RESEARCH ARTICLE

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Perinatal Outcomes in Women Exposed to Monoclonal Antibody Biologics During Pregnancy

Gebelik Sırasında Monoklonal Antikor Biyolojikleri Kullanan Kadınlarda Perinatal Sonuçlar

ABSTRACT

Objective

Biologics, often known as monoclonal antibody biologics (mAbs), have improved the treatment and quality of life for many patients with inflammatory and autoimmune diseases. Disease remission is the strongest predictor of perinatal outcomes in pregnancies exposed to monoclonal antibodies. The aim of this study was to evaluate maternal and perinatal outcomes in pregnancies receiving mAbs therapy.

Materials and Methods

We retrospectively reviewed 21 singleton pregnancies. Drug exposure during pregnancy was classified as: exposure throughout all trimesters, discontinuation in the first trimester, or discontinuation in the third trimester. mAbs drugs were classified into three groups based on their mechanism:Anti-TNF α, anti-cytokine, and anti-B cell agents.

Results

The most common underlying disease was Familial Mediterranean Fever. Certolizumab pegol and Anakinra were the most frequently administered anti-TNF α and anti-cytokine agents, respectively. The mean gestational age at delivery was 38±1.2 weeks, and the mean birth weight was 3083±416 g. Rates of fetal growth restriction, preterm birth, and neonatal intensive care unit admission were significantly higher in patients with multiple autoimmune or inflammatory diseases compared with patients without such conditions ($p < 0.05$).

Conclusion

This study demonstrated that the coexistence of multiple autoimmune or inflammatory diseases may be significantly associated with a higher incidence of adverse obstetric outcomes in pregnancy.

Key Words

Monoclonal antibody, Biologics, Perinatal outcome, Anti-TNF α, Anakinra, Certolizumab pegol

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ÖZ

Amaç

Biyolojikler, sıklıkla monoklonal antikor biyolojikleri (mAbs) olarak bilinmekte olup, inflamatuvar ve otoimmün hastalıkların tedavisinde ve hastaların yaşam kalitesinde önemli iyileşmeler sağlamıştır. Hastalığın remisyonu, mAbs maruziyeti olan gebeliklerde perinatal sonuçların en güçlü belirleyicisidir. Bu çalışmanın amacı, mAbs tedavisi alan gebeliklerde maternal ve perinatal sonuçların değerlendirilmesidir

Gereç ve Yöntemler

Bu çalışmada retrospektif olarak 21 tekil gebelik değerlendirildi. Gebelik boyunca ilaç kullanımı üç kategoriye ayrıldı: tüm trimesterlerde devam eden kullanım, birinci trimesterde sonlandırma ve üçüncü trimesterde sonlandırma. Monoklonal antikor biyolojikleri etki mekanizmaları temelinde Anti-TNF α, anti-sitokin ve anti-B hücre ajanları olarak sınıflandırıldı.

Bulgular

Çalışma popülasyonunda en sık görülen altta yatan hastalık Ailevi Akdeniz Ateşi olarak saptandı. İlaç kullanımında Certolizumab pegol, en yaygın anti-TNF α ajanı; Anakinra ise en sık kullanılan anti-sitokin ajanıydı. Ortalama doğum yaşı 38±1,2 hafta ve ortalama doğum ağırlığı 3083±416 g olarak hesaplandı. Çoklu otoimmün veya inflamatuar hastalığı bulunan gebelerde, fetal büyüme kısıtlılığı, preterm doğum ve yenidoğan yoğun bakım ünitesine yatış oranları, böyle bir eşlik eden hastalığı olmayan gebelerle karşılaştırıldığında anlamlı derecede yüksek saptandı ($p < 0,05$).

Sonuç

Çalışmamızın bulguları, birden fazla otoimmün veya inflamatuar hastalığa sahip olmanın, gebelikte olumsuz obstetrik sonuçların görülme sıklığını artırabileceğini göstermektedir.

