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RESEARCH

Anti-parietal cell antibody positivity in women with poor obstetric history and skin disorders: significance of preconception counseling

Kötü obstetrik öyküsü ve deri hastalıkları olan kadınlarda anti-parietal hücre antikor pozitifliği: gebelik öncesi danışmanlığın önemi

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Abstract

Purpose: The aim of this study was vto demonstrate the impact of anti-parietal cell antibody (APCA) positivity in women with poor obstetric history and skin disorders.
Materials and Methods: This retrospective cohort consisted of 63 women having skin disorders and poor obstetric history. Patients were grouped into the control (women with skin disorders only, n=50) and study groups (women with skin disorders and APCA positivity, n=13). The study groups were compared in terms of demographic findings, BOI, and risk factors for placenta-related obstetric complications.
Results: APCA (+) and APCA (–) groups showed no statistically significant difference in terms of demographic findings such as age, gravidity, parity, BOI, and the number of miscarriages.. We have demonstrated that 69.2% (9/13) of the APCA (+) cases have two or more skin diseases, while 34% of APCA (-) women have multiple skin diseases. There was a statistically significant difference between APCA (+) and APCA (–) groups in terms of the presence of single or multiple skin diseases (p=0.029). We could not demonstrate a statistically significant difference between APCA (+) and APCA (–) patients in terms of the presence of risk factors for obstetric complications such as immune system problems, *MTHFR* polymorphisms, hereditary thrombophilia, and diabetes mellitus type-2.
Conclusion: APCA positivity which is a risk factor for obstetric complications might be a good indicator used to identify susceptibility to multiple skin disorders during preconception counseling.
Keywords: Anti-parietal cell antibody, skin disorders, poor obstetric history, preconception counseling

Öz

Amaç: BU çalışmanın amacı kötü obstetrik öyküsü ve deri hastalıkları olan kadınlarda anti-parietal hücre antikor (APCA) pozitifliğinin anlamını göstermektir.
Gereç ve Yöntem: Bu retrospektif kohort, deri hastalıkları ve kötü obstetrik geçmişi olan 63 kadından oluşuyordu. Hastalar kontrol (sadece deri hastalıkları olan kadınlar, n=50) ve çalışma grubu (deri hastalıkları ve APCA pozitifliği olan kadınlar, n=13) olarak gruplandırılmıştır. Çalışma ve kontrol grubu demografik bulgular, BOI ve plasentaya bağlı obstetrik komplikasyonlarla ilişkili risk faktörleri açısından karşılaştırıldı.
Bulgular: APCA (+) ve APCA (–) grupları; yaş, gravida, parite, BOI ve düşük sayısı gibi demografik bulgular açısından istatistiksel olarak anlamlı farklılık göstermedi. APCA (+) vakaların %69,2'sinin (9/13) iki veya daha fazla deri hastalığına sahip olduğunu, ancak bu oranın APCA (-) olanlarda %34 bulunduğunu gösterdik. APCA (+) ve APCA (–) grupları arasında tekli ve çoklu deri hastalığı varlığı açısından istatistiksel olarak anlamlı fark vardı. APCA (+) ve APCA (-) hastalar arasında obstetrik komplikasyonlarla ilişkili risk faktörlerinin (bağışıklık sistemi sorunları, *MTHFR* polimorfizmleri, kalıtsal trombofili ve diyabetes mellitus tip-2 gibi) varlığı açısından istatistiksel olarak anlamlı bir farklılık gösteremedik.
Sonuç: Obstetrik komplikasyonlar için risk faktörü olan APCA pozitifliğinin, gebelik öncesi danışma sırasında belirlenmesi, kötü obstetrik öykü ve dermatolojik sorunları olan hastalarda çoklu deri hastalıklarının önceden belirlenmesinde önemli rol oynayabilir.

