HbA1c CONTROL:
CAN WE PREDICT HbA1c CONTROL IN TYPE 2 DIABETIC PATIENTS WITHOUT PERFORMING THIS TEST?

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ABSTRACT… Background: Diabetes Mellitus (DM) is a serious worldwide health concern. Pakistan is among the top 10 countries with the highest prevalence of diabetes in the world with estimates reaching as high as 21.6% in adults aged 30–79 years. HbA1C is the most useful diagnostic tool to assess the control and progression of disease and related complications. However, the predictors of good and bad control are not well established in our population.

Objective: 1). To assess the level of A1C control among type 2 diabetic patients. 2). To find out factors which can predict uncontrolled A1C.

Setting: Among type 2 diabetes mellitus patients attending the outpatient of Diabetes Endocrine and Metabolic Centre (DEMC) of Lahore General Hospital, Lahore. Period: June 2012 to Feb 2014. Material and methods: Total of 809 patients were randomly selected to assess A1C in this population. At the same time, we assessed other factors associated with uncontrolled A1C. Chart review of the included patients was done using a data collection sheet, structured for this purpose. Patient demographic data was gathered. Specific information including complications and laboratory results (HbA1C, Triglycerides (TG), Dyslipidemias) was collected. Diabetes complication data was obtained clinically and through laboratory workup. The outcome was calculated. Patients with A1C of <7% were considered well controlled. Other lab findings were categorized with results being controlled according to the accepted cut off points.

Results: A total of 809 patients were enrolled. Only 32.9% attained A1C control. Analyses showed that some factors were significantly associated with uncontrolled A1C. They were diabetes-related complications like presence of neuropathy, longer duration of diabetes and Dyslipidemias. When multivariate analysis was carried out, the chances of having uncontrolled A1C were significantly higher among patients who developed neuropathy and longer duration of diabetes, while triglycerides and other dyslipidemias were not statistically significant.

Conclusion: The level of HbA1C is significantly uncontrolled in our population. Uncontrolled HbA1C is more likely to exist in patients with neuropathy and longer duration of Diabetes. High triglycerides and other dyslipidemia are also present in our population, but not statistically significant.

Key words: Diabetes Mellitus, Neuropathy, Triglycerides, Duration of Diabetes

INTRODUCTION
Diabetes Mellitus (DM) is a serious worldwide health concern. Every system in the body gets affected, injuring vital organs, and is largely permanent damage. This results in major contribution economically on health expenditure.¹ Even the developed countries strive to reduce long term complications by early detection and education of population, as we understand that “prevention is better than cure.”²

There are many reasons for rise in the incidence of diabetes worldwide. It was initially thought that affluence is the main reason for this increase. This does not hold true today as we understand that most under developed countries have the highest incidence. Changing lifestyle seems to be the major contributor. With the surge of fast food culture, information technology and reduction in outdoor sports, there is encouragement for everyone to stay home and enjoy. This leads to obesity, which is common even in children.³

Pakistan is a developing country with economic restraints. However the incidence of diabetes in Pakistan is much more than many developed
countries. It is included in top 10 countries with the highest prevalence of diabetes in the world with estimates reaching as high as 21.6% in adults aged 30–79 years.4

HbA1C is the most useful diagnostic tool to assess the control for last three months. It is also recommended now for the initial diagnosis of diabetes.5 It measures the irreversible glycosylation of hemoglobin for the life span of Red Blood Cell. The cost of this test is not much, but for developing countries like Pakistan, it is still an economical hurdle for patients.

There are different criteria in diabetic patients, both clinical and investigational which can predict the control. They can be cost effective and at the same time reliable. Hence, scrutinizing them can give indirect evidence about the control of diabetes. Clinical criteria for this purpose include duration of diabetes, age of the patient, family history, history of diet and exercise capability, whereas investigational criteria include triglycerides, Body mass index, diabetic neuropathy and other dyslipidemias.6

The purpose of this study was to assess the level of HbA1c among type 2 diabetic patients presenting in Diabetes Endocrine and Metabolic Centre of Lahore General Hospital, a tertiary care centre, on their first visit. Overall aim was to find out associated clinical and investigational criteria which can help in predicting control of Diabetes in these patients.

