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PARTIAL CLINICAL REMISSION IN TYPE 1 DIABETES: PANCREATIC B - CELL FUNCTIONAL RESERVE, PREDIC-TORS, AND CLINICAL SIGNIFICANCE (A NARRATIVE RE-VIEW)

Daryna M. Bilous

Bogomolets National Medical University, Kyiv, Ukraine

ABSTRACT

Introduction. Partial clinical remission (the "honeymoon" phase) in type 1 diabetes (T1D) is characterized by transient recovery of pancreatic β-cell function and a temporary reduction in exogenous insulin requirements following the alleviation of glucotoxicity.

Aim. To synthesize current scientific evidence regarding the clinical significance, diagnostic criteria, and predictive factors of partial clinical remission in T1D.

Materials and methods. A narrative review of cohort studies, systematic reviews, and con-sensus guidelines on patients with newly diagnosed T1D was conducted using the PubMed and Google Scholar databases.

Results. The literature review indicates that the incidence of partial clinical remission ranges from 35% to 70%, with a typical duration of 3-12 months. Across the evaluated sources, the IDAA1c index (≤9) is highlighted as the current standardized surrogate marker of preserved stimulated C-peptide secretion (>300 pmol/L). Analysis of published data indicates that older age at T1D onset, absence of severe diabetic ketoacidosis (DKA), and higher baseline C-peptide levels are favorable predictors of partial remission. Preserved residual β-cell function facilitates glycemic control and may reduce the risk of severe hypoglycemia.

Conclusions. The remission phase represents an important therapeutic window in the clinical course of T1D. Intensive insulin therapy helps optimize glycemic control while reducing met-abolic stress on residual β-cells, whereas disease-modifying immunotherapies aimed at pre-serving or prolonging remission remain under active clinical investigation.

Keywords: C-peptide, diabetic ketoacidosis, Glycemic control, Insulin-Dependent Diabetes Mellitus, Insulin-Secreting Cells

INTRODUCTION

The "honeymoon" phenomenon, or the phase of partial clinical remission in type 1 diabetes mellitus (T1D), is a well-recognized clinical stage characterized by temporary improvement in glycemic control associated with preserved β-cell function [1, 3]. The clinical relevance of this period stems from its heterogeneity: the duration of remission may range from several months to several years [6, 7], and "approximately 80% of children and adolescents with T1D require a significant reduction in insulin dosage during this phase" [4].

Scientific interest in this phase focuses on immunometabolic mechanisms, as "precise control of blood glucose levels within a healthy range delays the harmful consequences arising from autoimmune mechanisms in the pancreatic islets" [7]. It has been demonstrated that "young age and severe disease course (DKA) at the time of treatment initiation are associated with reduced function of residual β-cells" [2], and that the likelihood of a prolonged "honeymoon period" in a "very young girl with severe decompensation is significantly lower compared with an adolescent with moderate hyperglycemia" [1].

A crucial feature of this phase is the preservation of the β-cell response to both oral glucose and other secretagogues, albeit at a subnormal level [3]. This observation challenges the traditional view of T1D as a condition characterized by complete and irreversible insulin dependence from the time of diagnosis, as the disease may include a distinct phase of residual endogenous insulin secretion [3, 8].

"The ultimate goal of therapy is to promote islet cell growth and to use pharmacological inter-

vention during this period to slow or halt the ongoing destruction of the remaining β-cells" [1, 2, 6]. Therefore, the development of strategies that allow for "effective glucose control to improve the mass, function, and markers of maturity of islet β-cells" [7] remains an important priority in modern endocrinology [4, 6].

AIM

The objective of this study is to analyze the factors influencing the onset and duration of the partial clinical remission phase in patients with type 1 diabetes based on a review of the current literature, and to assess the functional reserve of pancreatic β-cells at disease onset.

MATERIALS AND METHODS

Core publications examining β-cell functional reserve and the "hon-eymoon" phenomenon were identified through a literature search of the PubMed bibliographic database. To broaden the scope of the search, Google Scholar was also used, along with a targeted review of relevant full-text publications available through the Wiley platform. The review focused on published evidence concerning patients with newly diagnosed type 1 diabe-tes (T1D) during the phase of partial clinical remission [2, 6].

