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RESEARCH

Clinical and immunological factors influencing the onset and course of partial remission in pediatric type 1 diabetes

Pediatrik tip 1 diyabette kısmi remisyonun başlangıcını ve seyrini etkileyen klinik ve immünolojik faktörler

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Abstract

Purpose: This study examined key clinical and immunological factors influencing the onset and course of partial remission (PR) in children and adolescents with newly diagnosed type 1 diabetes(T1D).
Materials and Methods: A total of 201 pediatric patients with T1D were enrolled. PR was defined as an insulin dose-adjusted HbA1c(IDAA1c) of≤9. Participants were categorized into two groups: PR and NR (non-remission).
Results: Partial remission occurred in 138 (69%) patients. In the PR group, the mean age at diagnosis was 9.4 ± 3.8 years, with PR onset occurring 1.6 ± 1.4 months after diagnosis and lasting for a mean duration of 7.3 ± 5.2 months. Overweight/obesity was strongly associated with PR, as 81% of overweight/obese patients achieved remission. Anti-glutamic acid decarboxylase (anti-GAD) antibody positivity was more frequent in the PR group (63.0% vs. 33.3%). Longer remission was seen in patients with puberty, overweight/obesity, or coeliac disease, whereas positivity for anti-GAD and islet cell antibodies was associated with shorter remission.
Conclusion: Anti-GAD and ICA antibodies have distinct effects on PR, reflecting the complexity of autoimmune activity in pediatric T1D. The presence of obesity, puberty, and celiac disorder supports the need for a immuno-metabolic strategy for the early prediction and management of PR in pediatric T1D.

Keywords:. partial remission; anti-glutamic acid decarboxylase antibody; islet cell antibody

Öz

Amaç: Bu çalışmada yeni tanı konmuş tip 1 diyabetli (T1D) çocuk ve ergenlerde parsiyel remisyonun (PR) başlangıcını ve seyrini şekillendiren klinik ve immünolojik faktörleri incelenmiştir.
Gereç ve Yöntem: Çalışmaya T1D tanısı almış toplam 201 pediatrik hasta dahil edildi. PR, insülin dozu ile ayarlanmış HbA1c (IDAA1c) ≤9 olarak tanımlandı. Katılımcılar parsiyel remisyon yaşayanlar (PR grubu) ve remisyon yaşamayanlar (NR grubu) olmak üzere iki gruba ayrıldı.
Bulgular: Parsiyel remisyon 138 (%69) hastada gözlendi. PR grubunda tanı anındaki ortalama yaş 9,4 ± 3,8 yıl olup, remisyon başlangıcı tanıdan ortalama 1,6 ± 1,4 ay sonra gerçekleşmiş ve ortalama 7,3 ± 5,2 ay sürmüştür. Fazla kilolu/obez olmak PR ile güçlü bir şekilde ilişkiliydi; fazla kilolu/obez hastaların %81'inde parsiyel remisyon görüldü. Anti-glutamik asit dekarboksilaz (anti-GAD) antikor pozitifliği PR grubunda daha sık saptandı (%63,0 iken %33,3). Daha uzun remisyon süresi ergenlik dönemindeki, fazla kilolu/obez olan veya çölyak hastalığı pozitif olan hastalarda gözlenirken; anti-GAD ve adacık hücre antikoru pozitifliği daha kısa remisyon ile ilişkiliydi.
Sonuç: Bulgularımız, anti-GAD ve ICA gibi iyi bilinen belirteçlerin bile, çocukluk çağı T1D'de PR'nin seyri üzerinde farklı yönlü etkiler gösterebileceğini, bu belirteçlerin öngörüsel karmaşıklığını ve klinik önemini vurgulamaktadır. Ayrıca obezite, ergenlik ve çölyak hastalığı arasındaki etkileşim, T1D'nin başlangıç döneminde PR yönetiminde immünometabolik yaklaşımların gerekliliğini ortaya koymaktadır.