MATERIAL AND METHODS
We carried out a retrospective observational study among type 2 diabetes mellitus patients attending the outpatient clinic of Diabetes Endocrine and Metabolic Centre (DEMC) of Lahore General Hospital, a tertiary care centre, from June 2012 to Feb 2014. A total of 809 patients were randomly selected from the data. As a routine, level of A1C was assessed in them. At the same time, we also assessed the factors associated with uncontrolled A1C. It was carried out by review of the electronic medical record of the included patients and saving them on a data collection sheet, structured for this purpose. Information collected included Diabetes related variables that may influence values of A1C. Patient demographic data including age, gender, blood pressure and BMI were incorporated. Specific information included Diabetes duration, complications and laboratory results (HbA1C and Triglycerides (TG) was collected. Diabetes complication data was obtained clinically and through laboratory workup. For neuropathy, Neurothesiometer (Model W5410) was used to detect vibration sense in all diabetic patients. Hence it was possible to detect neuropathy more scientifically and at early stage by this method. A value of 15 volts or below was taken as normal, between 16 and 24 volts as mild impairment and above 25 volts as moderate to severe impairment in Diabetic Peripheral Neuropathy.7 The HbA1C in our patients was detected through the laboratory in Lahore General Hospital, which detects it by Direct Enzymatic Assay. It was more accurate, specific and cost effective and routinely done in the hospital.8 Patients with A1C of <7% were considered well controlled. Other findings were categorized with results being controlled according to the accepted cut off points, such as, blood pressure (BP) less than 130/80 mmHg.9

RESULTS
Demographic characteristics of the study sample stratified according to A1C control are presented in Table I. Of the 809 patients, 261 patients (32.7%) attained A1C control (A1C <7), whereas remaining (67.7%) were uncontrolled (A1C ⩾ 7). The average age was 47.5 years (SD 10.2) for the A1C controlled group, and 49.2 years (SD 10.8) for the A1C uncontrolled group, with no statistically significant difference (p = 0.31).

There was significant association between genders in two groups. In males, 50.7% were in the A1C uncontrolled group (A1C <7), whereas remaining (67.7%) were uncontrolled (A1C ⩾ 7). The average age was 47.5 years (SD 10.2) for the A1C controlled group, and 49.2 years (SD 10.8) for the A1C uncontrolled group, with no statistically significant difference (p = 0.31).

For BMI, there was no significant association between the two groups with p value 0.499. for obesity, A1C uncontrolled group had 213 patients
(38.86%), and 95 patients (36.4%) in A1c control group (OR 1.11, 95% CI 0.819–1.933). (Table I).

For smoking, 386 patients were current smokers, with 247 (64%) in uncontrolled A1c group, p = 0.029 (OR 1.182 95%CI 1.002 – 1.368). (Table I).

For the duration of DM, the A1C uncontrolled group were more likely to have a longer duration of DM. Mean duration in uncontrolled A1c was 6.82 (SD 3.59) and 3.90 (SD 2.77) in controlled group, with p value <0.0001 (OR 3.55 95%CI 2.59 – 4.87) (Graph 1) (Table I).

Neuropathy was more common in A1C uncontrolled group (p < 0.0001), with 474 patients (86.5%) of A1c uncontrolled group developing this complication. (Graph 2) (Table I).

In dyslipidemias, the A1C uncontrolled group was more likely to have uncontrolled levels of Triglycerides (TG) (≥150 mg/dl) and Total Cholesterol (TC) (≥100 mg/dl) as compared with the A1C controlled group (OR 1.268 95% CI 0.912 - 1.762 and OR 0.938, 95% CI 0.659 - 1.334, respectively). In the Uncontrolled A1c group 412 (75.2%) patients had uncontrolled Triglycerides levels and 420 (76.6%) patients had uncontrolled Cholesterol levels, but it was statistically insignificant. There was no significant difference in the means of Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) in the two groups of A1c. A laboratory data of study sample stratified according to A1C control is presented in Table II. Overall lipid profile (LDL, HDL, TG, and total cholesterol [TC]) was better for the controlled group. Uncontrolled group was more likely to have LDL level ≥100 mg/dl as compared to controlled group, which was not statistically significant p= 0.94 (OR 0.942 95% CI 0.69 - 1.26). For HDL, 663 (82%) patients were in controlled group and 146 (18%) patients in uncontrolled group with p value of 0.075 (Table II).

DISCUSSION
Diabetic control is very important from various perspectives. A good control can decrease complication rate.

There is a gold standard for measuring this control through HbA1c. In a tertiary care centre like ours, it was expected that the control will be better than average due to availability of all services and standard operating procedures in place. An important issue faced in a developing country like ours is affordability of investigations and treatment. It was therefore thought that if we can predict control by alternative ways, it can reduce the cost for the end user.10

It is documented in guidelines that the control should be individualized for every patient. Patients presenting in a tertiary care are different from primary care due to time elapsed between diagnosis and the start of treatment.
### Table-I. Study sample demographic characteristics stratified according to A1C control.