Across the reviewed studies, the main clinical and laboratory parameters assessed at hospital admission included the duration of symptoms before diagnosis (particularly <6 months), the presence of diabetic ketoacidosis (DKA), baseline blood glucose levels, and blood pH [1, 2]. Residual β-cell secretory capacity was assessed using C-peptide concentrations and re-sponses to intravenous glucose administration [3, 9].

Assessment of β-cell functional reserve and residual responses to various secretagogues in the included studies involved diagnostic stimulation proto-cols, including oral and intravenous glucose tolerance tests (OGTT and IVGTT), glibenclamide tests, mixed-meal tolerance tests (MMTT), and insu-lin tolerance tests (ITT), with assessment of corresponding insulin, C-peptide, and glucagon responses [3, 10]. Particular emphasis was placed on age-related determinants, including comparisons of remission rates between children older than 5 years and younger cohorts (3-5 years), with the re-viewed studies indicating higher odds of entering remission among children older than 5 years. The reviewed literature also evaluated the relationship between acid-base status, particularly blood pH at diagnosis, and the dura-tion of partial remission [2], with lower blood pH at admission consistently associated with a shorter duration of partial remission.

All statistical analyses, including assessments of associations and statistical significance ($p<0.001$), were performed by the authors of the original prima-ry studies [2, 7, 9]. Based on these findings, the original studies concluded that severe presentation with diabetic ketoacidosis and lower blood pH were associated with a lower probability of entering remission or a shorter dura-tion of remission. The reviewed literature also addressed immunometabolic mechanisms, particular-ly the potential influence of glucose metabolism on immune cell profiles within pancreatic islets [7, 9].

All statistical evaluations in the primary publications, including variance and correlation analyses with established significance levels ($p<0.001$), were conducted by the primary authors when comparing age cohorts and homeo-static markers [2]. Overall, the systematization of information aimed to ana-lyze immunometabolic factors capable of influencing the duration of the par-tial remission phase [7].

RESULTS

Definition and Criteria of Partial Remission

Analysis and systematization of published scientific evidence indicate that partial clinical remission, known as the "honeymoon" phase, is a transient period in the natural history of type 1 diabetes [1, 3]. Following the initia-tion of insulin therapy, this stage is characterized by a temporary reduction in exogenous insulin requirements owing to partially preserved secretory activity of the residual pancreatic β-cell mass [1, 3].

Synthesis of the available literature allows for a clear distinction between historical definitions and contemporary standardized diagnostic criteria [12]. For a long time, the primary criterion for defining remission was a re-duction in daily insulin requirements to below 0.5 IU/kg/day accompanied by satisfactory glycemic control (HbA1c 6.0-7.0%) [2]. However, analysis of clinical studies has highlighted the limitations of these earlier criteria: reli-ance solely on insulin dose and HbA1c is influenced by individual insulin sensitivity, dietary patterns, and physical activity levels and therefore may not accurately reflect the true functional reserve of the pancreatic islets [12].

According to contemporary publications, the international standard for as-sessing partial remission is the IDAA1c (insulin-dose-adjusted HbA1c) in-dex, calculated as the sum of HbA1c (%) and four times the daily insulin dose per kilogram of body weight [12]. An IDAA1c ≤9 is widely employed in the evaluated studies as a reliable surrogate marker of preserved stimulat-ed C-peptide secretion (specifically during standardized mixed-meal toler-ance testing), providing an objective assessment of functional β-cell status [12].

Remission Frequency and Duration

Analysis of published scientific literature indicates that partial remission rates range broadly from 50% to 75%, with an average duration typically spanning 3 to 12 months [2, 7]. Literature systematization demonstrates that this wide variance does not represent a single uniform finding, but ra-ther reflects inter-study heterogeneity [7]. Remission duration and frequency are significantly influenced by cohort age composition, specific remission criteria (classic metrics vs. IDAA1c), ethnic and population traits, initial insulin management protocols, and overall study design [7]. Furthermore, across multiple documented observations, a pronounced temporary de-crease in exogenous insulin requirements is observed in the majority of chil-dren and adolescents during the initial months following clinical onset [2, 4].

