DIABETES MELLITUS;
SIGNIFICANCE OF HbA1c DETERMINATION IN PATIENTS

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ABSTRACT… Objective: This study was done to find HbA1c levels in diabetes mellitus (DM) patients presenting at Bolan Medical Complex Hospital Quetta and observe the effects of antihyperglycemic treatment and physical exercise on HbA1c level. Study design: A cross sectional comparative study. Patients and methods: One hundred (100) patients were selected from Bolan Medical complex Hospital Quetta. Patients were divided in three groups. Group A included the patients who were on antihyperglycemic drugs, following dietary restrictions and doing physical exercises. Group B included patients who were on antihyperglycemic drugs following dietary restrictions but not doing physical exercises. Group C included the patients who were not using any antihyperglycemic drug, not following dietary restriction and not doing any physical exercise. HbA1c of all patients was determined, data was analyzed using SPSS. Anova was applied. Results: HbA1c of group A was higher than group B and group C. HbA1c of group B was higher than group C. Conclusions: HbA1c is a valuable test for monitoring glucose control over extended period of time and plays role in taking measures to avoid diabetes mellitus complications, therefore it should be tested regularly.

INTRODUCTION
Measurement of HbA1c, also known as HGBA1C, A1C and glycated hemoglobin, is an effective test in monitoring long term glucose control in people with diabetes mellitus (DM) as it provides retrospective index of the integrated plasma glucose values over an extended period of time and is not subject to wide fluctuations observed when assessing blood glucose concentration¹. HbA1c is formed by non-enzymatic condensation of glucose with N-terminal valine residue of each B-chain of HbA. Formation of HbA1c is essentially irreversible and blood level depends on both, life span of red blood cells (120days) and blood glucose concentration. It represents values of glucose over the preceding 6-8 weeks. In DM attachment of glucose to hemoglobin increases. The rate of HbA1c formation is directly proportional to ambient blood glucose concentration. A rise of 1% in HbA1c corresponds to approximate average increase of 36mg/dl in blood glucose.²

Persistent elevations in blood glucose (and therefore HbA1c) increases risk of long term complications of DM such as coronary heart disease, heart failure, stroke, kidney failure, blindness, neuropathy, gangrene, gastroparesis and poor wound healing³. American diabetes association (ADA) and international diabetes federation (IDF) guidelines are that HbA1c test be performed at least twice in a year in patients that are meeting treatment goals, and quarterly in patients not meeting treatment goals or diabetes patients whose therapy has been changed.⁴

HbA1c test is recommended for monitoring blood sugar control in DM patients and checking blood sugar control, in people who might be prediabetic⁵. The present study was conducted to find HbA1c levels in DM patients presenting at Bolan Medical Complex Hospital (B.M.C.H) Quetta and observe the effects of antihyperglycemic treatment and exercise on HbA1c level and therefore on glycemic control.

PATIENTS AND METHODS
One hundred (100) patients were selected from Bolan Medical Complex Hospital (BMCH) Quetta. Age of patients ranged from 25 to 62 years. Fifty eight (58) patients were males and forty two (42)
patients were females. Ninety one (91) patients knew that they have diabetes mellitus (DM). Out of these 91 patients who were aware of being DM patients, 57 patients were on antihyperglycemic treatment, following dietary restrictions and doing 150 minutes or more physical exercise per week regularly (group A). 34 patients were on antihyperglycemic drugs, following dietary restrictions but not performing any physical exercises (Group B). 09 patients were those who never knew before presenting at BMCH that they have DM. They were not getting any treatment (group C).

Subjects suffering from anaemia, chronic renal failure, sever liver disease, having recent blood loss or having recent blood transfusion were excluded from the study. Patients whole blood was analyzed for HbA1c level by method which combines chemical binding of boronate to HbA1c with fluorescent quenching effect that this binding exerts on a fluorescent marker bound to the boronate molecule. Decrease in the fluorescence of the active gradient is measured. Results were expressed in diabetes control and complications trial (DCCT) percentage. The international diabetes federation (IDF) recommend values below 6.5% DCCT.⁶

Statistical analysis: Data was analyzed using SPSS. Anova was applied. Mean ± SD was calculated in all three groups. Student’s t’ test was applied to find significance. ‘P’ value was read from specific table.

RESULTS AND OBSERVATIONS
HbA1c was determined in one hundred (100) patients. Fifty eight (58) patients were males and forty two (42) were females. The age of patients ranged from 25 to 62 years. Mean ± SD age in group A was 43.11 ± 9.58, mean ± SD age in group B was 43.41 ± 10.31 and mean ± SD age in group C was 37.56 ± 6.29.

