# Ethnic Differences in Glycemic Control and Diabetic Ketoacidosis Rate among Children with Diabetes Mellitus Type 1 in the Negev Area

Alnassara Hilmi MD[1], Yehonatan Pasternak BSc[1], Michael Friger PhD[2], Neta Loewenthal MD[1], Alon Haim MD[1] and Eli Hershkovitz MD[1]

[1]Pediatric Endocrinology and Metabolism Unit, Soroka Medical Center and Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel
[2]Department of Epidemiology and Health Services Evaluation, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel

**ABSTRACT:** **Background:** The existent glycemic control of type 1 diabetes mellitus (T1DM) patients in daily practice might not reach the goals determined in guidelines. Ethnic diversity was also shown to influence glycemic control.

**Objectives:** To evaluate glycemic control, prevalence of diabetic ketoacidosis (DKA) at presentation, diabetic complications rate, and associated autoimmune diseases in a pediatric T1DM patient population in the Negev area.

**Methods:** Clinical and demographic details of 168 T1DM patients were evaluated, including HbA1C levels, long-term complications, related autoimmune diseases, and insulin pump usage. The data were analyzed and the Jewish and Bedouin patient groups compared.

**Results:** Only 13.1% of the patients had reached the HbA1C levels recommended by the current guidelines at the first and second year follow-up visits, and 9.5% and 7.1% at the third and fourth year visits, respectively. A significant difference in HbA1c levels between Jewish and Bedouin patients was found ($P = 0.045$ at the first year follow-up, $P \leq 0.01$ thereafter). Significant difference was found between the Jewish and the Bedouin groups regarding presentation with DKA, 33% and 56% of the patients respectively ($P = 0.01$).

**Conclusions:** Existent glycemic control in daily practice is far from the guideline goals. Bedouin ethnicity was associated with less favorable diabetes control, emphasizing the need for better awareness of T1DM and its treatment options in this population. More resources should be directed to address T1DM in the general population, especially among the Bedouin.

*IMAJ* 2013; 15: 335–338

**KEY WORDS:** diabetes mellitus (DM), glycemic control, Negev, ethnic differences, hemoglobin A1c (HbA1c)

**For Editorial see page 363**

Type 1 diabetes mellitus is a common chronic disease in childhood. About half the subjects with T1DM are diagnosed within the first 15 years of life [1]. It was recently assumed that between the years 2005 and 2020 the prevalence of T1DM in children under age 15 will rise by 70%, making its prevalence even higher [2]. Strict metabolic control was proven efficient in reducing morbidity, mortality and long-term complications of T1DM [3,4].Therefore, achieving tight glycemic control with insulin – using either multiple daily injections or an insulin pump – as well as an appropriate diet and physical activity is of cardinal importance, especially early in the course of the disease before microvascular complications become established.

Hemoglobin A1C level was found to have the most predictive value for long-term diabetic complications [5]. According to the guidelines of the American Diabetes Association, treatment of T1DM should aim at reaching an HbA1C level ≤ 7% in adults, between 7.5% and 8.5% in preschool children, ≤ 8% in school-aged children, and ≤ 7.5% in adolescents and young adults [6,7].

The population in the Negev (desert area in southern Israel) consists of a large Bedouin minority, which has a different lifestyle and socioeconomic level compared to the general population in Israel. Previous studies have noted the influence of ethnic, cultural and socioeconomic factors on glycemic control of T1DM [8], while others have studied type 2 DM characteristics of Bedouin patients in the Negev [9,10].

In this study we evaluated the existent glycemic control, the prevalence of diabetic ketoacidosis at presentation and after diagnosis, the long-term diabetic complications rate, and associated celiac disease and autoimmune thyroid disease among a cohort of pediatric T1DM patients in the Pediatric Diabetes and Endocrinology Unit of Soroka Medical Center.

## PATIENTS AND METHODS

The study was approved by the local ethics institutional review board of Soroka Medical University Center, Beer Sheva. The subjects for this report were a cohort of 168 type

T1DM = type 1 diabetes mellitus

HbA1C = hemoglobin A1C

1 diabetes patients aged 1–18 years who were diagnosed and followed at the Pediatric Endocrinology and Diabetes Outpatient Clinic at Soroka Medical Center, Beer Sheva, during 2000–2008. The exclusion criterion was clinical follow-up of less than one year.