Age-Related Predictors

According to numerous published studies, age at T1D onset represents one of the most consistently verified prognostic factors [2, 7]. In patients older than 5 years and adolescents, partial remission occurs more frequently and persists longer than in younger children (under 5 years of age). This is at-tributed to a larger initial β -cell mass and a less aggressive autoimmune de-struction trajectory at an older age [2, 8].

Impact of Diabetic Ketoacidosis and pH

Based on the analyzed scientific literature, the severity of metabolic derangement at initial diagnosis represents an important prognostic determinant of the course of partial clinical remission [2, 6]. The reviewed studies indicate that diabetic ketoacidosis (DKA) and marked reductions in blood pH at admission are associated with a lower likelihood of partial remission and a shorter duration of the remission phase [2, 6].

The authors of the reviewed studies attribute this association to a cascade of pathophysiological disturbances triggered by DKA, including severe glucotoxicity, lipotoxicity, and profound electrolyte imbalances [8]. These metabolic disturbances may contribute to functional impairment and suppression of residual β-cell function, potentially accelerating the decline in residual β-cell mass before the initiation of insulin therapy [2, 8].

The available evidence indicates that the likelihood and duration of partial clinical remission are determined by a complex combination of clinical, laboratory, and demographic factors. Among the factors most consistently identified across the reviewed studies are age at disease onset, the absence of severe DKA and pronounced acidosis at hospital admission, and higher baseline C-peptide levels.

DISCUSSION

Findings from the literature analysis confirm that the partial clinical remission phase (the "honeymoon" period) represents an important stage in the natural course of type 1 diabetes (T1D) [4, 6]. Following the initiation of insulin therapy, this period is characterized by a temporary reduction in exogenous insulin requirements while glycemic control is maintained [1, 5]. This phenomenon is primarily associated with partial recovery of secretory activity in the residual pancreatic β-cell mass following alleviation of glucotoxicity and lipotoxicity after treatment initiation [3, 8].

At the same time, partial remission does not indicate cessation or reversal of the underlying autoimmune process [2, 8]. Progressive loss of β-cell mass may continue; however, temporary reduction of metabolic stress on residual β-cells allows partial compensation for insulin deficiency [8, 11]. In clinical practice, this period represents an important window for reinforcing diabetes self-management and optimizing individualized therapeutic regimens [4, 6].

Across the analyzed studies, the occurrence and duration of the "honeymoon" phase demonstrated considerable interindividual variability [4, 7]. Among the most consistently identified determinants of the remission trajectory are age at clinical onset, baseline C-peptide levels, and the degree of metabolic derangement at diagnosis [2, 5, 7]. The presence of diabetic ketoacidosis (DKA) and severe acidosis at admission is associated with greater impairment of pancreatic β-cell function and lower rates of remission or a shorter remission duration [2, 11]. Additional factors potentially associated with the remission trajectory include symptom duration before diagnosis, baseline glycated hemoglobin (HbA1c) levels, and body mass index [7].

Preservation of residual β-cell functional capacity during remission has important clinical implications [7, 9]. Endogenous C-peptide secretion facilitates achievement of glycemic targets, may reduce glycemic variability, and is associated with a lower risk of severe hypoglycemic events [5, 9].

For the assessment of partial remission in contemporary clinical research, standardized parameters, particularly the IDAA1c index and C-peptide measurements, are recommended, enabling objective assessment of residual pancreatic β-cell function and supporting individualized adjustment of insulin therapy [4, 12].

CONCLUSION

According to the analysis of the scientific literature, partial clinical remis-sion in type 1 diabetes is the

result of temporary functional recovery of surviving β-cells following the relief of glucotoxicity and lipotoxicity upon the initiation of insulin therapy. Alongside classical criteria of daily insulin dose and HbA1c, the IDAA1c ≤ 9 index is recognized as the modern standard for verification in research, serving as a reliable surrogate marker of preserved stimulated C-peptide secretion.

