to prenatally diagnosed trisomy 21 (1/22, 4.6%).

The mean age at diagnosis of TA was 24.54 ± 6.23 years (17–33), and the mean age at conception was 30.30 ± 4.80 years (20–38). There were two multiple pregnancies (one twin and one triplet) (9%) and a total of 19 newborns were delivered live. The mean gestational age at spontaneous abortion was 8.40 ± 1.14 weeks (7th to 10th week). The rates of hypertensive disorders of pregnancy (7 preeclampsia and 1 gestational hypertension), preterm birth, IUGR, oligohydramnios, and intrauterine fetal demise were 36.4% (8/22), 18.2% (4/22, two of them were

Table 1 Age at diagnosis, arterial involvement site, angiographic classification, and Ishikawa severity criteria of the patients before their pregnancies

Patient no.	Age at diagnosis	Arterial involvement site	Angiographic classification	Ishikawa severity criteria
1	33	Bilateral common carotid arteries	I	2a
2	20	Abdominal aorta and right pulmonary artery	IV P	2a
3	18	Abdominal aorta	IV	2a
4	28	Bilateral common carotid arteries	I	1
5	20	Abdominal aorta, arcus aorta, and left pulmonary artery	V P	2b
6	19	Right common carotid	I	1
7	30	Left subclavian artery and left pulmonary artery	IIa P	2a
8	31	Arcus aorta and left subclavian artery	IIa	3
9	17	Abdominal aorta and bilateral renal arteries	IV	3
10	32	Left common carotid artery and right pulmonary artery	I P	2a
11	22	Descending aorta	III	2b

multiple pregnancies), 13.6% (3/22), 13.6% (3/22), and 0% (0/22), respectively. The mean gestational age at birth was 37.25 ± 2.40 weeks (range 30–40 weeks), and the mean birthweight was 2682.10 ± 176.82 g (range 1390–3670 g). The median APGAR score was 8 (range 5–10). The CS rate was 50% (8/16). Regional anesthesia/analgesia was administered in 62.5% (10/16) of the deliveries. Of 19 (52.6%) live neonates, ten were admitted to the NICU, and eight neonates (42.1%) had neonatal respiratory complications [5 respiratory distress syndrome (RDS) and 3 tachypnea with intercostal retractions] (five of them were neonates from multiple pregnancies). Tables 2 and 3 show the clinical characteristics, obstetric complications, pregnancy outcomes, and neonatal outcomes of the pregnancies with TA.

Discussion

TA is a rare chronic inflammatory vascular disease of unknown origin that mainly affects the aorta and its primary branches [1]. TA is usually defined as "pulseless disease" because it causes full-layer arterial inflammation that leads to vascular stenosis/obstruction in the affected vessels [18]. Autoimmunity, sex hormones, genetic susceptibility, and *Mycobacterium tuberculosis* infection were hypothesized to take part in the etiology of TA, but the definitive cause of the disease is still unknown [2]. TA predominantly affects young women during their reproductive years (female to male ratio is 4:1) [23], and it has variable prevalence across different countries, with the highest the reported rates in Asian countries [2]. Clinical findings and patients' complaints depend on the severity of the disease and arterial involvement sites [5, 6]. The diagnosis of TA is made by the combination of clinical characteristics and radiologic imaging methods [8]. Histopathologic diagnosis is generally not possible because TA involves the large vessels [9]. In contrast, histopathologic studies indicate panarteritis by a variable inflammatory infiltrate, including acute exudative inflammation, chronic granulomatous inflammation with hyperplasia, and neovascularization [9]. Intimal leukocyte infiltration and myofibroblast proliferation cause stenosis and occlusion in the vessel lumens, whereas aneurysm formation occurs due to the release of metalloproteases from the inflammatory cells [9]. TA is a chronic vasculitis with exacerbations and remissions [11, 12]. Treatment includes medical, surgical, and interventional radiologic methods, depending on disease-related complications [11, 12]. Although many classification systems have been developed for the diagnosis and severity of TA to provide appropriate management protocols, none of them is ideal [2, 6, 10]. Owing to the rarity of TA and the presence of relatively limited number of studies in