The patients' medical charts are managed through an electronic database that includes the summaries and laboratory test results of all visits. The following demographic and clinical details were extracted from the patients' electronic charts: age, gender, age at presentation, diabetic ketoacidosis at presentation and after diagnosis, relatives with diabetes, treatment with insulin injection or pump, HbA1C levels, complications such as retinopathy and nephropathy, and related autoimmune diseases such as Hashimoto's thyroiditis and celiac.

HbA1C levels were evaluated at every visit in the outpatient clinic. The levels were stratified by years from presentation in order to compare the means for ethnicity, gender, age groups, and pump treatment.

### STATISTICAL ANALYSIS

Continuous variables are expressed as mean ± standard deviation and were compared between groups by the independent *t*-test. One-way ANOVA was used to compare continuous variables in multiple groups. Ordinal or continuous variables that do not distribute normally were compared by Kruskal-Wallis and Mann-Whitney tests. For nominal variables we used chi-square and Fisher exact tests. We used multiple linear regression to seek predictive variables for HbA1C levels, and logistic regression for insulin pump treatment. The variables analyzed were gender, ethnicity, and pump treatment. An estimation of the annual incidence of T1DM was based on our data, while the denominators in the incidence rate calculations were based on data published by the Israel Central Bureau of Statistics. For all tests, a $P$ value < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS 17 statistical software (IBM Corporation, Chicago, IL, USA).

## RESULTS

Overall, 168 patients with T1DM were enrolled to the study; 118 of them were Jewish (70.2%) and 50 were Bedouin (29.8%). There were 93 males (55.4%) and 75 females (44.6%). The average age was 10.2 ± 4.4 years in the Bedouin group and 9.6 ± 3.8 years in the Jewish group ($P$ = 0.9).

The annual incidence of T1DM per 100,000 cases/year was 10.8 (95% confidence interval 9.5–12.1) in the Jewish population and 5.1 (95% CI 3.8–6.4) among the Bedouin. Several clinical characteristics were evaluated [Table 1]. Seventy-eight (46.7%) of the patients had a family history of DM (mostly DM type 2).

CI = confidence interval

**Table 1.** Clinical characteristics of patients compared by ethnicity

| | Jewish | Bedouin | Total | *P* value |
|---|---|---|---|---|
| Family history of diabetes | 54 (46.2%) | 24 (48%) | 78 (46.7%) | 0.960 |
| DKA at diagnosis | 38 (33%) | 28 (56%) | 66 (40%) | 0.01 |
| DKA after diagnosis* | 23 (19%) | 16 (32%) | 39 (23%) | 0.076 |
| Insulin pump treatment | 78 (67.2%) | 10 (20%) | 88 (53%) | < 0.01 |
| Retinopathy | 5 (4.3%) | 1 (2%) | 6 (3.6%) | 0.670 |
| Nephropathy | 11 (9.4%) | 4 (8%) | 15 (9%) | 1.00 |
| Hashimoto thyroiditis | 15 (12.8%) | 4 (8%) | 19 (11.4%) | 0.527 |
| Celiac disease | 8 (6.8%) | 9 (18%) | 17 (10.2%) | 0.057 |

*One or more episodes

**Table 2.** HbA1C levels compared by ethnicity

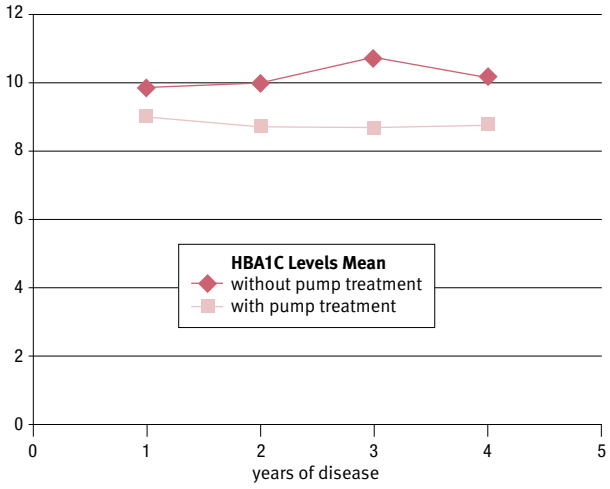
| Duration of DM | Ethnicity | N | Mean ± SD | *P* value |
|---|---|---|---|---|
| ≤ 1 yr | Bedouin<br>Jewish | 46<br>106 | 9.91 ± 2.08<br>9.18 ± 2.02 | 0.045 |
| › 1– ≤ 2 yr | Bedouin<br>Jewish | 41<br>95 | 10.23 ± 2.21<br>8.87 ± 1.57 | 0.01 |
| › 2– ≤ 3 yr | Bedouin<br>Jewish | 35<br>81 | 10.89 ± 1.1<br>9.00 ± 1.77 | ‹ 0.01 |
| › 3 yr | Bedouin<br>Jewish | 24<br>67 | 10.58 ± 1.95<br>8.94 ± 1.55 | ‹ 0.01 |