Article Declarations

Prospects for further research. Future research should focus on large-scale clinical trials and the validation of emerging immunotherapeutic and dis-ease-modifying strategies aimed at preserving and prolonging the pool of functionally active pancreatic ß -cells during the partial clinical remission phase in type 1 diabetes, as well as the identification of highly sensitive mo-lecular and genetic markers to predict the duration of the "honeymoon" pe-riod.

Study limitations. The authors acknowledge that the limitations of this re-view are determined both by the predefined scope of topics, timeframes, and study designs, and by resource accessibility. The search strategy encom-passed the PubMed bibliographic database (https://pubmed.ncbi.nlm.nih.gov/), Google Scholar resources, and the Wiley full-text platform. The review was narrative in nature and was based exclusively on published secondary data, without conducting an independ-ent formalized quantitative meta-analysis.

Primary data and materials. The authors explicitly state that primary med-ical records (patient case histories, outpatient charts, examination protocols, laboratory and instrumental test results of individual patients) and proprietary statistical databases were not utilized in this review.

Research ethics. The researchers adhered to all protocols and procedures established by the Biomedical Research Ethics Committee, as well as the requirements of Ukrainian healthcare legislation and the provisions of the Declaration of Helsinki (2000).

Declaration of AI use. During the preparation of this work, the authors uti-lized ChatGPT-4 to generate drafting options and phrasing. Following the use of this tool, the authors reviewed and edited the material as necessary and assume full responsibility for the content and integrity of the publica-tion.

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Author Contributions (CRediT taxonomy)

*Daryna M. Bilous: A,B,C,D,E,F. ORCID: 0009-0003-4932-0208

***Corresponding author:** dashabilous0120@gmail.com; **+380961215077**

REFERENCES

1. Pujia R, Maurotti S, Coppola A, Romeo S, Pujia A, Montalcini T. The potential role of C-peptide in sexual and reproductive functions in type 1 diabetes mellitus: An update. Curr Diabetes Rev. 2022;18(6):e051021196996. https://doi.org/10.2174/1573399817666211005093434
2. Nardelli GM, Guastamacchia E, Di Paolo S, Lattanzi V, Ciampolillo A, Montedoro P, Giorgino R. Remission from insulin dependence induced by continuous subcutaneous insulin infusion (CSII) in type I, newly diagnosed diabetics: role of some hormonal and immunologic factors. Acta Diabetol Lat. 1988;25(2):107-117. https://doi.org/10.1007/BF02581133
3. Torella R, Salvatore T, Cozzolino D, Grandillo F, Giugliano D. Pathophysiological study of the non-insulin-dependent phase of type I diabetes mellitus. Acta Diabetol Lat. 1988;25(4):313-322. https://doi.org/10.1007/BF02581381
4. Gomez-Muñoz L, Dominguez-Bendala J, Pastori RL, Vives-Pi M. Immunometabolic biomarkers of partial remission in type 1 diabetes. Front Immunol. 2022;13:825426. https://doi.org/10.1016/j.tem.2023.10.005
5. Chobot A, Stompor J, Shida K, Deja G, Polanska J, Jarosz-Chobot P. Remission phase in children diagnosed with type 1 diabetes in years 2012 to 2013 in Silesia, Poland: An observational study. Pediatr Diabetes. 2019;20(3):286-292. https://doi.org/10.1111/pedi.12824
6. Fonolleda M, Murillo M, Vazquez F, Bel J, Vives-Pi M. Remission phase in type 1 diabetes: New insight and emerging biomarkers. Horm Res Paediatr. 2017;88(5):307-315. https://doi.org/10.1159/000479030