Anahtar kelimeler: parsiyel remisyon; anti-glutamik asit dekarboksilaz antikoru; adacık hücresi antikoru

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INTRODUCTION

Type 1 diabetes (T1D) is a chronic autoimmune disease marked by progressive destruction of pancreatic β-cells, culminating in insulin deficiency and lifelong insulin dependence[1]. Notably, approximately 60% of children and adolescents with newly diagnosed T1D experience a transient partial remission (PR) phase, characterized by reduced exogenous insulin requirements, improved glycemic control, and a brief recovery of residual β-cell function shortly after the initiation of insulin therapy[1]. An insulin dose-adjusted HbA1c (IDAA1c) of ≤9, has provided a standardized, noninvasive, reliable metric correlating well with stimulated C-peptide and is now widely used in pediatric cohorts[2].

Over the past decade, multiple clinical and metabolic predictors of PR have been explored, including age at onset, sex, diabetic ketoacidosis at diagnosis, body mass index (BMI), and diabetes-related autoantibodies residual C-peptide levels[2-4]. Recent evidence highlights the emerging role of immunometabolic mechanisms in shaping the partial remission phase, suggesting that optimal glycemic control may attenuate immune-mediated β-cell damage and thereby prolong remission by modulating inflammatory pathways[4]. While these factors have been identified, results still vary across studies, and the precise mechanisms underlying the development and progression of PR remain unclear[4-7].

The global rise in childhood overweight and obesity has introduced new complexity to T1D pathophysiology[8]. Concurrently, metabolic factors such as overweight and obesity are gaining prominence, with accumulating evidence suggesting that excess weight may influence both the onset and duration of partial remission in pediatric T1D through its effects on insulin resistance and β-cell stress, although the underlying mechanisms remain unclear[5,7,8]. Obesity may paradoxically favor partial remission in type 1 diabetes, as recent studies suggest this is linked to a relative improvement in insulin sensitivity after treatment initiation[5,9]. Moreover, autoantibody profiles are key immunological predictors of β-cell preservation and remission dynamics, though their associations vary across studies, reflecting the heterogeneity of underlying immune pathways[3,6,7]. Collectively, this variability highlights the need to reassess the roles of both obesity and autoantibodies as potentially underestimated factors in determining remission[4,5]. While prior research has identified metabolic and immunological correlates of partial remission, few investigations have explored their combined and interacting effects in pediatric populations[2,5]. Addressing this gap, the present study evaluates the influence of overweight/obesity and diabetes-related autoantibodies on the onset and duration of partial remission in children and adolescents with newly diagnosed T1D, thereby re-examining established predictors in light of current epidemiological trends and evolving insights into T1D pathophysiology.

MATERIALS AND METHODS

Sample

This retrospective study included patients diagnosed with T1D between 2010 and 2021 who were followed at the Pediatric Endocrinology Department of Çukurova University. Clinical evaluations, treatment procedures, and follow-up were performed by pediatric endocrinologists in accordance with institutional protocols, ensuring reliability and consistency of data collection. The diagnosis of T1D was based on the criteria defined by the International Society for Pediatric and Adolescent Diabetes (ISPAD)[10].

The study protocol was approved by the Clinical Research Ethics Committee of Cukurova University (Approval No: 111/19-2021, Date: 21 May 2021) and conducted in accordance with the Declaration of Helsinki. Inclusion criteria were applied to minimize selection bias, only patients who met all inclusion criteria and had complete medical records were enrolled.

Among 863 patients initially evaluated, 201 were included in the final analysis. Patients were excluded if key clinical or laboratory data were missing (e.g., islet autoantibodies, HbA1c, insulin dose [U/kg/day]), or if regular follow-up during the first year after T1D onset could not be confirmed. C-peptide levels were not included in the analysis due to incomplete data, as they were not systematically measured during the partial remission phase in all patients. Patients were included in the study if they met all of the following criteria: Diagnosed with T1D before the age of 18 years at the time of onset, at our center, in accordance with the ISPAD guidelines[10]. The children were defined as either having diabetic ketoacidosis (DKA) (i.e., plasma glucose > 200 mg/dL, venous pH < 7.3, and/or bicarbonate < 15

mmol/L, ketonemia or ketonuria positive) or non-DKA (i.e., glucose > 200 mg/dL, ketonemia or ketonuria negative, venous pH > 7.3, or bicarbonate> 15 mmol/ L), and this information was documented in their medical records[11].