Anahtar Kelimeler

Monoklonal antikor, Biyolojik, Perinatal sonuç, Anti-TNF α, Anakinra, Certolizumab pegol

INTRODUCTION

Biologics, often known as monoclonal antibody biologics (mAbs), have improved the treatment and quality of life for many patients with inflammatory and autoimmune diseases. These medications have made a considerable difference not just in reducing disease activity, but also in preventing illness-related structural damage and improving patients' quality of life (1). mAbs have an immunoglobulin G (IgG) structure and bind to receptors or critical inflammatory molecules (1). They may control inflammation by decreasing cytokine synthesis, lymphocyte trafficking, blocking costimulation signals, or depleting B cells (1). With a greater understanding of the mechanisms, effects, and safe reporting of their usage during the perinatal period, increasing numbers of women of reproductive age are using these medicines (2).

Remission of the disease is the most significant predictor of pregnancy outcomes in autoimmune and inflammatory diseases, particularly in the 6 months preceding conception, and has been related to improved maternal and fetal outcomes (1, 3, 4). Consequently, physicians may opt to maintain immunosuppressive therapy during pregnancy, including mAbs such as anti-tumor necrosis factor alpha (anti-TNF α), anti-cytokine, or anti-B cell agents (2). Using mAbs therapy (mostly anti-TNF α) during pregnancy is not associated with an increase in adverse outcomes such as preterm birth, congenital anomalies, or miscarriage, according to recent studies (5-7).

The goal of this research was to evaluate maternal and fetal outcomes of patients receiving mAbs therapy during pregnancy.

MATERIAL and METHODS

The study comprised a retrospective analysis of 21 pregnancies receiving mAbs therapy that were followed-up and delivered in the Obstetrics and Gynecology Department of the İstanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty between 2018 and 2022. The study received approval from the local Ethical Committee (protocol number: E-83045809-604.01-960883). During the follow-up of these pregnancies, full cooperation was established with the relevant departments, including gastroenterology and rheumatology.

At the time of the first antenatal visit, the following parameters were recorded: age, parity, co-existing systemic disease, duration of disease, and drugs administered. The gestational age of the pregnancies was estimated by utilizing the precise date of the last menstrual cycle and using ultrasonographic measurement of the crown-rump length during the first trimester. The frequency of consultations with relevant departments and the schedule of obstetric visits were individualized for each patient. All fetuses were examined for anatomical screening. Between 24 and 28 weeks of pregnancy, 50 g of oral glucose was used to screen for gestational diabetes mellitus. Depending on

gestational status, cardiotocography, a modified biophysical profile, or Doppler ultrasonography was performed weekly or biweekly to assess fetal well-being.

Maternal and perinatal outcomes were analyzed. Maternal outcomes studied were frequency of cesarean section, the incidences of gestational hypertension, preeclampsia and gestational diabetes mellitus. Perinatal outcomes studied were duration of gestation, birth weight, incidence of stillbirth, neonatal death, preterm birth, fetal growth restriction, and congenital anomalies. Drug exposure during pregnancy was classified as continuous exposure throughout all trimesters, discontinuation in the first trimester, or discontinuation in the third trimester. mAbs drugs were classified into three groups based on their mechanism:Anti-TNF α, anti-cytokine, and anti-B cell agents and additional medications used by patients were documented. Patients affected by more than one autoimmune or inflammatory disease were recorded.

The data were processed with Statistical Package for Social Sciences software version 25.0 for Windows (SPSS Inc., Chicago, USA). Categorical data were presented as frequencies and percentages, whereas mean and standard deviation were given for continuous variables. The categorical data were analyzed using non-parametric statistical tests, including the Kruskal-Wallis, Mann-Whitney U, and chi-square tests, if applicable. Continuous data were analyzed using relevant statistical tests such as one-way ANOVA, Student's t-test, and paired sample t-test. The Pearson's rank correlation was calculated to evaluate the association between the duration of the disease and the gestational age at delivery and birth weight ($p< 0.05$).