<table>
<thead>
<tr>
<th></th>
<th>Total N (%)</th>
<th>Uncontrolled (A1c &gt;7) N (%)</th>
<th>Controlled (A1c &lt;7) N (%)</th>
<th>OR (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Sample</strong></td>
<td>N = 809</td>
<td>N = 548 (67.7%)</td>
<td>N = 261 (32.3%)</td>
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<tr>
<td><strong>Age (Years)</strong></td>
<td>Mean (SD)</td>
<td>48.66 (10.63)</td>
<td>49.21 (10.8)</td>
<td>47.49 (10.2)</td>
<td>0.031</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
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<tr>
<td>Male</td>
<td>387 (47.8%)</td>
<td>278 (50.7%)</td>
<td>109 (41.8%)</td>
<td>0.82 (0.69 - 0.97)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Female</td>
<td>422 (52.2%)</td>
<td>270 (49.3%)</td>
<td>152 (58.2%)</td>
<td>1.18 (1.03 - 1.35)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>Mean (SD)</td>
<td>28.37 (5.84)</td>
<td>28.23 (5.69)</td>
<td>28.67 (6.14)</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>233 (28.8%)</td>
<td>162 (29.6%)</td>
<td>71 (27.2%)</td>
<td></td>
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</tr>
<tr>
<td>Over Weight</td>
<td>268 (33.1%)</td>
<td>173 (31.6%)</td>
<td>95 (36.4%)</td>
<td></td>
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</tr>
<tr>
<td>Obese</td>
<td>308 (38.1%)</td>
<td>213 (38.8%)</td>
<td>95 (36.4%)</td>
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<tr>
<td><strong>Current Smokers</strong></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>386</td>
<td>247</td>
<td>139</td>
<td>1.18 (1.02 - 1.36)</td>
<td>0.029</td>
</tr>
<tr>
<td><strong>Diabetes Duration</strong></td>
<td>Mean (SD)</td>
<td>5.88 (3.69)</td>
<td>6.82 (3.59)</td>
<td>3.90 (2.77)</td>
<td></td>
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<tr>
<td>Upto 5 Years</td>
<td>394 (48.7%)</td>
<td>213 (38.9%)</td>
<td>181 (69.3%)</td>
<td>1.78 (1.58- 2.03)</td>
<td></td>
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<tr>
<td>&gt; 5 Years</td>
<td>415 (51.3%)</td>
<td>335 (61.1%)</td>
<td>80 (30.7%)</td>
<td>0.50 (0.41 - .61)</td>
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<td><strong>Neuropathy</strong></td>
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<tr>
<td>Yes</td>
<td>624 (77.1%)</td>
<td>474 (86.5%)</td>
<td>150 (57.5%)</td>
<td>0.66 (0.59 - 0.74)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>185 (22.9%)</td>
<td>74 (13.5%)</td>
<td>111 (42.5%)</td>
<td>3.15 (2.44 - 4.06)</td>
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<tr>
<td><strong>SBP</strong></td>
<td>Mean (SD)</td>
<td>134.02 (48.41)</td>
<td>134.08 (54.5)</td>
<td>133.9 (21.05)</td>
<td></td>
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<tr>
<td>DBP</td>
<td>Mean (SD)</td>
<td>83.75 (11.04)</td>
<td>83.42 (10.93)</td>
<td>84.4 (11.26)</td>
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</table>

There is lesser resistance in changing lifestyle, accepting change in treatment and coming for follow up. It is not difficult to assess the effect of these changes. Different clinical and investigational findings clearly document positive and negative effects. Literature has documented variable HbA1c in different parts of the world. Improvement in education alone has shown good effect on control. The primary care physicians see majority of these patients and have their own preferences to refer poor control patients to a tertiary care centre for control, which can be a factor in poor control of these high HbA1c in patients presenting here.

Several documentations are available in the literature with different findings on HbA1c control. Taleb et al documented a prevalence of 30% HbA1c control in patients from Lebanon. In Amman, Jordan, Al-Khawaldeh and colleagues documented a less than 50% control of diabetes in their cohort of patients. Similarly, bad control has been reported from Canada by Harris et al, with almost half of T2DM patients in primary
care did not achieve glycemic target. Improving program quality resulted in better results. \[^{15}\]

We documented in this study that population presenting here has a 32.7% control, comparable to other studies in different parts of the world, but this was not what was expected (Table I). There was no effect of being cared for in a tertiary care centre. There could be many reasons for this finding. Lack of education, poor follow up, poor family support and high cost of medicine and investigation could be important factors. Point to note here is that although services were free in our hospital, there was difficulty to provide them 100% to everyone due to lack of resources, overcrowding and time wasting at places where these services were provided. \[^{16}\]

In this study, there were more male patients in the uncontrolled group and more female patients in the control group (Table I). It was also statistically significant. Bahijri SM et al \[^{17}\] have documented similar finding in Saudi Arabia, where males were more likely to have poor control of diabetes. Exact cause is unknown, but more careless attitude towards lifestyle change and irregular medicine intake could be possible reasons. We also found in our study that smoking, systolic and diastolic blood pressure, were not related with control of diabetes.