Table 2 Demographic features, obstetric outcomes, pregnancy complications, and neonatal outcomes of pregnant women with Takayasu arteritis

Variable	*n* (%)
Total pregnancies	22
Multiple pregnancy	2/22 (9%) (one twin, one triplet)
Live births	16/22 (72.7%)
Relapse of TA during pregnancy	5/22 (22.7%)
Spontaneous abortion	5/22 (22.7%)
Spontaneous abortion week (mean ± SD, range)	8.40 ± 1.14 (7–10)
Termination of pregnancy	1/22 (4.6%)
Hypertensive disorders of pregnancy	8/22 (36.4%)
Preterm birth	4/22 (18.2%)
IUGR	3/22 (13.6%)
Oligohydramnios	3/22 (13.6%)
Intrauterine fetal demise	0/22 (0%)
Maternal age at conception (years) (mean ± SD, range)	30.30 ± 4.80 (20–38)
Age at diagnosis of TA (years) (mean ± SD, range)	24.54 ± 6.23 (17–33)
Gestational age at birth (mean ± SD, range)	37.25 ± 2.40 (30–40)
Birthweight (g) (mean ± SD, range)	2682.10 ± 176.82 (1390–3670)
CS rate	8/16 (50%)
Regional anesthesia/analgesia rate	10/16 (62.5%)
APGAR (median, range)	8 (5–10)
NICU administration rate	10/19 (52.6%)
Neonatal respiratory complication rate	8/19 (42.1%)

IUGR intrauterine growth retardation, *SD* standard deviation, *TA* Takayasu arteritis, *NICU* neonatal intensive care unit, *CS* cesarean, regional anesthesia rate

Table 3 Clinical characteristics, obstetric complications, pregnancy outcomes, and neonatal outcomes of pregnant women with Takayasu arteritis

Patient no.	Pregnancy no.	Maternal age at conception (years)	Pregnancy outcome	Obstetric complications	Medications	Gestational age at birth	Mode of delivery	Labor anesthesia	Birthweight (g)	5th-minute APGAR Score	Neonatal outcome	NICU admission	Maternal disease
1	1	36	LB	PB	Prd 10, Asp 100, enx 0.2, Euthyrox 50	30	CS	General	1390/1400/1450	8/8/7	RDS	Yes/yes/yes	Hashimoto, IVF pregnancy
2	1	23	SA (8th GW)										HTN, TA relapse during current pregnancy
	2	27	LB	PE	Prd 10, Asp 100, enx 0.2, a-met 2×250	37	VB	Regional	3050	9	Tachypnea	Yes	
3	1	20	LB		Prd 5, Asp 100, enx 0.4, a-met 2×250	39	VB	Regional	3670	10	Healthy	No	HTN, Crohn, AS, F5Lhet, MTHFR677 Homo
	2	26	SA (10th GW)		Prd 5, Asp 100, enx 0.4, a-met 2×250								TA relapse during current pregnancy
	3	27	LB	PB, oligo, IUGR	Prd 5, Asp 100, enx 0.4, a-met 2×250	35	CS	General	2050	5	RDS	Yes	TA relapse during current pregnancy
4	1	30	LB		Prd 5, Asp 100, Enx 0.4, Euthyrox 75	39	VB	Regional	3450	9	Healthy	No	AS, Hashimoto
	2	32	LB		Prd 5, Asp 100, enx 0.4, Euthyrox 75	38	VB	Regional	3500	9	Healthy	No	
	3	34	LB		Prd 5, Asp 100, enx 0.4, Euthyrox 75	38	VB	Regional	3620	10	Healthy	No	

Table 3 (continued)