7. Vague P, Vialettes B, Lassmann V, Moulin JP, Mercier P. Sustained initial remission induced by intensive insulin treatment in type I diabetes: possible role of the genetic background. Acta Diabetol Lat. 1985;22(4):307-313. https://doi.org/10.1007/bf02624748
8. Guo Y, Lei L, Che G, Gao H, Hu Q. Xist-mediated B cell modulation: Implications for immune dysregulation in T1DM. Biochim Biophys Acta Mol Basis Dis. 2026;1872(6):168376. https://doi.org/10.1016/j.bbadis.2026.168376
9. Nyburch A.K., Jensen A.K., Mortensen H.B., et al. Prevalence, duration, and predictors of partial remission in children and adolescents with type 1 diabetes: A nationwide prospective cohort study. Pediatric Diabetes. 2022;23(4):475-484. https://doi.org/10.3389/fimmu.2022.825426
10. Jamiołkowska-Sztabkowska M, Głowińska-Olszewska B, Bossowski A. C-peptide and residual β -cell function in pediatric diabetes - state of the art. Pediatr Endocrinol Diabetes Metab. 2021;27(2):123-133. https://doi.org/10.5114/pedm.2021.107165
11. Ludvigsson J, Heding LG. Beta-cell function in children with diabetes. Diabetes.1978;27(Suppl1):230-234. https://doi.org/10.2337/diab.27.1.s230
12. Moole H, Moole V, Mamidipalli A, Dharmapuri S, Boddireddy R, Taneja D, Sfeir H, Gajula S. Spontaneous complete remission of type 1 diabetes mellitus in an adult - review and case report. J Community Hosp Intern Med Perspect. 2015;5(5):28709. https://doi.org/10.3402/jchimp.v5.28709

ЧАСТКОВА КЛІНІЧНА РЕМІСІЯ ПРИ ЦУКРОВОМУ ДІАБЕТІ 1 ТИПУ: ФУНКЦІОНАЛЬНИЙ РЕЗЕРВ В-КЛІТИН, ПРЕДИКТОРИ ТА КЛІНІЧНЕ ЗНАЧЕННЯ (НАРАТИВНИЙ ОГЛЯД)

Дарина М. Білоус

Національний медичний університет імені О. О. Богомольця, м. Київ, Україна

РЕЗЮМЕ

Мета. Узагальнити сучасні наукові дані щодо клінічного значення фази часткової клінічної ремісії («медового місяця») при цукровому діабеті 1 типу (ЦД1), критеріїв її верифікації, прогностичних факторів та збереження функціонального резерву β-клітин підшлункової залози.

Матеріали та методи. Предметом огляду стали результати проспективних когортних досліджень, систематичних оглядів та міжнародних консенсусних рекомендацій щодо пацієнтів із вперше діагностованим ЦД1, опубліковані в базах даних PubMed та Google Scholar. Проведено аналіз класичних діагностичних підходів і стандартизованого індексу IDAA1c, ролі ендогенного С-пептиду та клініко-лабораторних факторів, пов'язаних із перебігом ремісії.

Результати. За даними проаналізованих джерел, часткова ремісія спостерігається в узагальненому діапазоні від 35% до 70% пацієнтів, із типовою тривалістю від кількох місяців до одного року, що суттєво залежить від віку, популяції та використаного критерію верифікації. Застосування стандартизованого індексу IDAA1c (≤9) дозволяє оцінювати збереження функціональної секреції β-клітин. До підтверджених сприятливих прогностичних факторів перебігу ремісії належать старший вік на момент маніфестації, відсутність тяжкого діабетичного кетоацидозу та вираженого ацидозу при госпіталізації, а також вищий початковий рівень стимульованого С-пептиду. Збереження залишкової ендогенної секреції інсуліну асоціюється з кращим глікемічним контролем, зменшенням варіабельності глікемії та зниженням частоти тяжких гіпоглікемій.

Висновки. Фаза часткової клінічної ремісії є важливим періодом перебігу ЦД1, який може розглядатися як потенційне терапевтичне вікно для збереження залишкового пулу β-клітин. Досягнення стабільного глікемічного контролю за допомогою сучасних режимів інсулінотерапії сприяє зменшенню глюкотоксичності та оптимізації ведення пацієнтів, тоді як методи експериментальної імунотерапії наразі залишаються предметом клінічних досліджень.

Ключові слова: С-пептид, діабетичний кетоацидоз, глікемічний контроль, цукровий діабет 1 типу, інсулінсекретуючі клітини

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