

GLYCOSYLATED HEMOGLOBIN AND GLYCEMIC CONTROL OF CHILDREN WITH TYPE 1 DIABETES MELLITUS PRESENTING TO A DIABETIC CLINIC

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ABSTRACT

Objective: To describe the association of frequency of visits and glycosylated hemoglobin on glycemic control of children attending pediatric diabetic clinic of a tertiary care hospital.

Material and Methods: A retrospective longitudinal cohort study of 43 patients with type 1 diabetes followed at the pediatric diabetic clinic of Khyber Teaching Hospital, Peshawar, Pakistan from January 2015 to December 2017.

Results: The number of patients enrolled were 43 (24 males and 19 females) with age range of 06 months to 15 years. The initial mean HbA1c of the patients was 10.25 ± 2.7 SD and the final was a mean of 9.5 ± 2.5 SD. 18 patients had improved glycemic control. The patients with regular follow up visits were 35 times more likely to have better glycemic control (OR 1.07) as compared to the ones with worsened glycemic control and irregular visits. The patients with HbA1c testing 3 times were 51 times more likely to have a better glycemic control (OR=1.4, CI=2.2-3.2) as compared to worsened glycemic control.

Conclusion: Regular follow up visits and HbA1c testing were associated with better glycemic control.

Key Words: Diabetes mellitus, HbA1c, glycemic control.

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INTRODUCTION

Achieving good glycemic control is essential to prevent acute complications and risk of long term complications in children with diabetes. It requires continuous medical care, patient and parent self-management education and daily blood glucose monitoring^{1,2}. Pediatric diabetic management has remained a major challenge to the patient, parents and health care providers.^{3,4,5}

Glycemic control is monitored by self-monitoring of blood glucose (SMBG) and HbA1c. HbA1c is glycosylated hemoglobin which is formed by non-enzymatic attachment of glucose in blood to hemoglobin. It is a slow process that is dependent on the prevailing con-

centration of blood glucose, it continues throughout the life span of RBC which is approximately 120 days. The higher the blood glucose concentration and the longer the red blood cell's exposure to it the higher is the HbA1c level expressed as percentage of total hemoglobin. HbA1c measurement reflects the average blood glucose concentration from the preceding 2-3 months. When measured by standardized methods to remove labile forms, the fraction of HbA1c is not influenced by an isolated episode of hyperglycemia.⁶

HbA1c is monitored at least three to four times each year to obtain a profile of long term glycemic control. The lower its value the lesser are the micro vascular complications such as retinopathy and nephropathy. American Diabetic Association (ADA) target values for HbA1c in relation to age are as follows: 7.5% to 8.5% at age <6 years, <8.0% at age 6 to 12 years, <7.5% at age 13 to 18 years and <7.0% at 19 years and above. Individuals who met the ADA target were classified as good control; those with HbA1c > 9, 5% regardless of age were classified as poor control. The value between poor and good are classified as intermediate control⁷. The American diabetic association recommend two

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visits and glycosylated hemoglobin for patients with good glycemic control and quarterly visits and three HbA1c in patients with poor glycemic control².

In children, demographic characteristics such as age, gender, and socioeconomic status affect glycemic control. In addition diabetic factors including type of insulin, dose of insulin, frequency of self-monitoring, diet, duration of diabetes, monitoring of blood glucose and regularity in visiting diabetic clinic also affect glycemic control³.

This study is conducted to find the association of the number of follow up visits and the number of glycosylated hemoglobin performed on the glycemic control of diabetic children enrolled in pediatric diabetic clinic.

MATERIAL AND METHODS

This retrospective longitudinal cohort study was conducted in pediatric diabetic clinic of Khyber Teaching Hospital, Peshawar, Pakistan, from January 2015 to December 2017. The information was retrieved from patients' records; which has their registration Proforma filled on their initial visit with history, examination, date of diagnosis of diabetes and date of registration and investigations advised like HbA1c, urine for micro albumin and their eye fundus examination. The follow up visits were recorded on a separate Proforma each time with all the diabetes related observation and any planning done especially adjustment of insulin dose. The HbA1c levels were recorded. The HbA1c's were all performed from Khyber Teaching Hospital laboratory.

All children with type 1 diabetes under 18 years of age at enrollment in the clinic were included; (from January 2015 till December 2017). The newly diagnosed children (less than 1 year since diagnosis), with no HbA1c or who had a single visit and loss to follow up were excluded.

On enrollment a thorough history which included diabetes related information, physical examination, eye examination, micro albumin and HbA1c value were noted. Follow-up visits were individualized. The follow up visits were counted and interpreted as regular or irregular according to their scheduled visit.

The HbA1c at the time of enrollment was taken as initial and the one noted at the end of the study was taken as final. The final HbA1c is interpreted as improved, static or worsened by comparing it with the initial value at the start of the study.

Multinomial regression test was applied; with glycemic control at the end of the study being dependent variable and number of HbA1c performed per year and

the follow up visits being independent variables.

RESULTS

The data extracted from the patient record was analyzed by SPSS version 20. The total number of patient who fulfilled the criteria were 43, males were 24(55.8%) and 19(44.2%) were females. Mean HbA1c at the time of enrollment was $10.25 \pm 2.7SD$ and at the end of the study $9.5 \pm 2.7SD$. Table 1 shows the number and percentages of glycemic control (improved, static, worsened), follow up visits and the number of HbA1c performed. The total number of visits of all the patients over these 3 years were 573 (OR 1.07 CI 1.4-.7) with a mean of 13.3 visits. In 2015 there were 160 visits, in 2016 there were 146 and in 2017 there were 178 visits.