Patients were excluded from the study if they met any of the following criteria: genetically confirmed monogenic diabetes, type 2 diabetes, onset of diabetes before the age of one year, presence of a chronic systemic illness prior to T1D diagnosis (e.g., liver disease, kidney disease, adrenal insufficiency, or malignancy), or use of medications known to affect insulin secretion (e.g., sulfonylureas, corticosteroids, diazoxide, or somatostatin analogues).

Procedure

Availability of comprehensive medical records at the time of T1D diagnosis, including: Biochemical data (HbA1c, daily insulin dose [U/kg/day]), immunological markers such as: anti-glutamic acid decarboxylase antibodies (anti-GAD), islet cell antibodies (ICA), thyroid autoantibodies (anti-thyroglobulin and anti-microsomal antibodies), assessment of coeliac disease status based on the ESPGHAN criteria[12]. We evaluated ICA and anti-GAD antibodies, both of which were included in the correlation and regression analyses.

Regular follow-up at our center for at least 24 months, with clinical visits occurring at three-month intervals. Availability of serial data across outpatient visits, including glycated hemoglobin (HbA1c), and daily insulin requirements. Pubertal status at diagnosis was retrospectively obtained from clinical records documented by pediatric endocrinologists, based on the Tanner criteria; puberty was defined as testicular volume of ≥4 mL in males (via Prader orchidometer) and breast development at Tanner stage ≥2 in females. As this was a retrospective study, blinding and inter-rater assessment were not applicable. Additionally, height, weight, and BMI were converted into standard deviation scores (SDS) using age- and sex-specific reference values for Turkish children, Patients with a BMI **from** ≥85th **to** <95th percentile were classified as overweight, and those ≥95th percentile as obese[14].

All participants followed an insulin regimen consisting of once-daily, stable-time, long-acting glargine and rapid-acting insulin analogs (e.g., insulin lispro, aspart) administered with each main meal. All 201 patients were using both rapid-acting and long-acting insulin therapy for the treatment of T1D; none of the patients were undergoing insulin pump therapy. Insulin dosages were individualized based on each patient's total daily insulin requirement and pre-meal glucose levels. Adjustments to insulin dosages were made according to self-monitored blood glucose (SMBG) readings and the glycemic targets outlined in the ISPAD guidelines[15]. Participants provided data from self-monitoring of blood glucose (≥ eight measurements per day) over a 14-day period, which were recorded on charts. These data were reviewed during each follow-up visit, and the accuracy and completeness of the blood glucose measurement records were assessed using glucometer data.

Insulin Dose-Adjusted HbA1c (IDAA1c) was calculated using the formula: IDA A1c = HbA1c (%) + [4 × total daily insulin dose (U/kg/day)] and the PR criteria included IDAA1c ≤ 9[16]. The patients were divided into two groups: PR and non-remission (NR). Patients who experienced PR within the first year after diagnosis were categorized based solely on the presence of PR. The time from diagnosis to PR onset and the duration of PR were recorded separately and treated as continuous variables in the analysis. A total of 201 patients 138 and 63 were placed in the PR and NR groups, respectively.

