

# Blood glucose monitoring in children and adolescents with Type 1 Diabetes Mellitus

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## Abstract

**Aim:** The aims of this review are to explore and quantify the importance of blood glucose monitoring on glycaemic control in children and adolescents with Type 1 Diabetes Mellitus (T1DM).

**Methods:** A literature search of the major bibliographic databases found 11 observational studies which met the inclusion criteria of this review.

**Results:** 9 of the 11 papers found a significant link between self-monitoring of blood glucose (SMBG) frequency and HbA1c reduction, with SMBG monitoring 4 times daily leading to a further reduction in HbA1c of 1% compared to once daily monitoring. Frequent SMBG was correlated to higher social status, higher self-efficacy and increased parental involvement and was a sign of better global self-care behaviour. It was also noted that frequent SMBG leads to improved glycaemic control only if patients are taught what to do with the results and if they have an insulin regimen that allows for adjustment of insulin doses in response to blood glucose values.

**Conclusion:** Frequent SMBG monitoring is an important part of diabetes self-management in children and adolescents with T1DM because it results in a significant reduction in HbA1c. In the long-term this will lead to a reduction in the late complications of T1DM. Providing children and adolescents with T1DM in Malta with an adequate supply of glucose test strips should serve as an incentive for them to check their blood glucose regularly.

## Keywords

Type 1 Diabetes Mellitus, self-monitoring of blood glucose, HbA1c, children, adolescents

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## Introduction

The Diabetes Control and Complications Trial in 1994 had shown that an entire programme of intensive diabetes management with multiple daily injections of insulin or continuous subcutaneous insulin infusion by pumps, together with frequent self-monitoring of blood glucose (SMBG), significantly reduces and delays the micro- and macro-vascular complications of T1DM in adolescents and may also play a role in preserving residual beta cell function.<sup>1-3</sup> However, it did not assess the effectiveness of SMBG on glycaemic control in its own right.

This review looks at the advantages of SMBG, and discusses the evidence for the correlation between the frequency of SMBG and decrease in HbA1c in children and adolescents with T1DM. The results of a systematic search for studies which have looked at the frequency of SMBG and its impact on health outcomes in children and adolescents with T1DM are presented and results discussed.

## Aim

The aims of this study are to explore and quantify the importance of blood glucose monitoring on glycaemic control in children and adolescents with Type 1 Diabetes Mellitus (T1DM).

## Background

### *Intermittent self-monitoring of blood glucose*

SMBG is recommended in all current clinical guidelines of management of T1DM in children and adolescents.<sup>4,5</sup> SMBG makes intensive diabetes management of glycaemia possible by assisting patients and health care providers evaluate therapeutic effectiveness, adjust insulin doses to correct out-of-target glucose values and detect or prevent hypoglycaemia. All patients on an intensive multiple daily injection insulin regimen or on insulin pump therapy should monitor at least 3-4 times daily. Whilst periodic HbA1c testing indicates the mean blood glucose value over the preceding 2 to 3 months, SMBG provides immediate real-time feedback to

patients regarding glucose levels at various intervals throughout the day. Both tests are essential for assessing glycaemic control.

The best way in which to systematically interpret SMBG data to optimise glucose control is by pattern management.<sup>6</sup> A pattern of high readings at the same testing time each day, lasting at least three days in a row, or a pattern of low readings lasting two days in a row requires further examination to determine the source of the problem and insulin dose adjustment to improve control. Patients can document SMBG readings either by using a written logbook in which daily readings are entered in a single row so that the readings at the same time each day line up in a column, together with notes on insulin doses, exercise, food consumption and hypoglycaemic episodes. Meter data can also be downloaded on to a computer in the clinic, patients' homes or on the internet and it is important that the time and date are properly entered into the meter to ensure accurate downloads. The latter two options will allow more time for data interpretation during clinic visits.

Computerised data management allows for a better assessment of relationships between blood glucose, insulin, meals and activity. Most meter software programmes can provide pie-charts, bar-graphs and electronic logbooks which show the average frequency of meter readings, their mean value over a certain number of days and during set time periods within each day, as well as the percentage of readings above, below and within target ranges. Standard deviation (SD) values are also provided. An SD less than half of the mean blood glucose indicates severe insulin deficiency either because of missed insulin doses, poor matching of carbohydrate intake and insulin, missed meals or erratic insulin absorption secondary to lipohypertrophy.