HbA1c in group A ranged from 3.6% to 7.2%. In this group 88% patients had HbA1c lower than recommended value by international diabetes federation (IDF) i.e. 6.5% and 12% patients had higher than 6.5%. Mean ± SD HbA1c in group A was 5.49 ± 0.85. In group B HbA1c ranged from 4.8% to 8.9%. In this group 50% subjects had higher than and 50% patients lower than IDF recommended HbA1c. Mean ± SD HbA1c in group B was 6.54 ± 0.88. HbA1c in group C ranged from 5.4% to 11.9%. In this group 90% patients had HbA1c higher than and 10% patients lower than IDF recommended value. Mean ± SD HbA1c in group C was 8.97 ± 2.09.

HbA1c of group A was comparable to group B and significant statistically (P < 0.005). HbA1c of group B and group C was comparable and significant statistically (P< 0.005). HbA1c of group A and group C was also comparable and significant statistically (<0.005), Table-I.

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean ± SD HbA1c (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>5.49± 0.85 (n=57)</td>
</tr>
<tr>
<td>Group B</td>
<td>6.54 ± 0.88 (n=34)</td>
</tr>
<tr>
<td>Group C</td>
<td>8.97 ± 2.09 (n=9)</td>
</tr>
</tbody>
</table>

Table-I. Comparison of HbA1c results among group A, group B and group C.

Key: n = number of patients    S = Significant

DISCUSSIONS
Diabetes mellitus (DM) is a group of metabolic disorders in which glucose is underutilized leading to hyperglycemia. DM patients may experience acute life threatening hyperglycemic attacks of ketoacidosis or hyperosmolar coma. With progression of disease, patients are at risk of developing late complications like retinopathy, neuropathy, and renal failure, atherosclerosis resulting in stroke, gangrene, coronary heart diseases, blindness and other morbidities.³

DM management requires prevention of hyperglycemia and decreasing risk of developing late complications⁷. To ascertain effects of DM
management (medicines, exercises, and life style adjustments) various investigations are done, like blood glucose estimation, fructosamine, microalbumin, HbA1c and others. HbA1c is considered a useful test as it reflects glycemic control over previous 6-8 weeks. There is a linear relationship between average blood glucose and HbA1c in previous 6-8 weeks.8

The present study was conducted at Bolan Medical Complex Hospital (BMCH) Quetta, focusing on HbA1c level of DM patients divided in three groups. First group (group A) comprised of those DM patients who were taking antihyperglycemic drugs, following dietary restrictions and doing physical exercises. The second group (group B) included patients who were taking antihyperglycemic drugs and following dietary restrictions but not doing any physical exercises. The third group (group C) comprised patients who before presenting at BMCH, never knew that they have DM. They were not using any drug for DM, not following any dietary restrictions and not doing any physical exercise.

The results of present study showed that the mean and range of HbA1c in group A was higher than group B and C. Mean and range of HbA1c of group B was also higher than group C on comparison. The findings of present study are consistent with findings of previous similar studies which reported that HbA1c of DM patients with good glucose control was close to or within reference range while higher levels were found in DM patients with persistently elevated glucose. Good dietary control, antihyperglycemic therapy and physical exercises reduced HbA1c significantly. In studies proving that intensive measures reduce the risk of retinopathy, neuropathy and nephropathy, HbA1c was the corner stone. For example risk of retinopathy increased with increase in HbA1c and a single measure of HbA1c predicted the progression of retinopathy four years later. A 10% lower HbA1c decreased the 45% risk of having retinopathy7. It has been reported that the risk of main complications of DM decreases notably with decrease in HbA1c level8. The Selvin, Elizabeth et al9 have shown in their study that the HbA1c is a strong predictor of individuals who will develop DM, and is an important marker of subsequent cardiovascular risk.

American diabetes association (ADA) believes that as HbA1c test does not require the patient to fast this added convenience will encourage people to get tested. Early diagnosis of prediabetes can enable patients to make life style or drug changes to thwart diabetes on set10. Diabetes Prevention Programme (DPP) research group has proved that the life style interventions (e.g.; weight loss) delay DM by 58%11. The high association of HbA1c with diabetes risk, complications and mortality makes it important biomarker for DM and other high risk individuals.

Use of HbA1c increases patient centeredness of care given the improved convenience and comfort of testing.12

CONCLUSIONS
HbA1c is a valuable laboratory test. It reflects glycemic control over an extended period, therefore it is useful in monitoring blood glucose control in DM patients and checking blood glucose in prediabetes. HbA1c determination is cornerstone for drugs and lifestyle intervention to prevent complications of DM. It is suggested that HbA1c should be tested twice in a year in patients who are reaching treatment goals and quarterly in patients not reaching the treatment goals.

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REFERENCES