Statistical analysis

Data were analysed using SPSS (Statistical Package for the Social Sciences) version 25.0 software. Categorical measurements were summarised as numbers and percentages, and continuous measurements as means ± standard deviations (median and minimum-maximum, where appropriate). Chi-square and Fisher's exact tests were used to analyse categorical variables**.** The Shapiro–Wilk test was used to determine whether the parameters in the study showed normal distribution. The independent Student's *t*-test was used for normally distributed pairwise comparisons, and the Mann–Whitney U test was used for the pairwise analysis of non-normally distributed parameters. Pearson's correlation test was used to determine the relationship between continuous measurements with normal distribution and Spearman's rho correlation test for those without normal distribution. A post-hoc power analysis was conducted to assess the adequacy of the sample size. Based on a total of 201 participants and a significance level of 0.05, the statistical power was calculated to be approximately

81% for detecting a moderate effect size (Cohen'sd = 0.4), indicating that the sample size was sufficient to detect clinically relevant associations regarding partial remission. Logistic and multiple linear regression analyses were used to determine the factors affecting the development and duration of remission in patients. A *p*-value of < 0.05 was considered statistically significant. For the multivariate regression analysis, candidate variables were selected based on their clinical relevance supported by prior literature and/or a p-value < 0.1 in univariate analyses. The final model included sex (female/male), overweight or obesity status, pubertal stage at diagnosis (prepubertal vs. pubertal), age at diagnosis, presence of coeliac disease, and positivity for islet autoantibodies (anti-GAD and ICA), given their established or proposed roles in β-cell function, immune-mediated β-cell destruction, and metabolic stress at disease onset. Model fit was assessed using the coefficient of determination (R^2) for linear models and the Hosmer–Lemeshow goodness-of-fit test for logistic models, both indicating an acceptable fit to the data. The multivariate linear regression model explained 24.7% of the variance in partial remission duration (R^2 = 0.247). Multicollinearity among independent variables was evaluated using variance inflation factor (VIF) values, all of which were below 2, indicating the absence of significant multicollinearity.

RESULTS

A total of 201 pediatric patients with T1D were evaluated, of whom 79 (39.3%) were female and 122 (60.7%) were male. At the time of type 1 diabetes diagnosis, 107 patients (53.2%) had entered puberty. PR was observed in 138 of the 201 patients (68.7%). In the PR group, the mean age at diagnosis was 9.4 ± 3.8 years, and PR onset occurred at a mean of 1.55 ± 1.4 months (range: 0.1–6) after diagnosis. The mean duration of the remission phase was 7.28 ± 5.2 months.

Compared with the NR group, patients in the PR group had significantly higher rates of overweight/obesity and anti-GAD antibody positivity (p = 0.001 and p < 0.001, respectively). Notably, 68 out of 84 overweight/obese patients (81.0%) experienced PR. Additionally, height SDS was significantly higher among patients with PR (p = 0.005) (Table 1).

Table 1. Demographic, auxological findings, biochemical parameters, and immunological autoantibody of patients with partial remission and non-remission

Variable	**Non-remission** (n=63)	**Partial remission** (n=138)	**p**
	n(%)	n(%)	
Sex			
Female	23 (36.5)	56 (40.6)	0.584
Male	40 (63.5)	82 (59.4)	
Puberty	34 (54)	73 (52.9)	0.888
DKA	40 (63,5)	94 (68.1)	0.519
Overweight/Obesity	16(25.4)	68(49.3)	0.001
ICA	34 (54)	73 (52.9)	0.880
Anti-GAD	21 (33.3)	87 (63.0)	<0.001**
Coeliac disease	6 (9.5)	12 (8.7)	0.849
	Non-remission	**Partial remission**	**p**
	(n=63)	(n=138)	
Age of diagnosis (year)	9.31±3.9	9.49±3.8	0.739[b]
Coeliac disease duration (years)	0.75 (0-8)	1 (0-20)	0.270[b]
Height SDS	-0.21±1.2	0.29±1.1	0.005**,[a]
Weight SDS	0.03±1.2	-0.07±1.2	0.546[a]

PR: Partial remission, DKA: diabetic ketoacidosis, ICA: Islet cell antibody, anti-GAD: anti-glutamic acid decarboxylase antibody, BMI: Body mass index, SDS:standard deviation score (* p<0.05, **p<0.001, a: Independen student t-test, b: Mann whitney u test, c: Chi-square and Fisher exact test