Patient no.	Pregnancy no.	Maternal age at conception (years)	Pregnancy outcome	Obstetric complications	Medications	Gestational age at birth	Mode of delivery	Labor anesthesia	Birthweight (g)	5th-minute APGAR Score	Neonatal outcome	NICU admission	Maternal disease
	4	35	SA (7th GW)		Prd 5, Asp 100, enx 0.4, Euthyrox 75								
5	1	25	LB	PB, PE	Prd 10, Asp 100, enx 0.4, a-met 4×250	35	CS	General	2190/2300	7/8	RDS, jaundice	Yes/yes	Bilateral renal artery stent
6	1	26	LB	GHT	Prd 5, Asp 100, enx 0.2, a-met 3×250	40	VB	Regional	3170	9	Healthy	No	
	2	28	LB	PE	Prd 5, Asp 100, enx 0.2, a-met 3×250	38	VB	Regional	2980	6	Tachypnea	Yes	TA relapse during current pregnancy
7	1	32	SA (8th GW)										
	2	33	SA (9th GW)										
	3	34	LB		Prd 10, Asp 100, enx 0.4	39	VB	Regional	3330	9	Healthy	No	
8	1	32	LB	PE	Prd 10, Asp 100, enx 0.4	39	CS	General	3000	7	Healthy	No	
	2	35	LB	PE	Prd 10, Asp 100, enx 0.4	38	CS	Regional	2800	8	Healthy	No	
	3	38	LB	PE, oligo, IUGR	Prd 10, Asp 100, enx 0.4	37	CS	Regional	2180	6	RDS	Yes	

Table 3 (continued)

Patient no.	Pregnancy no.	Maternal age at conception (years)	Pregnancy outcome	Obstetric complications	Medications	Gestational age at birth	Mode of delivery	Labor anesthesia	Birthweight (g)	5th-minute APGAR Score	Neonatal outcome	NICU admission	Maternal disease
9	1	27	LB	PB, PE, oligo, IUGR	Prd 10, Asp 100, enx 0.2	36	CS	General	2120	7	Tachypnea	Yes	Graft at abdominal aorta, HTN, MTHFR 1298 Het, TA relapse during current pregnancy
10	1	37	LB		Prd 5, Asp 100, enx 0.6	38	CS	Regional	3310	8	Healthy	No	HTN, SVT, TIA
11	1	30	TOP (14th GW)	Trisomy 21	Prd 5, Asp 100, enx 0.2								

LB live birth, *PB* preterm birth, *Prd* prednisolone, *Asp* aspirin, *enx* enoxaparin, *CS* cesarean section, *RDS* respiratory distress syndrome, *NICU* neonatal intensive care unit, *IVF* in vitro fertilization, *SA* spontaneous abortion, *HTN* hypertension, *PE* preeclampsia, *VB* vaginal birth, *a-met* alpha methyldopa, *AS* ankylosing spondylitis, *F5LHet* factor 5 Leiden heterozygous, *oligo* oligohydramnios, *IUGR* intrauterine growth retardation, *GHT* gestational hypertension, *GW* gestational week, *TOP* termination of pregnancy, *TIA* transient ischemic attack, *SVT* supraventricular tachycardia, *MTHFR 1298 Het* methylenetetrahydrofolate reductase 1298 heterozygous, *TA* Takayasu arteritis

literature, we do not have adequate knowledge regarding the optimal management protocols for pregnant women with TA [15–22].