Anahtar kelimeler: Anti-parietal hücre antikoru, deri hastalıkları, kötü obstetrik öykü, gebelik öncesi danışmanlık

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INTRODUCTION

The skin is sensitive to allergic reactions, internal organ problems, metabolic changes/disorders, immune system problems, inflammation, paraneoplastic syndromes, bacterial/viral infections, and epigenetic disorders[1-4]. Some skin disorders are particularly associated with immune system problems, autoimmune antibody positivity, and folate/vitamin B12 metabolism disorders[1-4]. Anti-parietal cell antibody (APCA) is an autoimmune antibody that may affect folate/vitamin B12 metabolism associated with health problems such as skin disorders[5,6]. Furthermore, serum APCA level is prevalent in patients with atrophic gastritis (AAG), pernicious anemia (PA), type-1 diabetes mellitus, autoimmune thyroid diseases, vitiligo, immune system-related skin disorders, and celiac disease[1,2,4]. Thus, people with autoimmune problems (autoimmune diseases and chronic inflammatory diseases) and skin disorders should be closely screened for APCA and other autoimmune antibodies[5-7].

Autoimmune diseases and autoimmune antibody positivities such as APCA were commonly investigated for possible etiologic factors for obstetric complications, such as miscarriage, fetal growth restriction preterm birth, and stillbirth[6-13]. It has also been shown that some skin disorders go together with immune system-related gestational problems[1,14]. According to Lorini et al, autoantibodies were more prevalent in vitiligo patients, particularly APCA.[15] In addition, APCA was found higher in Indians with alopecia areata.[16] Thus, the heterogeneous clinical presentation of skin disorders and overlap of the autoimmune disorders make autoantibodies possible risk factors for obstetric complications[1,6-9,14]. At this point, APCA should be the concern of investigators searching for autoimmune disorders associated with skin disorders and obstetric complications. APCA positivity which is a risk factor for obstetric complications might be a good indicator used to identify susceptibility to multiple skin disorders during preconception counseling.

In this study, we tried to demonstrate the impact of APCA positivity among women with a history of poor obstetric outcomes and skin disorders.

MATERIALS AND METHODS

Sample

This retrospective cohort consisted of 63 women having skin disorders and poor obstetric history. Patients were grouped into the control group (women with skin disorders only, n=50) and the study group (women with skin disorders and APCA positivity n=13). All patients were admitted to preconception counseling between January 2016 to January 2020. The study was approved by the Local Ethics Committee of Hacettepe University (Nov 2019, GO19/1064). This study was conducted according to the Helsinki Declaration.

Procedure

Skin diseases (ICD-10-CM Diagnosis Code I10) were assessed in patients by a dermatologist (BB) as infections (viral, bacterial, fungal diseases), autoimmune diseases (psoriasis vulgaris), acneiform diseases, dermatitis, hypertrophic disorders of the skin, hair, and nail problems, hyperpigmentation, lichen planus, and vitiligo.

Poor obstetric history defines a woman who had problems in previous pregnancies such as miscarriage, fetal growth restriction, preterm birth, preeclampsia, and stillbirth. In the context of a pre-pregnancy care program managed by obstetricians (MSB and MC), patients with skin diseases were checked and assessed for the existence of APCA positivity. Necessary laboratory tests (CBC, biochemical tests, etc.) were performed together with the physical/obstetric examinations. Vitamin B12, folate, homocysteine, autoimmune antibodies (anti-smooth muscle antibody=ASMA, anti-parietal cell antibody=APCA, anti-thyroglobulin, anti-TPO), biochemical tests, blood count, factor V Leiden mutation, G20210A mutation in the prothrombin gene, C677T and A1298C homozygous mutations in *MTHFR* gene, etc. were performed. Beksac Obstetric Index (BOI) was used to assess the patient's obstetric history by following the formula: (number of living child + π/10)/Gravida).

Demographical and clinical findings, BOIp, and risk factors for placenta-related obstetric complications were compared. Placenta-related risk factors for obstetric complications were defined as factor V Leiden mutation, prothrombin gene mutation (G20210A), B12/folate deficiencies,

hyperhomocysteinemia, C677T and A1298C homozygous mutations in *MTHFR* gene, immune system problems including autoimmune diseases (systemic lupus erythematosus, Sjogren's disease, and antiphospholipid syndrome) and chronic inflammatory diseases (Celiac Disease, Crohn's Disease, Ulcerative Colitis, Takayasu's arteritis, Behcet's Disease, etc.).