Table 2. Demographic, auxological findings, biochemical parameters, and immunological autoantibody affecting the duration of partial remission

Variable	Duration of remission (month)	
	Med (Min-Max)	p
Sex		
Female	4.75 (2-23)	0.442
Male	6 (2-20)	
Overweight/Obesity		
Negative	4(2-23)	<0.001**
Positive	8.5(2-23)	
Puberty		
Negative	4 (2-18)	<0.001**
Positive	8 (2-23)	
DKA		
Negative	4 (2-23)	0.17
Positive	6 (2-20)	
ICA		
Negative	7 (2-23)	0.002**
Positive	4 (2-20)	
Anti-GAD		
Negative	7 (2-20)	0.044*
Positive	5 (2-23)	
Coeliac disease		
Negative	5 (2-22)	0.039*
Positive	10.5 (4-23)	
Duration of partial remission		
	R	pd
Age of diagnosis	0.329**	<0.001
Height SDS	0.08	0.354
Weight SDS	0.033	0.7

DKA: diabetic ketoacidosis. ICA: Islet cell antibody. Anti-GAD: Anti glutamic acid decarboxylase
* p<0.05, **p<0.001, b: Mann whitney u test. r: Spearman's rho correlation test

Table 3. Univariate and multivariate regression analysis affecting the presence of partial remission

Variable	Univariate		Multivariate	
	Odd Ratio (%95 CI)	p	Odd Ratio (%95 CI)	p
Sex				
Female	1	0,584	_	
Male	0.842 (0.455-1.558)			
Overweight/Obesity	2.854 (1.478-5.511)	0.002**	2.099 (0.937-4.700)	0,072
Puberty	0.507 (0.399-0.645)	<0.001**	0.520 (0.392-0.688)	<0.001**
Anti-GAD	3.750 (1.997-7.042)	<0.001**	2.446 (1.073-5.580)	0.033*
Coeliac disease	0.905 (0.323-2.531)	0,849		
Age of diagnosis	1.013 (0.937-1.095)	0,739		

DKA: diabetic ketoacidosis. Anti-GAD: Anti glutamic acid decarboxylase.* p<0.05. **p<0.001. p1: logistic regression test. p2: multiple logistic regression test

Table 4. Univariate and multivariate regression analysis affecting the presence duration of partial remission

	Univariate	Multivariate			
		Non-standardized coefficients		Odd Ratio (%95 CI)	p[2]
	p[1]	β	Std Error		
Sex					
Female	0.690				
Male					
Overweight/Obesity	<0.001**	2.716	0.749	0.262	<0.001**
Puberty	<0.001**	0.872	1.283	0.084	0.498
ICA	0.022*	-1.905	0.779	-0.177	0.016*
Anti-GAD	0.269				
Coeliac disease	0.015*	2.388	1.374	0.130	0.085
Age of diagnosis	0.001**	0.195	0.166	0.144	0.241

ICA: Islet cell antibody. Anti-GAD: Anti glutamic acid decarboxylase. * p<0.05. **p<0.001. p1: linear regression test. p2: multiple linear regression test

Longer PR duration was significantly associated with the presence of puberty, overweight/obesity, and coeliac disease positivity ($p < 0.001$, $p < 0.001$, and $p = 0.039$, respectively). In contrast, anti-GAD antibody and islet cell antibody (ICA) positivity were associated with shorter PR duration ($p = 0.044$ and $p = 0.002$, respectively). There was a moderate positive correlation between age at diagnosis and PR duration ($r = 0.329$). No other significant associations were found between PR duration and the remaining variables analyzed ($p > 0.05$) (Table 2).

A multivariate logistic regression model was conducted to identify independent predictors of PR presence. The variables included were sex, overweight/obesity, pubertal status, anti-GAD positivity, and coeliac disease. In this model, anti-GAD positivity (OR = 2.44, 95% CI: 1.07–5.58; $p = 0.033$) and pubertal status (OR = 0.52, 95% CI: 0.39–0.68; $p < 0.001$) emerged as independent predictors of PR (Table 3).