Model fitting showed significance of 0.000 so the model was fit. Goodness of fit showed p value of 1 so the model is adequate, pseudo R square showed cox of 0.6 and negeljerke of 0.72 so variation in number of HbA1c performed and the follow up visits affect the glycemic control. Likelihood ratio for number of HbA1c is 0.001 and follow up visit is 0.05. Parameter estimation in which worsened glycemic control is compared with improved and static glycemic control showed that a diabetic child with HbA1c performed only once; is 14 times more likely to have improved glycemic control (CI 2.1-2.8) while when performed twice is 33(OR 6.9 CI 1.4-2.5) times more likely and with thrice is 54(CI 0.7-1.5) times more likely to have improved rather than worsened glycemic control. More frequent HbA1c were performed for children with poor glycemic control.

Table 1: Case Processing Summary

Variables		Number & Percentage
glycemic control	Improved	18 (41.9%)
	Static	13 (30.2%)
	Worsened	12 (27.9%)
followup visits	Regular	20 (46.5%)
	Irregular	23 (53.5%)
number of HbA1c	1	12 (27.9%)
	2	13 (30.2%)
	3	6 (14.0%)
	4	4 (9.3%)
	5	2 (4.7%)
	6	3 (7.0%)
	7	2 (4.7%)
	10	1 (2.3%)
Total		43 (100%)

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Children with regular follow up visits were 35 times more likely to have improved glycemic control (CI 1.02-1.52). Table 2 and 3 shows comparison of glycemic control with number of HbA1c and follow up visits respectively.

Classification of the dependent variable shows an overall percentage of 72% so the independent variable though are able to assess the glycemic control of patients but other variables will further help to increase the percentage to nearly 100%.

Table 2: number of HbA1c versus glycemic control

No. of HbA1c performed	Glycemic Control			Total
	Im-proved	Static	Wors-ened	
1	0	6	6	12
2	5	3	5	13
3	5	1	0	6
4	2	1	1	4
5	1	1	0	2
6	3	0	0	3
7	2	0	0	2
10	0	1	0	1
Total	18	13	12	43

Table 3: glycemic control versus follow-up visits

Glycemic control	Follow-up visits		Total
	Regular	Irregular	
Improved	14	4	18
Static	6	7	13
Worsened	0	12	12
Total	20	23	43

DISCUSSION

The paediatric diabetic clinic is set in Khyber Teaching Hospital to improve the care of diabetic children. The HbA1c level was found to be 10.5 at beginning which improved to 9.3 at the end; this level is roughly comparable to other international studies^{8,9}. and a study conducted by Ayeha Abdul Qayyum et al at NICH Karachi¹⁰. The reason for this high mean HbA1c in this study can be the variable ages of the children, their initial HbA1c level, their duration of diabetes being different and a lack of endocrinologist in this diabetic clinic¹¹. Age being a factor affecting glycemic control is shown in many studies and pubertal age is found to be the one associated with poor glycemic control because of psychosocial and hormonal changes occurring at

pubertal age^{11,12}. the children with unsatisfactory HbA1c level in the first and second year of their disease is found to predict a poor glycemic control in future^{13,14}. The longer the duration of the diabetes the control worsens¹⁵. The absence of an endocrinologist in a diabetic clinic in a tertiary care hospital where all the complicated and uncontrolled patients are referred was found to be the reason for poor glycemic control¹⁶.

Regular follow up visit has a positive effect on the glycemic control of the children. The same was clearly evident by multinomial regression test that a child with regular visit was 37 times more likely to have improved glycemic control than the one with worsened glycemic control. The reason being face to face diabetic education about diet, insulin injection technique, site of injection, site rotation and insulin dose adjustment^{17,18}. Irregular visit would obviously result in loss of this opportunity^{19,20}.

The recommended number of glycosylated hemoglobin is three to four per year. Though the recommendation is twice per year for well controlled and more frequent for poorly controlled. This study showed that the patient with only one HbA1c were less likely to have an improved glycemic control and as the number increased to 2 and 3 there were 16 and 33 times improved glycemic control. For better glycemic control 4 HbA1c is required, less frequent HbA1c is required after achieving better glycemic control and more frequent for poorly controlled patients¹⁹. In this study more HbA1c were required for the patient in the beginning and for ones with poorly controlled diabetes. The similar fact was noted by other studies as well²⁰.

Apart from these two factors i.e. the follow up visit and the number of glycosylated hemoglobin other factors affect the glycemic control of diabetic children which are demographic and disease related. These factors along with the ones already studied will better explain the glycemic control of the children enrolled in diabetic clinic.

CONCLUSION

At least 4 times estimation of HbA1c per year and regular follow up visits improved the glycemic control in type I diabetes mellitus.

RECOMMENDATIONS

It is recommended that for prevention of micro-vascular and macro-vascular complications an age appropriate HbA1c is required which can be achieved by a multidisciplinary team including an endocrinologist, a diabetic nurse and nutritionist.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

- Amir S:** Case collection ,data analysis, typing , references
- Afridi JM:** Case Collection & data
- Muneer A:** Literature review
- Raheem F:** Overall supervision

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.