Statistical analysis

Power analysis was performed for the two independent group model (t- test) model using the G*Power 3.1 program. Effect size d=0.88, type I error α=0.05 and type II error β=0.20 (power of the test 0.80), the total sample size was 64 for the two groups (APCA (–) and APCA (+)), however due to missing data this retrospective cohort consisted of 63 women having both skin disorders and poor obstetric history.

Statistical Package for the Social Sciences (SPSS, version 23, IBM, Chicago, USA) was used for statistical analysis. The Shapiro-Wilk test was used to analyze the normality of numerical data. Non-parametric Mann-Whitney U test was used for the comparison of maternal age, gravidity, parity, BOIp, and the number of miscarriages. Yates' Chi-square and Fisher's exact tests were used to compare APCA positivity with skin diseases (multiple vs. single) and with the presence of risk factors for obstetric complications (Immune system problems, *MTHFR* polymorphisms, Hereditary thrombophilia, and Diabetes Mellitus Type-2). A p-value less than 0.05 is statistically significant.

RESULTS

This retrospective cohort consisted of 63 women having skin disorders and poor obstetric history. Fifty women (79.4%) have only skin disorders without APCA positivity, however, 13 (20.6%) women with both skin disorders and APCA positivity. Demographic features and clinical characteristics are in Table 1. APCA (+) and APCA (–) groups showed no statistically significant difference in terms of demographic findings such as age, gravidity, parity, BOI, and the number of miscarriages (p>0.05 for all).

Table 1. The demographic and clinical characteristics of the patients

	APCA (-) n=50	APCA (+) n=13	Total n=63	*p*
Age	33.38±4.71	34.76±4.62	33.66±4.69	0.311
Gravidity	3.64±1.94	3.38±1.60	3.58±1.87	0.618
Parity	1.52±0.86	1.53±1.12	1.52±0.91	0.920
BOIp	0.39±0.33	0.44±0.32	0.40±0.32	0.545
Miscarriage numbers	1.30±1.55	1.08±1.18	1.25±1.48	0.852

BOIp: Beksac Obstetric Index during pregnancy, SD: Standard deviation, Mann-Whitney U test, p>0.05, *Mean±SD*

We have demonstrated that 69.2% (9/13) of the APCA (+) cases have two or more skin diseases, however, 30.8% of women have only one skin disease (Table 2). There was a statistically significant difference between APCA (+) and APCA (–) groups in terms of the presence of single and multiple skin diseases (p=0.029). Detailed frequencies of skin diseases in APCA (+) women are given in Table 3.

Table 4 indicates the comparison of APCA (+) and APCA (–) patients in terms of the presence of risk factors for obstetric complications. Immune system problems, *MTHFR* polymorphisms, hereditary thrombophilia, and diabetes mellitus type-2 showed similar rates. There was no statistically significant difference between groups (p>0.05 for all).

Table 2. Frequencies of APCA positivity in single and multiple skin diseases

Skin diseases	APCA (-)	APCA (+)	Total	*p*
Single	33 (66)	4 (30.8)	37 (58.7)	0.029*
Multiple	17 (34)	9 (69.2)	26 (41.3)	
Total	50 (100)	13 (100)	63 (100)	

APCA: Antiparietal cell antibody, Fisher's exact test, *:p<0.05

Table 3. Frequencies of skin diseases in APCA (+) patients

Frequencies of skin diseases	APCA (+), n (%)
Single skin disease (n=4, 30.8%)	
Vitiligo	1 (7.7)
Dermatitis	1 (7.7)
Urticaria	2 (15.4)
Multiple skin diseases (n=9, 69.2%)	
Acneiform diseases, dermatitis	2 (15.4)
Hypertrophic disorders of the skin, fungal disease, Hidradenitis suppurativa	1 (7.7)
Viral warts, melanocytic nevi, hair and nail problems	1 (7.7)
Hypertrophic disorders of the skin, melanocytic nevi, dermatitis	1 (7.7)
Urticaria, hypertrophic disorders of the skin	1 (7.7)
Urticaria, dermatitis, acneiform diseases, hypertrophic disorders of the skin, psoriasis	1 (7.7)
Dermatitis, psoriasis	1 (7.7)
Hypertrophic disorders of the skin, hair and nail problems	1 (7.7)
Total	13 (100)

APCA: Antiparietal cell antibody

Table 4. Presence of risk factors for obstetric complications and APCA positivity.