RESULTS

The clinical features and drug exposure of pregnancies with receiving mAbs therapy are listed in Table I. The mean maternal age was 30.5±4.6 and the rates of nulliparity and history of miscarriages were 52.4%, 23.8% respectively. The mean duration of disease was 7.05±4.3 years and all pregnancies were in clinical remission for more than six months. The most common type of underlying disease was Familial Mediterranean Fever (FMF) (28.5%). In the study group, 5 (23.8%), 4 (19%), 4 (19%) and 3 (14.2%) of the pregnancies were affected by ulcerative colitis, ankylosing spondylitis, rheumatoid arthritis and Crohn disease respectively. The frequency of pregnancies affected by more than one autoimmune or inflammatory disease was 33.3%. Anti-TNF α, anti-cytokine, and anti-B cell agents were used in 13 (61.9%), 6 (28.6%) and 2 (9.5%) of pregnancies receiving mAbs therapy, respectively. Certolizimuab pegol and Anakinra were the most frequently administered anti-TNF α, and anti-cytokine agents in this study. The rate of drug exposure over all trimesters was 52.4%, and the rate of drug discontinuation in the first trimester was 47.6% in our study group.

Table I. The clinical features and drug exposure of pregnancies with receiving mAbs therapy.

N	21	
Age (years)	30.5±4.6	
Duration of disease (years)	7.05±4.3	
Nulliparity	n	%
	11	52.4
History of miscarriages	5	23.8
Type of disease		
FMF	6	28.5
Ulcerative colitis	5	23.8
Ankylosing spondylitis	4	19
Rheumatoid arthritis	4	19
Crohn disease	3	14.2
Other	6	28.5
Behçet disease	2	9.5
Wegener's granulomatosis	1	4.7
Adult-onset Still's disease	1	4.7
Juvenile rheumatoid arthritis	1	4.7
Vasculitis	1	4.7
Several autoimmune or inflammatory disease	7	33.3
Exposure of mAbs during pregnancy		
All trimester	4	19
Discontinued drugs in the first trimester	11	52.4
Discontinued drugs in the third trimester	10	47.6
mAbs therapy		
Anti-TNF α	13	61.9
Certolizumab pegol	9/13	69.2
Infliximab	2/13	15.3
Adalimumab	1/13	7.6
Golimumab	1/13	7.6
Anticytokine	6	28.6
Anakinra	4/6	66.6
Canakinumab	2/6	33.3
Anti-B cell	2	9.5
Rituximab	2/2	100
Use of glucocorticoids	8	38.1
Use the combination of mAbs and thiopurine	3	14.2
Co-existing disease		
Chronic kidney disease	1	4.7
Maternal morbidity	1	4.7

Data are expressed as mean ± standard deviation; n, % where appropriate.
mAbs, monoclonal antibody biologics; FMF, Familial Mediterranean Fever; TNF, Tumor necrosis factor

Glucocorticoids and thiopurines were used by 38.1% and 14.2% of pregnancies, respectively. We observed no disease activation during pregnancy in pregnancies with receiving mAbs therapy. Only one patient using Anakinra during pregnancy for Adult-onset Still Disease was admitted to the intensive care unit on the seventh postpartum day with a prediagnosis of macrophage activation syndrome and sepsis. The obstetric outcomes of pregnancies with receiving mAbs therapy are illustrated in Table II. The mean gestational age at delivery was 38±1.2 weeks, and mean birth weight was 3083±416 g in the study group. Deliveries ≤37 gestational weeks were detected in 9.5% of the pregnancies, and no births were observed before 34 weeks. The incidences of fetal growth restriction, gestational diabetes, gestational hypertension during pregnancy of the study population were 9.5%, 33.1% and 4.7%, respectively. The frequency of livebirth was 100% and 23.8% of newborns were admitted to the NICU in our study group. There was no neonatal death and con-