The glucose meters available today are capable of producing results that meet established standards of accuracy. However accuracy of SMBG data depends on proper use of meters by patients. Errors might arise due to insufficient cleansing of finger tips, inappropriate squeezing to obtain a drop of blood, failure to match calibration codes to strips and soiled meters. Glucose strips exposed to humidity, excess of temperature or high altitude may give falsely elevated results.

## Methods

The main question addressed in this review was 'Does self-monitoring of blood glucose levels lead to improved glycaemic control as measured by HbA1c in children and adolescents with T1DM.' A literature search of major bibliographic databases including Ovid Medline (1950 to week 3, 2011) and EMBASE (1980 to week 14, 2011) was undertaken in April 2011. The inclusion criteria included children up to 18 years of age with T1DM. Study designs could be experimental and observational studies. Case reports were excluded. The intervention studied was SMBG and the outcome was impact on HbA1c. The search

strategy combined the following key words: Type 1 diabetes mellitus, self-monitoring of blood glucose, HbA1c and was limited to 'all child 0-18 years'. The references of articles judged to be relevant were also manually searched for any additional studies.

## Results

The initial search yielded 380 references. Analysis of the abstracts identified 13 articles which were deemed relevant to answer the question addressed in this review. Two were review articles on SMBG which focussed mainly on adults.<sup>6,7</sup> The other 11 papers were observational studies. No randomised controlled trials were identified. Two of the 11 papers did not find a link between SMBG frequency and HbA1c.<sup>8,9</sup> Table 1 gives a summary of the 9 studies which found a positive correlation between SMBG and HbA1c. Of these, 7 were cross-sectional studies and 2 were long term observational studies.

## Discussion

The correlation between frequency of SMBG and better HbA1c levels in children, as in adults,<sup>7</sup> comes mainly from observational studies. Non-experimental studies may be of value in assessing the importance of SMBG in diabetes because there are ethical issues associated with conducting a randomised controlled trial in which a group of patients are denied an intervention which, despite a lack of high-quality supportive evidence, is a well-established part of routine clinical diabetes management. Observational studies also assess efficacy of SMBG under real-life conditions and most involve a large number of patients.

Seven of the studies were cross-sectional and thus examined the association of blood glucose monitoring with HbA1c at one point in time<sup>13-18</sup> or over a relatively short time-frame of two weeks.<sup>10</sup> Two recent studies examined the association over a longer period of time.<sup>11,12</sup>

Anderson et al<sup>13</sup> and Levine B-S et al<sup>14</sup> assessed the frequency of SMBG by self-report measures (questionnaires or from data on logbooks). Haller et al<sup>10</sup> and Helgeson et al<sup>11</sup> downloaded data from meters in the clinic or at home. The studies by Dorchy et al<sup>15</sup>, Moreland et al<sup>16</sup> and Svensson et al<sup>12</sup> used both data from meters and from logbooks. In the study by Evans et al<sup>17</sup>, SMBG was inferred from dispensing of glucose test strips whilst Ziegler et al<sup>18</sup> extracted data from a database of diabetes care and outcome.

When data is determined exclusively by self-report, a relation between SMBG frequency and HbA1c may be under- or over-estimated as patients can easily manufacture or distort the number of times they check blood glucose. In fact, the two studies<sup>8,9</sup> in the literature which found no links between SMBG