Pregnancy has been reported to neither interfere with disease progression nor negatively affect fertility [15, 17, 18, 21, 24]. However, conception during the remission phase of TA is recommended to achieve optimal obstetric and neonatal outcomes [15, 25]. A study by Hidaka et al. reported good maternal and neonatal outcomes in 26 pregnancies of 24 patients who were in remission during the study period [18]. In addition, Assad et al. reported improvement in TA disease activity and symptoms during pregnancy in their study, which consisted of 156 pregnancies of 89 patients with TA [21]. Furthermore, Matsumura et al. reported lowered C-reactive protein levels and improved hemodynamic stability in their study, which included 22 pregnancies of 18 patients with TA [24]. Immunologic adaptive changes during pregnancy, immunomodulatory effect of progesterone, and T-helper 2 cell-related cytokines might be responsible for the course of TA during pregnancy based on various studies [15, 21, 24]. However, relapse of TA was observed in five pregnancies in our study (22.7%). Furthermore, relapse of the disease resulted in poor obstetric outcomes, such as spontaneous abortion, IUGR, and preeclampsia, in four of the five pregnancies. These negative outcomes were most probably due to the inflammation of placenta, which might be observed in pregnant women with autoimmune diseases [26, 27]. The injury of the syncytiotrophoblasts, endovascular trophoblasts covering the tip of the spiral arteries, endothelial cells of the spiral veins, superficial/glandular epithelial cells of the decidua (intervillous space of the placenta), induced by autoantibody inflammatory processes, and the entrance of cell degradants of these tissues into the maternal circulation might result in impaired implantation and disturbed fetal perfusion in these patients [26, 27]. Thus, stabilization of the disease before conception and appropriate management of placental inflammation during the pregnancy seem to be the key points for achieving optimal pregnancy outcomes [26, 27]. Low-dose corticosteroids, low-dose acetylsalicylic acid, and low-dose LMWH were the main components of the treatment of these patients [26, 27]. Another important point was that three of the five spontaneous abortions (60%) occurred in pregnant women without preconceptional counseling.

Although pregnancy is believed to have a positive effect on the course of TA, this disease can adversely affect pregnancy [15, 17, 18, 21, 22]. Particularly, increased blood volume with increased cardiac load during pregnancy may cause worsening of TA-related vascular lesions and may result in fatal complications [15, 17, 18, 21, 22]. Aortic regurgitation, congestive heart failure, renal insufficiency, antepartum hemorrhage, pulmonary embolism, and myocardial infarction were some of the most serious reported complications in the literature [17, 18, 25]. Fortunately, none of the patients in our study died or had serious morbidity.

Obstetric complications, such as gestational hypertension, preeclampsia, spontaneous abortion, IUGR, placental ablation, preterm labor, and low birthweight were found to be more frequent in pregnancies of patients with TA [15, 17, 21, 22]. The most common complication in pregnant patients with TA was hypertension, and the overall incidence reached 54% in large cohort studies [14, 15, 17, 18, 21, 22]. Hypertensive disorders were reported to be associated with premature birth, low birthweight, and maternal mortality/morbidity [15, 18, 21, 28]. Thus, close monitoring of blood pressure and appropriate treatment during pregnancy are mandatory. We also started low-dose salicylic acid and low-dose LMWH in all patients with preconceptional counseling for preeclampsia prophylaxis. Furthermore, medical treatment with alpha methyldopa was administered to patients with elevated blood pressure during pregnancy. Hypertensive disorders were observed in eight pregnant women (36.4%) in our study (7 preeclampsia and 1 gestational hypertension). However, most of them had late-onset hypertensive diseases (6/8, 75%), and only two pregnant women with early-onset preeclampsia developed oligohydramnios and IUGR. In contrast, two patients had pregestational hypertension and two spontaneous abortions, one oligohydramnios and one superimposed preeclampsia occurred in five pregnancies of these patients. Pregnancy outcomes seemed to be worse in patients with pregestational hypertension, which was consistent with previous literature [15, 18, 21].

The spontaneous abortion rate was 22.7% in our study (5/22), which was slightly higher than the reported rates in the literature [14]. The spontaneous abortion rates ranged between 8.3 and 19% in various studies [15, 16, 18, 22]. However, three of the five spontaneous abortions (60%) occurred in pregnancies without preconceptional counseling, and two patients had pregestational hypertension.