genital anomaly in the newborns. The clinical characteristics and obstetric outcomes of 21 pregnancies treated with mAbs therapy are summarized in Table III. The obstetric outcomes of pregnancies according to the use of corticosteroids and thiopurines, period of drug exposure and having been affected by more than one autoimmune or inflammatory diseases are shown in Table IV. The obstetric outcomes of mean gestational age, fetal growth restriction, gestational diabetes, and NICU admission were not significantly different between use of glucocorticoids and non users. Fetal growth restriction, preterm birth and NICU admission were significantly higher in patients with multiple autoimmune or inflammatory diseases compared with those without ($p < 0.05$). There was no correlation between duration of disease and mean gestational age at delivery (Pearson's $r = -0.3$, $p = 0.186$) and mean birth weight (Pearson's $r = -0.05$, $p = 0.984$).

Table II. The obstetric outcomes of pregnancies with receiving mAbs therapy.

N	21	
Birth weight (gram)	38±1.2	
Gestational age at delivery (weeks)	3083±416	
	n	%
Preterm birth ≤ 37 weeks ≤34 weeks	 2 -	 9.5 -
Fetal growth restriction	2	9.5
Preeclampsia	-	-
Gestational hypertension	1	4.8
Gestational diabetes	7	33.3
Cesarean section rate	19	90.5
Neonatal Intensive Care Unit admission	5	23.8
Live birth	21	100
Perinatal mortality	-	-

Data are expressed as mean ± standard deviation; n, % where appropriate.
mAbs, monoclonal antibody biologics

The obstetric outcomes of pregnancies based on the subgroups of mAbs therapy are demonstrated in Table V. The obstetric outcomes of mean gestational age, fetal growth restriction, gestational diabetes, gestational hypertension and NICU admission were not significantly different among anti-TNF α, anti-cytokine, and anti-B cell treatments.

Table III. The clinical characteristics and obstetric outcomes of 21 pregnancies treated with mAbs therapy.

Patient	Age (years)	Gravida n	Misscarriage n	Disease	Duration of disease (years)	Medication	mAbs exposure	Maternal outcomes	Gestational age at delivery (weeks, days)	Perinatal outcomes
1	29	1	-	Ulcerative colitis	6	Mesalazine, Azathioprine, Prednisolone, Adalimumab	All trimesters	-	39	-
2	27	1	-	Ulcerative colitis	1	Mesalazine, Methylprednisolone, Infliximab	Discontinued in first trimester, continued second and third trimester	-	39	-
3	33	2	1	Rheumatoid arthritis	3	Certolizumab pegol	All trimesters	GDM	38,4	-
4	33	2	1	FMF,Ankylosing spondylitis	10	Colchicine, Prednisolone, Certolizumab pegol	Continued between 12 and 24 gestation weeks	-	35,2	Preterm delivery, PPROM, NICU admission
5	39	1	-	Rheumatoid arthritis	11	Certolizumab pegol	Discontinued in first trimester, continued second and third trimester	GDM	37	-
6	31	5	-	Ulcerative colitis, celiac disease	6	Mesalazine, Azathioprine, Methylprednisolone, Certolizumab pegol	All trimesters	GDM	35	Preterm delivery, FGR, NICU admission
7	32	2	-	Wegener's granulomatosis	8	Rituximab	Continued between 12 and 24 gestation weeks	-	37	Fetal distress, NICU admission
8	29	1	-	FMF, vasculitis, chronic kidney disease	5	Colchicine, Anakinra	All trimesters	GHT	38,3	-
9	41	3	-	Rheumatoid arthritis	10	Leflunomide, Golimumab	Discontinued leflunomide in early first	GDM	38	-