**Table 1:** Non-experimental studies assessing the impact of SMBG in T1DM children/adolescents

Reference Study design	Setting	Inclusion criteria including treatment	Number of subjects	Main measures	Main Outcomes
Anderson et al (1997) Cross-sectional study	U.S. Pediatric hospital clinic	Preadolescents and adolescents with diabetes for > 1 year ? insulin regimen	51 (10-12 yrs) 38 (13-15 yrs)	1. HbA1c 2. Assessment of adherence to SMBG based on blood glucose data at O/P visit 3. Parental involvement in SMBG	1. ↑ frequency of SMBG associated with lower HbA1c level SMBG ≤1/day: HbA1c 9.9±0.44% SMBG 2-3/day: HbA1c 8.7±0.17% SMBG ≥4/day: HbA1c 8.3±0.22% 2. ↑ frequency of SMBG significant predictor of better glycaemic control. $r^2=0.19$ , $p<0.02$ 3. Parental involvement in SMBG significantly related to adherence to SMBG 4. SMBG performed more often in younger than in older patients
Evans et al (1999) Cross-sectional study	U.K. diabetes database	Adults and children with T1DM ? insulin regimen	807	1. SMBG frequency inferred from number of strips dispensed. 2. 1 <sup>st</sup> HbA1c	In 258 patients with one valid HbA1c the total number of strips dispensed was a significant predictor of HbA1c ( $p<0.001$ ) with a decline in HbA1c of 0.7% for every 180 strips dispensed over the 6 month period prior to taking HbA1c i.e. equivalent to one extra test/day
Levine et al (2001) Cross-sectional study	U.S. Pediatric Hospital clinic	Children 7-16 yrs T1DM >6months. One O/P visit 1.yr prior study. No medical or psychiatric problem. 35%: 1-2 inj daily 61%: 3 inj daily 4%: ≥4 inj daily	300	1. Frequency of SMBG determined by clinician's notes in patients' charts. 2. HbA1c.	Frequency of SMBG was a significant modifiable predictor of HbA1c $r^2=0.12$ , $p<0.0001$ SMBG ≤1/day: HbA1c 9.1%±0.34% SMBG 3/day : HbA1c 8.9%±0.16% SMBG ≥5/day: HbA1c 8.0%±0.31%
Dorchy et al (1997) Cross-sectional study	Belgian Outpatients clinic	Children <18 years of age with T1DM for >5 months. 89.5%:conventional 11.6%:MDI	144	1. HbA1c. 2. Frequency of SMBG from data in log book and from meter.	After 2 years of diabetes, HbA1c negatively correlated with frequency of SMBG
Haller et al (2004) Cross-sectional study	Children/ adolescents attending a diabetes camp.	9-15 yr children with T1DM >1 yr. 31%: MDI 10%: pump 59%: conventional	229	Frequency of SMBG in parent records of meter data of children two weeks prior to camp.	1. ↑SMBG frequency correlated with lower HbA1c ( $r=0.15$ , $p=0.006$ ) 2. HbA1c decreased by 0.4% for each additional SMBG/day
Moreland et al (2004) Cross-sectional study	U.S. Pediatric Hospital Clinic	8-16 year olds with T1DM for ≥6months	153	1. HbA1c 2. Frequency of SMBG from meters & data from logbook	BGM frequency was an independent predictor of HbA1c ( $p=0.03$ ) SMBG 1/day: HbA1c 9.1% SMBG 2-3/day: HbA1c 8.7% SMBG 4-5/day: HbA1c 8.2% SMBG 6+/day: HbA1c 7.5%
Svensson et al (2009) >10 year observational Multicentre	Danish registry for Childhood Diabetes	T1DM ≤18 yrs age 16.3%: MDI 25.9%: 3 inj daily 57.8%: ≤2 inj daily	2705	SMBG based on electronic or written data	1. SMBG frequency increased over the 10 year period ( $p<0.001$ ) 2. HbA1c of -0.9% with SMBG ≥4 times/day
Ziegler et al (2011) Cross-sectional study	German/Austrian DPV-Weiss database (a standardized prospective computer based documentation of care and outcomes)	T1DM ≤18 years of age on database between 1995-2006 from 233 centers. 11.7%: pump 69.5%: MDI 18.8%: <3 inj/day	26,723	Mean/median values of data from the most recent year of diabetes care were extracted from database for: 1. SMBG Frequency 2. HbA1c	1. ↑frequency significantly associated with lower HbA1c up to 5 SMBG/day; for pump therapy showed further improvement in HbA1c with >5 SMBG/day 2. HbA1c ↓-0.2% every added SMBG/day $p<0.001$ 3. This ↓HbA1c was most pronounced with CSII - 0.27% vs -0.24% with MDI vs. -0.09% with conventional therapy ( $p<0.001$ )
Helgeson et al (2011) 5-yr study observational longitudinal examining relation x5 occasions	U.S. Pediatric Hospital Clinic	Adolescents with T1DM 72%: MDI 26%: pump 2%: 2 injections daily	136	1. Frequency of SMBG assessed by data downloaded from meters in clinic or in 16% of cases from patient's logbook. 2. HbA1c	1. ↑frequency of SMBG significantly correlated with better glycaemic control; $r = -0.32$ ; $p<0.001$ (Similar results when monitoring based on logbook was excluded) 2. SMBG 2/day: HbA1c 9.07% SMBG >5/day: HbA1c 8.12%

frequency and HbA1c, used self-report measures to assess frequency of SMBG. In the 3 year observational study by Belmonte et al<sup>9</sup> there were other reasons why an association between HbA1c and SMBG frequency was not found. Patients were instructed to check their capillary blood glucose only twice daily and they were on a conventional insulin regime of 1-2 injections of intermediate acting insulin together with short acting insulin. In the cross-sectional study by Urbach et al<sup>8</sup>, even though an independent association between frequency of glucose monitoring and HbA1c was not shown, a significant association ( $p < 0.001$ ) between the marital status of the biological parents (an important predictor of HbA1c in this study) and the number of glucose checks performed each day was found. Only 30.4% of children who checked their capillary glucose two or fewer times per day had married parents, compared with 75.2% of those children who checked three or more times daily. This suggests that the marital status of the parents influences glucose control through better compliance with good diabetes self-care skills such as blood glucose monitoring.