Significant differences were found between Jewish and Bedouin patients regarding DKA at presentation: 33% vs. 56%, respectively ($P$ = 0.01), and insulin pump treatment for at least 6 months 67% vs. 20%, respectively ($P$ < 0.01). No differences were found between genders regarding DKA at presentation and insulin pump treatment. No significant differences between the ethnic groups were noted for DM complications and related autoimmune diseases. DKA occurrence after diagnosis was not significantly different between the ethnic groups [Table 1].

Only 13.1% of the patients had reached a goal of 7.5 mg/dl HbA1C at the first and second year follow-up visits, and 9.5% and 7.1% at the third and fourth year visits, respectively. A significant difference in HbA1C levels between Jewish and Bedouin patients was found in every year of follow-up [Table 2], with lower HbA1C levels in the Jewish group. A significant difference was not found between the years of follow-up within the ethnic groups.

Lower levels of HbA1C were found in those who used an insulin pump [Figure 1]. This difference was found to be significant in every year of follow-up ($P$ = 0.01 in the first year and $P$ < 0.01 thereafter). When adjusted to ethnic origin the significance was lost for the first year of follow-up ($P$ = 0.26) but maintained its significance in the subsequent years. No significant differences in HbA1C were found between gender and different age groups (data not shown).

**Figure 1.** HbA1C levels compared by insulin pump usage during follow-up. The differences between groups in each year are significant ($P \leq 0.01$)




During the first year no variable predicted HbA1C. Pump treatment was found to be predictive for HbA1C levels in every year after the diagnosis, with lower HbA1C levels for the treated group ($P = 0.07$ and $P = 0.01$ for the first and second year, respectively, and $P < 0.01$ thereafter). From the second year onward, ethnicity was also predictive for HbA1C levels with lower levels for the Jewish group ($P = 0.35$ and $P = 0.01$ for the first and second year, respectively, and $P < 0.01$ thereafter).

## DISCUSSION

For the Jewish population, an annual incidence of 10.8/100,000 for T1DM was found, a similar finding to the 11.7/100,000 in recent studies [11]. The Bedouin population reached an annual incidence of 5.1/100,000, which was lower than the 8.0/100,000 reported for Arabs in Israel. These results might reflect lower diagnosis rates in the Bedouin population due to a decreased predisposition for T1DM in this population.

The glycemic control evaluated in our study as represented by HbA1C levels was unsatisfactory. HbA1C levels in all groups overall were higher than recommended by the American Diabetes Association [6]. These outcomes represent the daily reality at a large pediatric diabetes outpatient clinic that provides health care services to a low-medium socioeconomic population in Israel. Our clinic provides no-charge treatment by pediatric endocrinologists, skilled diabetes nurses, dieticians and social workers, offered at least every 3 months for all patients. Monthly follow-up appointments as recommended by the Diabetes Control Complications Trial (DCCT) are hard to achieve in current reality due to limited resources and the large number of patients.

Poor glycemic control among T1DM patients was found in previous studies, with 13.2% of patients reaching the glycemic goal in a recent Brazilian study [12], and better results with 34.2% reaching the glycemic goal in American academic medical centers [13]. Those results reflect the difficulty worldwide of reaching the recommended HbA1C levels in daily practice.

Previous studies have demonstrated the strong influence of ethnicity and socioeconomic status on glycemic control [8,14,15]. As mentioned, the Bedouins are a minority whose cultural and social uniqueness has been much studied. Diabetes has become a major health problem in this population [9], and our findings demonstrated statistically significant poorer glycemic control in the Bedouin group. A recent study investigating diabetes control in the adult Bedouin population in southern Israel revealed a higher prevalence of both types of diabetes and poorer glycemic control [10]. This difference could be explained by a variety of socioeconomic and cultural differences in this unique ethnic population.