Table III. Devamı

							trimester, Discontinued golimumab in first trimester, continued second and thirdh trimester			
10	36	3	1	Neuro-Behçet disease	10	Prednisolone, Certolizumab pegol	Discontinued in first trimester, continued second and thirdh trimester	-	38,3	-
11	25	1	-	Crohn disease	4	Certolizumab pegol	Discontinued in first trimester, continued second and thirdh trimester	-	40,4	-
12	30	3	1	Ulcerative colitis, Ankylosing spondylitis	11	Mesalazine, Certolizumab pegol	All trimesters	-	37,6	NICU admission (tachypnea)
13	33	1	-	FMF, Ankylosing spondylitis	7	Anakinra	All trimesters	-	39	-
14	36	2	1	Rheumatoid arthritis	8	Rituximab, Methylprednisolone	Continued between 12 and 24 gestation weeks	GDM	39	-
15	30	2	-	FMF	20	Colchicine, Anakinra	Continued between 12 and 24 gestation weeks	-	38,4	-
16	29	2	-	Ankylosing spondylitis	6	Certolizumab pegol	All trimesters	-	38,1	-
17	24	2	-	Crohn disease,Behçet disease, Juvenile rheumatoid arthritis	4	Certolizumab pegol, Methylprednisolone	All trimesters	-	38,5	FGR, NICU admission
18	28	2	-	Crohn disease	2	Azathioprine, Infliximab	Discontinued in first trimester, continued second and third trimester	-	37,6	-
19	24	1	-	FMF, Ulcerative colitis	5	Colchicine, Canakinumab	All trimesters	-	38,6	-
20	25	2	-	Adult-onset Still's disease	1	Anakinra, Methylprednisolone	All trimesters	GDM, She was admitted to the intensive care unit on the fourth postoperative day with the initial diagnoses of sepsis and macrophage activation syndrome.	38,3	-
21	28	1	-	FMF	10	Colchicine, Canakinumab	All trimesters	GDM	39	-

mAbs, monoclonal antibody biologics; GDM, gestational diabetes mellitus; GHT, gestational hypertension; NICU, neonatal intensive care admission; FGR, fetal growth restriction; FMF, Familial Mediterranean Fever

DISCUSSION

In recent years, biologics have been prescribed for disease remission during pregnancy (2). This study demonstrates that the maternal and fetal outcomes of pregnancies in women who received mAbs therapy were comparable to those of the general population. The mean maternal age and duration of disease in our study population were 30.5 and 7, respectively. In a recent multicenter PIANO study (Pregnancy and Neonatal Outcomes after Fetal Exposure To Biologics and Thiopurines among Women with Inflammatory Bowel Disease), involving pregnancy outcomes in women receiving mAbs therapy, mean maternal age and duration of disease were reported as 31.8 and 8.7, respectively (8). Anti-TNF α drugs are well-known among biologic agents and are most commonly administered during pregnancy (9). Similarly, 62.9% of patients were receiving Anti-TNF α medication in our study group were receiving anti-TNF medication. Many biologic drugs that target TNF-a have been developed such as certolizumab pegol, adalimumab, infiliximab and golimumab, which are essential therapeutics for patients whose condition is uncontrolled by initial treatments, mostly 5ASA, steroids, and immunosuppressants (9). According to a large cohort study (the EVASION study) of pregnancies with inflammatory bowel disease who were exposed to anti-TNF α, 14.1% of births occurred between 24 and 37 weeks of

Table IV. The obstetric outcomes of pregnancies with receiving mAbs therapy according to the use of glucocorticoids and thiopurines, period of drug exposure and having affected from more than one autoimmune or inflammatory diseases