Even though one must be cautious in interpreting the association of SMBG frequency and HbA1c on cross-sectional analysis, the results of all these studies, which included a large number of patients in a clinic setting, are consistent and support the view that SMBG is an essential tool in diabetes management. The frequency of SMBG was statistically significant in predicting glycaemic control in all of these studies. However it explains only a relatively small proportion of the variability in HbA1c as shown by the square of correlation coefficient  $r^2 = 0.19$  in Anderson et al<sup>13</sup> and  $r^2 = 0.12$  in Levine B-S et al.<sup>14</sup> There are other factors and good health behaviours that relate to metabolic control and act as confounding factors e.g. physical activity, education, diet, family structure, socioeconomic status.

Anderson et al<sup>13</sup> and Helgeson et al<sup>11</sup> have studied the characteristics of patients that might affect blood glucose monitoring. Increased frequency was significantly correlated to higher social status, higher self-efficacy and increased parental involvement whilst decreased frequency was correlated to low self-esteem, stressful life events, lower parental support and poor relationships with parents.<sup>11,13</sup> Frequent SMBG was also a sign of better global self-care behaviour ( $r = 0.60$ ;  $p < 0.001$ ).<sup>15</sup>

The studies by Ziegler et al<sup>18</sup> and Helgeson et al<sup>11</sup> have made it clear that successful utilisation of SMBG requires patient knowledge, motivation and self-care skills and an insulin regimen that allows for adjustment of insulin dose in response to blood glucose values. With a conventional twice-daily insulin regimen there was a limited benefit of increasing SMBG frequency whilst the most benefit was found in insulin pump patients who can adjust treatment with each blood glucose measurement. In practice,

providing algorithms on how to adjust insulin according to blood glucose readings, can be helpful.

### Conclusion

When assessing these studies blood glucose monitoring four times daily or more, compared to once-daily blood glucose monitoring, is associated with a further reduction in HbA1c of about 1%, in children and adolescents with T1DM on insulin. This decrease will significantly contribute to reduce the occurrence of late diabetic complications in this group of patients, who are at an increased risk of developing late diabetes complications as a result of an expected long duration of the condition. These studies have also highlighted the importance of patient education and empowerment. There is no glycaemic benefit if patients are not capable of interpreting the SMBG result and using it to positively modify diabetes self-management.

At present, Maltese children and adolescents with type 1 diabetes are entitled to receive 50 blood glucose test strips free of charge every 28 days from the Department of Health. This amount is equivalent to about 1.79 blood glucose self-testing opportunities per day. In actual fact, type 1 diabetic children need to perform a minimum of 4 blood glucose tests every day, and on even more occasions if they run into situations where their blood glucose may suddenly become significantly destabilized (e.g. hypoglycaemic episodes, concurrent illness, unusual physical activity). The overwhelming majority of Maltese children already test 4 times daily as a minimum and all of our patients are taught how to adjust insulin doses depending on blood glucose results so that persistently high or low blood glucose readings are not maintained until the next clinic visit. They are also advised to contact the local diabetes team if they don't feel confident to make the necessary adjustments themselves. All patients are given algorithms on how to adjust short acting insulin doses depending on blood glucose results. However a significant number complain that although they accept regular blood glucose monitoring as necessary, it imposes a considerable financial burden on their families. For this reason, it would be ideal for the Department of Health to provide each type 1 diabetic with the minimum requisite of 4 test-strips per day. This would serve as a strong incentive for patients to continue checking their blood glucose regularly as required. Such a change in free glucose test-strip entitlement would increase the cost to the Department of Health from €0.57 per patient per day to €1.28 per patient per day, but the financial savings from a reduction in long-term diabetes-related complications (including diabetic retinopathy, nephropathy and neuropathy) in terms of

provision of healthcare and social services would be incalculable.

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