IUGR and preterm labor are other major concerns in the pregnancies of patients with TA [14, 15, 17, 21, 22]. The incidence of IUGR ranged between 17 and 51.7% in various studies [14, 15, 17, 21], whereas preterm delivery rates were reported to be between 4 and 30% [14, 16, 18]. Placental insufficiency, hypertension-related complications, and maternal vascular lesions lead to impaired blood flow to the fetus, resulting in IUGR according to most researchers [14, 15, 17, 21]. In addition, placental inflammation as previously mentioned might be another important factor behind the higher rates of obstetric and neonatal complications in these patients [26, 27]. Furthermore, iatrogenic prematurity and intrauterine fetal demise were other important issues [14, 15, 17, 21]. In this series, 16 pregnancies resulted in live births (72.7%), and the rates of preterm birth, IUGR, oligohydramnios, and intrauterine fetal demise were 18.2% (4/22, two of them were multiple pregnancies), 13.6% (3/22),

13.6% (3/22), and 0% (0/22), respectively. These outcomes appeared to be better than that in existing literature most probably due to the appropriate management of pregnancies and sufficient preconceptional counseling.

Arterial involvement site (especially renal arteries) and maternal vascular complications are important precursors of pregnancy outcomes [16, 29]. Two patients with severe TA-related complications (one patient with bilateral stent in renal arteries together with twin gestation and another with abdominal aorta graft) experienced preeclampsia, but delivery was successful without neonatal or maternal mortality/morbidity. The most common risk of multiple pregnancy is preterm delivery, which is associated with increased perinatal mortality and morbidity due to complications related to immaturity [30]. Multiple pregnancy accounts for approximately 17% of births before 37 weeks of gestation and 23% of births before 32 weeks [31]. Additionally, the risk of preeclampsia is significantly higher in multiple pregnancy compared to singletons [32]. Thus, physicians should be more cautious in the management of multiple pregnancies complicated with TA. In our series, the patient with twin pregnancy developed preeclampsia and delivered by CS at the 35th week of gestation. Both fetuses were admitted to NICU and they were complicated by RDS. Moreover, one pregnancy with IVF triplets was delivered by CS due to preterm labor at the 30th week of gestation. All three neonates were admitted to NICU and RDS was observed in all. Our findings were consistent with the current literature [31, 32]. However, successful results can be obtained with appropriate management protocols even in the most difficult cases. Relatively lower mean gestational age at birth and birthweight values in our study depended on the prelabor deliveries performed for maternal and fetal indications (such as preeclampsia, multiple pregnancy, IUGR). Although vaginal birth was preferred in uncomplicated pregnancies, physicians should be cautious, particularly during the second stage of labor. Fluctuations in blood pressure and increased cardiovascular load may worsen maternal health [14, 18]. In contrast, CS might be performed more frequently in deliveries of patients with TA due to increased rates of CS indications (fetal distress, maternal cardiac complications, preeclampsia, etc.) [14, 33]. The CS rate was 50% (8/16) in this study, which was mostly associated with obstetric indications. Regional anesthesia/analgesia was generally recommended for deliveries of patients with TA to minimize maternal complications [34]. The regional anesthesia/analgesia rate was 62.5% (10/16) in our study, and general anesthesia/analgesia was mostly administered for emergency CS deliveries.

Neonatal outcomes were reported to be favorable in the absence of pregnancy complications [18, 33]. However, prematurity, RDS, NICU admission, and postpartum neonatal death were some of the main concerns of neonatologists because the incidences of these neonatal complications increased in pregnancies with TA due to disease-related complications [17, 22]. The median 5th-minute APGAR score was 8 (5–10) in our study, and none of the fetuses died in the neonatal period. In contrast, the NICU admission rate and neonatal respiratory complication rate were 52.6% (10/19) and 42.1% (8/19), respectively, in our study. Nevertheless, five of these neonates were from multiple pregnancies, and they were delivered prematurely.

In conclusion, appropriate management of pregnancies with TA within the framework of antenatal care programs and providing multidisciplinary approach are crucial for successful outcomes.

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Compliance with ethical standards

Conflict of interest Atakan Tanacan declares that he has no conflict of interest. Canan Unal declares that she has no conflict of interest. Halise Meltem Yucesoy declares that she has no conflict of interest. Sinem Ayse Duru declares that she has no conflict of interest. Mehmet Sinan Beksac declares that he has no conflict of interest.

Ethical approval The study protocol was approved by Hacettepe University Ethics Committee (GO 18/68).

Informed consent Informed consent was obtained from all individual participants included in the study.

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