	APCA (-) n (%)	APCA (+) n (%)	Total n (%)	*p*
Immune system problems (+)	11 (22)	3 (23.1)	14 (22.2)	1.000
MTHFR polymorphisms (+)	16 (32)	6 (46.2)	22 (34.9)	0.350
Hereditary thrombophilia (+)	11 (22)	0 (0)	11 (17.5)	0.100
Diabetes Mellitus Type-2 (+)	13 (26)	2 (15.4)	15 (23.8)	0.716

MTHFR: Methylenetetrahydrofolate reductase, APCA: Antiparietal cell antibody, Fisher's exact test, $p>0.05$

DISCUSSION

Autoimmune antibody positivity is a risk factor for both skin disorders and obstetric complications[1,3,14]. APCA positivity is a risk factor for poor gestational outcome[6]. Moreover, APCA is prevalent in the serum of patients with AAG, PA, diabetes mellitus, and some chronic inflammatory diseases[1,4,17]. However, there is a lack of information about the relationship between APCA and skin diseases.[15,16] In this study, we have demonstrated that APCA positivity is a risk factor for the presence of multiple skin disorders in women with dermatological problems and poor obstetric history. Thus, the presence of various types of skin disorders or the history of the presence of repeated skin disorders should be the concern of perinatologists in the pre-pregnancy evaluations of women with poor obstetric histories, because awareness of skin disorders among patients is much more prevalent compared to health problems which necessitate complicated diagnostic tests.

Some skin disorders are particularly associated with immune system problems and folate/vitamin B12 metabolism disorders[1-4]. APCA is an autoimmune antibody which has an impact on folate/vitamin B12 metabolism associated with health problems including some skin disorders[5,6]. Thus, the interaction of skin disorders and obstetric complications is also something expected in perinatology practice. In this study, we have demonstrated that APCA positivity is a risk factor for the presence of multiple skin disorders in women with poor obstetric history.

In this study, we could not demonstrate a statistically significant difference between APCA (+) and APCA (–) patients in terms of the presence of risk factors for obstetric complications such as immune system problems, *MTHFR* polymorphisms, hereditary thrombophilia, and diabetes mellitus type-2 most probably due to the patient characteristics of the study population. The population was composed of APCA (+) or APCA (–) women with poor obstetric history and skin disorders. APCA (+) and APCA (–) patients showed no statistically significant difference in terms of gravidity, parity, BOI, and the number of miscarriages. This setup was one of the advantages of this study.

The main limitation of this study is the number of patients. This is the reason why we could not demonstrate the specific skin disorders which

participate in the negative interaction of skin pathophysiology, APCA positivity, and poor obstetric outcome. However, it is difficult to find a patient population having both skin disorders and a history of poor obstetric outcomes to evaluate the impact of APCA positivity on these health issues.

In conclusion, the relationship between APCA and skin diseases has not been fully revealed. However, APCA positivity which is a risk factor for obstetric complications might be a good indicator used to identify susceptibility to multiple skin disorders during preconception counseling.

Yazar Katkıları: Çalışma konsepti/Tasarımı: BB, MSB; Veri toplama: HGD, MC; Veri analizi ve yorumlama: BB, HGD, MC; Yazı taslağı: BB, HGD, MSB; İçeriğin eleştirel incelenmesi: MSB; Son onay ve sorumluluk: BB, HGD, MC, MSB; Teknik ve malzeme desteği: -; Süpervizyon: MSB; Fon sağlama (mevcut ise): yok.
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