	Use of glucocorticoids				p	Use of thiopurines				p	Drug exposure				p	Affected from more than one autoimmune or inflammatory diseases				p
	yes		no			yes		no			All trimesters		Discontinued drugs in the first trimester			yes		no		
N	8		13			3		18			11		10			7		14		
Birth weight (gram)	3050±565		3103±318		0.782	2996±775		3102±361		0.613	3061±493		3107±337		0.807	2855±498		3197±332		0.075
Gestational age at delivery (weeks)	37.7±1.6		38.2±0.9		0.411	37.2±2		38.2±1		0.193	38.1±1.1		37.9±1.4		0.758	37.4±1.6		38.3±0.8		0.106
	n	%	n	%		n	%	n	%		n	%	n	%		n	%	n	%	
Preterm birth	2/8	25	-	-	0.062	1/3	33.3	1/18	5.5	0.143	1/11	9	1/10	10	0.947	2/7	28.5	-	-	**0.036**
Fetal growth restriction	2/8,	25	-	-	0.062	1/3	33.3	1/18	5.5	0.143	2/11	18.1	-	-	0.172	2/7	28.5	-	-	**0.036**
Gestational diabetes	3/8	37.5	4/13	30.7	0.765	1/3	33.3	6/18	33.2	1	4/11	36.3	3/10	33.3	0.772	1/7	14.2	6/14	42.8	0.209
Neonatal Intensive Care Unit admission	3/8	37.5	2/13	15.3	0.270	1/3	33.3	4/18	22.2	0.694	3/11	27.2	2/10	20	0.713	4/7	57.1	1/14	7.1	**0.009**

Data are expressed as mean ± standard deviation; n, % where appropriate. mAbs, monoclonal antibody biologics

Table V. The obstetric outcomes of pregnancies based on the subgroups of mAbs therapy.

	Anti-TNF α		Anticytokine		Anti-B cell		p
N	13		6		2		
Birth weight (gram)	3052±463		3153±358		3075±459		0.896
Gestational age at delivery (weeks)	37.8±1.4		38.6±0.3		38±1.4		0.5
	n	%	n	%	n	%	
Preterm birth	2/13	15.3	-	-	-	-	0.547
Fetal growth restriction	2/13	15.3	-	-	-	-	0.547
Gestational diabetes	4/13	30.7	2/6	33.3	1/2	50	0.883
Neonatal Intensive Care Unit admission	4/13	30.7	-	-	1/2	50	0.252

Data are expressed as mean ± standard deviation; n, % where appropriate. mAbs, monoclonal antibody biologics

gestation (10). In the same study, a congenital anomaly was detected during pregnancy in 1 of 1457 pregnancies, and this number increased to 49 (6.3 %) after one year of monitoring, and this rate was similar to pregnancies not exposed to mAbs treatment (10). In our study, deliveries ≤37 gestational weeks were detected in 15.3% of the pregnancies using anti-TNF α agents and no births were observed before 34 weeks. Prenatally and during the first 28 days of life, no anomalies were detected. This may be due in part to the small sample size of our study. In the meta-analysis that reported pregnancy and neonatal complications of women using anti-TNF α agents during pregnancy, showed significantly increased risks of preterm birth (OR=2.62, 95% CI= 2.12-3.23 and low birth weight (OR= 5.95, 95% CI=1.17-30.38) compared to the general population, but had comparable outcomes with non-users (5). In our study, the mean gestational week and birth weight for anti-TNF α users were 3052±463 and 37.8±1.4, and frequency of fetal growth restriction was 15.3%.

Another commonly used among mAbs drugs is anakinra, which blocks interleukin 1 (IL-1) and is often used in colchicine-resistant FMF during pregnancy (4). Similarly, in our study, FMF was the most common diagnosis among pregnancies using anakinra (3/4, 75%). Anakinra treatment during pregnancy does not lead to an increased risk of congenital anomalies or miscarriage, according to the information presented at a meeting of the European League Against Rheumatism (EULAR) (4). Although there are reports indicating that the use of anakinra in the early first trimester may be associated with miscarriage and renal agenesis, our study revealed no congenital anomalies in the offspring of three pregnancies in which the drug was used without interruption during pregnancy (4). A systematic review about blocking the IL-1 system in pregnancy revealed that the rate of preterm birth was 17.4% for pregnancies with receiving anakinra (11). Canakinumab, a less frequently used IL-1-blocking drug than anakinra, has limited data, but over 90% of term births have been reported (11). Preterm birth, congenital anomalies, and neonatal intensive care admission were not observed in six pregnancies treated with anakinra and canakinumab in our study. Rituximab, which promotes targeted CD20+ B cell depletion, was another mAbs therapy used in our study. In a study of 19 women who received rituximab during their pregnancies, the incidences of preterm birth and low birth weight were reported to be 10% and 10%, respectively (12). Multiple haemangiomas, bilateral hip dysplasia, and a laryngeal cleft were observed in the same case series (12). At the EULAR meeting, it was emphasized that rituximab does not increase the incidence of congenital anomalies; however, anatomical screening should be performed on fetuses, and B-cell depletion may occur in the fetus when rituximab is administered in the third trimester (4). In our study, two women received rituximab between 12 and 24 weeks of pregnancy and no preterm birth or congenital anomalies were observed.