Numerous studies have found insulin pump treatment to improve glycemic control and diabetes outcome [16,17]. Our study yielded similar findings. We also found an association between non-Bedouin ethnicity and pump treatment. Noting that insulin pump therapy is included in the national health "basket," this disparity could be attributed to the Bedouin's low interest in such treatment, or to biased patient selection by health care practitioners based on their perception of the families' ability to manage the complexity of such treatment. Moreover, insulin pump treatment might have been a confounder, lowering the HbA1C levels among a larger fraction of the Jewish patients; however, since this study is retrospective, we can only point to this association as a possibility.

Microalbuminuria is a marker for renal damage occurring early in the development of the disease. In childhood-onset T1DM the cumulative prevalence of microalbuminuria is 12–25% [18]. Retinopathy is another common complication of diabetes and its prevalence was reported to be 10–35% in several studies [19]. In our study, diabetic retinopathy and nephropathy were noted in a small proportion of the patients (3.6% and 9%, respectively) with more than 3 years of diabetes duration, a fact that can be explained by the young age of patients and the relatively short duration of the disease.

Celiac and Hashimoto's thyroiditis are two autoimmune diseases that have been associated with the incidence of T1DM [20,21]. Hashimoto's thyroiditis was diagnosed in 11.4%, results similar to those found in the literature. Celiac disease, diagnosed with gastrointestinal biopsy, was found in 10.2% of our subjects, a result somewhat higher than the 4.8% in a similar study [21].

DKA is a consequence of severe insulin deficiency resulting in hyperglycemia and an accumulation of ketone bodies

DKA = diabetic ketoacidosis

in the blood, with subsequent metabolic acidosis. DKA is a life-threatening condition with the potential of permanent medical and neurological sequelae. Approximately 30% of new-onset patients present with ketoacidosis [22]. While the prevalence of DKA at presentation in the Jewish group was similar to that in the literature (33%) [23], the prevalence in the Bedouin group was significantly higher (56%). This difference can partly be explained by lower awareness of the disease and its symptoms, leading to this life-threatening situation. However, no significant differences were found between the groups regarding DKA after diagnosis as this situation might not be overlooked by the families of known diabetic patients from both ethnic origins.

Parents of diagnosed diabetic patients should learn how to recognize and treat impending DKA with additional rapid- or short-acting insulin and oral fluids, while the entire population should be guided to be aware of DM symptoms and to seek medical assistance early in the course of the disease to prevent DKA in new-onset T1DM patients [24]. Efficient prevention programs for the entire population have been implemented with great success, significantly lowering the cumulative frequency of DKA in presentation of new-onset type 1 diabetes [25].

## CONCLUSIONS

The unsatisfactory clinical outcomes in our study reflect the urgent need for new initiatives and aggressive campaigns to facilitate better awareness of type 1 diabetes mellitus and its treatment options among patients and families. More resources should be directed to address T1DM in the general population and especially among the Bedouin communities.

**Corresponding author**
**Dr. E. Hershkovitz**
Pediatric Endocrinology Unit, Soroka Medical University Center, P.O. Box 151, Beer Sheva 84101, Israel
**Phone:** (972-8) 640-3517
**Fax:** (972-8) 640-0528
**email:** elih@bgu.ac.il