To evaluate predictors of PR duration, a multiple linear regression analysis was performed using the same variables. Overweight/obesity was significantly associated with longer PR duration ($\beta = 2.71$, $p < 0.001$), while ICA positivity was associated with a shorter PR duration ($\beta = –1.90$, $p = 0.016$) (Table 4).

DISCUSSION

In this study, we aimed to identify the predictors and duration of PR in pediatric patients with T1D at the time of onset. The findings reveal several key factors associated with both the presence and duration of PR, thereby enhancing the understanding of disease progression in children and adolescents with T1D. In the present study, we examined the combined effects of puberty, overweight/obesity, and autoimmune markers in the context of PR in pediatric T1D, while also revisiting certain variables previously assessed in pediatric cohorts with diabetes but not consistently explored concerning PR.

Our results indicate that 68.7% of pediatric patients with T1D experienced PR, consistent with previous studies that reported high remission rates in the early stages of pediatric T1D[12–17]. The onset of PR occurred relatively early, with a mean of 1.55 months after diagnosis, and the duration of PR was, on average, 7.28 months. This early remission phase supports previous research emphasizing the role of the early post-diagnosis period in the disease's pathophysiological progression[2–17].

The proportion of patients in puberty was relatively high (53.2%) in the present sample, and T1D is more common during the pubertal period[18]. Puberty is a critical period for growth and development, during which hormonal changes may influence insulin sensitivity in T1D[19]. Cimbek et al.[2] reported the presence of PR during puberty, noting that the PR period was prolonged. The presence of puberty was significantly associated with the duration of PR. In our study, pubertal patients had longer remission durations, suggesting that hormonal factors related to growth and metabolic changes could contribute to the modulation of insulin requirements during this phase.

Prior studies have shown that higher BMI-SDS at T1D onset is associated with higher PR rates[3,17,20]. Insulin resistance although their clinical relevance along with obesity's impact on pancreatic autoimmunity and possible distinct metabolic or phenotypic features compared with non-diabetic populations remains unclear[21]. While overweight/obesity may be linked to PR, potential

long-term complications such as insulin resistance could worsen T1D progression, emphasizing the need for careful interpretation[22,23].

We also found that is more common in these patients, and early hyperglycemia may precede β-cell loss[3]. While BMI is widely used to assess obesity, it offers limited insight into adipose tissue distribution, which can vary in T1D[21]. Notably, our study found that 81% of overweight or obese children with T1D experienced PR, a finding consistent with the study suggesting potential β-cell–protective and anti-inflammatory effects of excess adiposity, overweight/obesity at T1D onset was associated with prolonged PR duration, possibly due to insulin resistance resulting from excess adiposity. However, increased insulin demand may accelerate β-cell stress and dysfunction, as seen in animal models fed high-fat diets[24,25]. In obese children, insulin therapy and proper diet may reduce inflammation, leading to a milder T1D presentation. Further research is needed to clarify the mechanisms and long-term effects of overweight/obesity on PR and T1D outcomes, as potential benefits may be offset by adverse complications.

In our study, prolonged PR was observed in individuals diagnosed with coeliac disease. The autoimmune nature of T1D may contribute to early signs of disease and the preservation of β-cells through multiple immune system responses[17]. Ozen et al.[26] found that the frequency of additional autoimmune diseases increased in patients with a prolonged PR period. Studies in animals support the correlation between gluten's influence on β-cells and the progression of T1D[27,28]. Studies also emphasise the effect of a gluten-free diet on glycaemic and metabolic control as well as growth patterns in children with T1D[29,30]. However, the decrease in the systemic inflammatory response resulting from the initiation of a gluten-free diet after CD diagnosis may have contributed to a more extended PR period in children in whom CD and T1D coexisted.