The current consensus opinion about the ideal time for conception is 6 months after clinical remission in autoimmune and inflammatory diseases, and the continuation of mAbs therapy during pregnancy is critical for maintaining remission (1, 3, 4). In our study group, all pregnancies were in clinical remission before conception and 52.4% of the pregnancies continued to use mAbs therapy in all trimesters. 47.6% and 19% of pregnancies discontinued using drug in the first trimester and third trimester in our study group, respectively. Although there was no correlation between duration of drug use and obstetric outcomes, patients with multiple autoimmune or inflammatory diseases who were currently in remission reported a higher rate of fetal growth restriction, premature birth, and NICU admission. Glucocorticoids are safe to use during pregnancy; however, there is an increased incidence for gestational diabetes and pregnancy-induced hypertension (13). We observed gestational diabetes in 33.3% of pregnancies and there is no association with use of glucocorticoids. A number of adverse effects, such as gestational hypertension and gestational diabetes mellitus, have been associated with elevated TNF α levels (14, 15). Increased TNF α levels in complicated pregnancies may cause differentiation in trophoblast biology, particularly migratory activity, syncytialization, and in endocrine function (16, 17). Furthermore, increased TNF α levels may alter the maternal-fetal relationship by altering the secretory profile of placental immunomodulatory substances, which affects maternal immune cells (17). The excessive release of cytokines and chemokines in syncytiotrophoblasts may be caused by chronic inflammatory rheumatic and gastroenterological diseases that release inflammatory and immunomodulatory factors (17). Elevated TNF α levels have been shown to be associated with preeclampsia, and increasing data indicates that metabolic/pro-inflammatory cytokines can regulate early placental growth and activities during the first trimester of pregnancy (18, 19). In our study, there was no pregnancy with complicated preeclampsia. Although it is not possible to declare that mAbs medications, particularly anti-TNF α, prevent preeclampsia at this time, it is reasonable given the pathophysiological basis. More research, including in healthy populations, is needed on the use of mAbs drugs in preeclampsia, which is a major cause of maternal and fetal mortality and morbidity.

CONCLUSION

Clinical remission of the disease is the most critical factor determining obstetric outcomes in pregnancies receiving mAbs therapy. Although there is no increase in adverse obstetric outcomes in these pregnancies, multidisciplinary follow-up is recommended. Multiple autoimmune or inflammatory diseases may be associated with increasing adverse obstetric outcomes in pregnancies.

Ethics Committee Approval

This research complies with all the relevant national regulations, institutional policies and is in accordance the tenets of the Helsinki Declaration, and has been approved by the Cerrahpaşa Medical Faculty Ethical Committee, İstanbul University-Cerrahpaşa (E-83045809-604.01-960883)

Author Contributions

Concept – D.K., R.M.; Design – D.K., E.A.D.; Supervision – R.M., S.U, M.V.; Resources – D.K., A.F.Ş., E.A.D., S.U., R.M., M.V.; Materials - D.K., A.F.Ş., E.A.D.; Data Collection and/ or Processing - D.K., A.F.Ş., E.A.D.; Analysis and/ or Interpretation - D.K., A.F.Ş., E.A.D., S.U., R.M.; Literature search - D.K., E.A.D.; Writing Manuscript - D.K., R.M.; Critical Review - D.K., R.M.

Conflict of Interest

Authors declare that they have no conflict of interest.

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