## References

1. Vandewalle CL, Coeckelberghs MI, De Leeuw IH, et al. Epidemiology, clinical aspects, and biology of IDDM patients under age 40 years. The Belgian Diabetes registry. *Diabetes Care* 1997; 20: 1556-61.
2. Patterson CC, Dahlquist GG, Gyürüs E, Green A, Soltesz G. Incidence trends for childhood type 1 diabetes in Europe during 1989-2003 and predicted new cases 2005-20: a multi centre prospective registration study. *Lancet* 2009; 373: 2027-33.
3. Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Eng J Med* 1993; 329: 977-86.
4. Nordwall M, Arnqvist HJ, Bojestig M, Ludvigsson J. Good glycemic control remains crucial in prevention of late diabetic complications – the Linköping Diabetes Complications Study. *Pediatr Diabetes* 2009; 10 (3): 168-76.
5. Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with microvascular and macrovascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 2000; 321: 405-12.
6. American Diabetes Association. Standards of Medical Care in Diabetes – 2010. *Diabetes Care* 2010; 33 (Suppl. 1): S11–61.
7. Silverstein J, Klingensmith G, Copeland K, et al. American Diabetes Association. Care of children and adolescents with type 1 diabetes: a statement of the American Diabetes Association. *Diabetes Care* 2005; 28: 186-212.
8. Carter PJ, Cutfield WS, Hofman PL, et al. Ethnicity and social deprivation independently influence metabolic control in children with type 1 diabetes. *Diabetologia* 2008; 51 (10): 1835-42.
9. Abou-Rbiah Y, Weitzman S. Diabetes among Bedouins in the Negev: the transition from a rare to a highly prevalent condition. *IMAJ Isr Med Assoc J* 2002; 4: 687-9.
10. Cohen AD, Gefen K, Ozer A, et al. Diabetes control in the Bedouin population in southern Israel. *Med Sci Monit* 2005; 11: CR376-80.
11. Kotton S; Israel IDDM Registry Study Group – IIRSG: Incidence of type 1 diabetes mellitus in the 0- to 17-yr-old Israel population, 1997–2003. *Diabetes Care* 2007; 8: 60-6.
12. Gomes MB, Coral M, Cobas RA, et al. Prevalence of adults with type 1 diabetes who meet the goals of care in daily clinical practice: a nationwide multi center study in Brazil. *Diabetes Res Clin Pract* 2012; 97: 63-70.
13. Grant RW, Buse JB, Meigs JB; University Health System Consortium (UHC) Diabetes Benchmarking Project Team: quality of diabetes care in U.S. academic medical centers: low rates of medical regimen change. *Diabetes Care* 2005; 28: 337-442.
14. Mayer-Davis EJ, Bell RA, Dabelea D, et al. SEARCH for Diabetes in Youth Study Group The many faces of diabetes in American youth: type 1 and type 2 diabetes in five race and ethnic populations: the SEARCH for diabetes in youth study. *Diabetes Care* 2009; 32 (Suppl 2): S99-101.
15. Kamps JL, Hempe JM, Chalew SA. Racial disparity in A1C independent of mean blood glucose in children with type 1 diabetes. *Diabetes Care* 2010; 33: 1025-7.
16. Doyle EA, Weinzimer SA, Steffen AT, Ahern JA, Vincent M, Tamborlane WV. A randomized, prospective trial comparing the efficacy of continuous subcutaneous insulin infusion with multiple daily injections using insulin glargine. *Diabetes Care* 2004; 27: 1554-8.
17. Ahern JH, Boland EA, Doane R, Vincent M, Tamborlane WV. Insulin pump therapy in pediatrics: a therapeutic alternative to safely lower HbA1C levels across all age groups. *Pediatr Diabetes* 2002; 3: 10-15.
18. Amin R, Widmer B, Prevost AT, et al. Risk of microalbuminuria and progression to macroalbuminuria in a cohort study with childhood onset type 1 diabetes: prospective observation study. *BMJ* 2008; 336: 697-701.
19. Massin P, Erginay A, Mercat-Caudal I, et al. Prevalence of diabetic retinopathy in children and adolescents with type-1 diabetes attending summer camps in France. *Diabetes Metab* 2007; 33: 284-9.
20. Glastras SJ, Craig ME, Verge CF, Chan AK, Cusumano JM, Donaghue KC. The role of autoimmunity at diagnosis of type 1 diabetes in the development of thyroid and celiac disease and microvascular complications. *Diabetes Care* 2005; 28: 2170-5.
21. Crone J, Rami B, Huber WD, Granditsch G, Schober E. Prevalence of celiac disease and follow-up of EMA in children and adolescents with type 1 diabetes mellitus. *J Pediatr Gastroenterol Nutr* 2003; 37: 67-71.
22. Rewers A, Klingensmith G, Davis C, et al. Presence of diabetic ketoacidosis at diagnosis of diabetes mellitus in youth: the search for diabetes in youth study. *Pediatrics* 2008; 121: e1258-66.
23. Lansdown AJ, Barton J, Warner J, et al., Brecon Group. Prevalence of ketoacidosis at diagnosis of childhood onset Type 1 diabetes in Wales from 1991 to 2009 and effect of a publicity campaign. *Diabet Med* 2012; 29 (12): 1506-9.
24. Wolfsdorf J, Glaser N, Sperling MA; American Diabetes Association. Diabetic ketoacidosis in infants, children, and adolescents: a consensus statement from the American Diabetes Association. *Diabetes Care* 2006; 29: 1150-9.
25. Vanelli M, Chiari G, Ghizzoni L, Costi G, Giacalone T, Chiarelli F. Effectiveness of a prevention program for diabetic ketoacidosis in children. An 8-year study in schools and private practices. *Diabetes Care* 1999: 22: 7-9.