In our study, patients with neuropathy were 86.5% in uncontrolled A1C (Table I, Graph 2), which was very high as well as statistically significant. El-Salem et al showed in their study that A1C is strongly associated with neuropathy. This study was different from ours in many respects. Patient number was less in their study than our study. Other reason could be an earlier poor control in our population, with lack of awareness, and late presentation. However they used nerve conduction assessment as tool to identify neuropathy which was gold standard. His results of more than 50% were also less than in our population. Possible reason for this difference could be geographical,
smaller patient pool, delay in treating the early stages of the disease in our population or any other unknown factor. It was documented by Fox et al that there was no correlation of control of diabetes with neuropathy.\textsuperscript{18} They did not find an association between neuropathy and A1C control. Higher prevalence of significant neuropathy can be regarded as a predictor for poor control from our study findings.

High percentage of patient in this study were obese and were more in uncontrolled group (38.8\%) (Table I). Similarly high number of patients were present in the over-weight and normal weight patient group among uncontrolled group. However they were not statistically significant. Yan Y et al have documented that BMI has a significant role in poor control of diabetes.\textsuperscript{19} This prevalence in this study suggests that more steps need to be taken for decreasing BMI in our population.

In addition, the duration of Diabetes in our study was very significant and affecting A1C control (Table I, Graph 1). It was 6.82 years in uncontrolled group as compared to 3.9 years in the controlled group with a p value of <0.0001. Noureddin et al has documented that duration of diabetes was important but insignificant statistically.\textsuperscript{6} Increasing duration of diabetes can result in higher A1C levels by affecting resistance to medication and need for higher doses. Long duration can also cause depression resulting in poor control with time. This is in addition to few established facts like beta cell deterioration with time and increasing resistance.

In our study, diabetics with poor A1C levels were more likely to have higher triglycerides (TG), total cholesterol (TC), HDL and LDL, but it was similar for those with good control. Hence it was not statistically significant (Table II). It was also observed that in uncontrolled group, men were <40 and women were <50. Mullugeta et al found similar results in their study with high dyslipidemias and significantly high TG’s.\textsuperscript{20} They reported that strong relationship exists between A1C and dyslipidemia, especially serum Triglycerides (TG). Similarly, Goudswaard et al documented that poor glycemic control is strongly associated with high levels of TG. They also documented in a bigger patient pool that fasting blood sugar was relatively a better indicator for control and it is difficult to assess predictors of poor A1c. It can be suggested on this basis that insulin resistance attributes in causing high TG levels in the blood.\textsuperscript{21} These findings were closer to our findings in this study, however not statistically same. It suggests that there is global similarity in association of triglycerides with poor A1c control. Difference in our setup can be attributed to our patient dietary habits and other cultural differences. Patient pool is also small, and more studies are required to confirm these findings.

**CONCLUSION**

The level of HbA1C is significantly uncontrolled in our population, and similar to documented literature elsewhere. Uncontrolled HbA1C is more likely to exist in patients with longer duration of diabetes and neuropathy. Uncontrolled dyslipidemia is documented high, but not statistically significant in our population of diabetics.

**LIMITATIONS**

There are several limitations in our study. First is that our hospital is a tertiary care institute, catering specialty patients. It may not be a true reflection of population of diabetic patients in our community. Second is that this was a smaller pool of patients selected on convenience sampling technique. There is need to carry out more studies with holistic selection of patients, to decrease chances of bias and more representative sample. There is poor co-ordination between different departments, which are also dealing with similar patients in their wards. We therefore suggest a relatively larger registry, just like for Dengue patients established at government level, to predict true figures and plan better for assessment and risk reduction.

**REFERENCES**


“Vision is the art of seeing what is invisible to others.”

Jonathan Swift

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<tr>
<th>Sr. #</th>
<th>Author's Full Name</th>
<th>Contribution to the paper</th>
<th>Author’s Signature</th>
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<tr>
<td>1</td>
<td>Dr. M. Imran Hasan Khan</td>
<td>Research idea, Supervision, Review of literature, Write up and Final review of the manuscript</td>
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<tr>
<td>2</td>
<td>Ehsan Ullah</td>
<td>Data Collection, Write Up</td>
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<tr>
<td>3</td>
<td>Zohaib Abbas Khan</td>
<td>Statistical Analysis Result calculation and writing.</td>
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<tr>
<td>4</td>
<td>Salman Shakeel</td>
<td>Data collection and entry in the SPSS</td>
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<td>5</td>
<td>Amina Javid Qaiser</td>
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