In our study, both ICA and anti-GAD positivity were associated with a shorter PR duration. This aligns with findings from a Brazilian cohort reporting similar associations between autoantibody positivity and PR outcomes[31]. However, Pecheur et al.[32] found no significant relationship between anti-GAD positivity and the occurrence of PR. The inverse relationship between PR duration and the time from T1D onset to PR may reflect cumulative β-cell damage due to ongoing autoimmunity. Consistent with this, another observational study reported shorter or absent PR phases in children who were autoantibody-positive at diagnosis[20].

In our study, anti-GAD positivity was associated with both a higher likelihood of entering partial remission and a shorter remission duration. This paradox suggests that the clinical significance of anti-GAD positivity may vary depending on its context and the presence of additional islet autoantibodies. Literature indicates that isolated anti-GAD positivity can be linked to a greater propensity for remission, potentially due to a slower and more limited autoimmune response that preserves β-cell function for longer[6,34]. In contrast, the coexistence of multiple autoantibodies is often associated with a more aggressive immune attack and a reduced remission period. Therefore, the role of anti-GAD should be interpreted within the broader antibody profile, including the number and combination of antibodies, and the clinical context[33,34].

We found that ICA positivity appeared linked to shorter remission duration, supporting recent evidence suggesting that a broader autoantibody profile, including ICA, is more predictive of disease progression and autoimmune aggressiveness than single-marker positivity[33,35]. Additionally, the coexistence of multiple islet autoantibodies, including ICA, is indicative of aggressive islet inflammation[34,35]. In particular, the absence of ICA at diagnosis has been linked to preserved C-peptide secretion up to two years later in European cohorts[36].

Collectively, these findings reinforce that ICA positivity at diagnosis particularly within multiple autoantibody profiles may signal a less favorable prognosis for partial remission. Moreover, autoantibody-negative children (for anti-GAD and ICA) demonstrated slower disease progression, better β-cell preservation, and improved glycemic control at 12 months[33]. These observations underscore the potential prognostic value of comprehensive autoantibody profiling. The use of extended autoantibody panels including ICA, anti-GAD, IA-2A, IAA, and ZnT8A may offer greater predictive power for PR onset and duration. In this context, longitudinal reassessment of autoantibody status during the PR phase may also provide insights into the dynamics of autoimmune activity and β-cell function[33,34].

The current study has limitations. Data were analyzed from a single center in the same geographic area,

albeit thought in a city with cosmopolitan population characteristics. The absence of C-peptide measurements at diagnosis and longitudinal follow-up, as well as the lack of insulin reserve assessment, represents a limitation of our study. Due to the retrospective design, we did not have sufficient data on insulinoma-associated-2 autoantibodies (IA-2A), insulin autoantibodies (IAA), and zinc transporter-8 autoantibodies (ZnT8A) in patients with PR. Another limitation is the retrospective design itself, which restricts the possibility of assessing factors that influence obesity/overweight, such as C-peptide levels, eating behavior, or physical activity. Additionally, changes in weight status among overweight and obese children during follow-up were not evaluated.

Considering the multiple factors that contribute to the pathophysiology of T1D and the clinical variation among individuals, there is a requirement for new and more sensitive biomarkers for disease prevention, diagnosis, prediction, and management, which are the subject of current research. Future studies should incorporate genetic susceptibility markers, such as HLA typing, alongside extended autoantibody profiling, including ZnT8A, to better stratify patients according to their risk of entering and sustaining partial remission. Integrating both immunological and genetic markers in longitudinal follow-up could enhance our understanding of disease heterogeneity and guide more personalized therapeutic strategies.

In conclusion, the presence of overweight/obesity and higher rates of anti-GAD antibody positivity were associated with partial remission. Patients with puberty, overweight/obesity, and coeliac disease positivity had longer remission periods than those with ICA and anti-GAD positivity. Our findings suggest that diabetes-related autoantibody positivity may serve as an important parameter in the management of PR in T1D. In addition, anti-GAD positivity may serve as a useful marker in both diagnostic and monitoring settings to help identify patients at higher risk for shorter PR duration and to inform closer follow-up strategies.

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