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Original Research Article

Correlation between HbA1c and Diabetic Complications

Muhammad Usman Nazir, Fatima Qayyum, Sikander Khan Tanoli, Sania Saeed, Umair Toqueer, Elaf Aslam

Department of General Medicine, Medical A Ward, Ayub Teaching Hospital.

***Corresponding Author Email: drabdul.haq15@gmail.com**

Abstract

Diabetes mellitus is a syndrome of faulty insulin secretion, action or both with multiple complications. Those that affect the eyes, kidneys and peripheral nervous system are collectively called the microvascular complications in contrast to the less diabetes-specific macrovascular complications. Multiple studies in different countries confirm that a higher HbA1c level is an independent risk factor for the development of diabetic complications. Therefore, a descriptive cross sectional study was performed using data from 194 patients in the medical ward in Ayub Teaching Hospital Abbottabad. This study included 105 females and 89 males with documented diabetes. The values of HbA1c were recorded and any macro vascular or micro vascular complication was noted. Most of the patients were using insulin and the oral drug used in most cases was from the class of drugs called sulfonylureas. The majority of the patients had HbA1c values between 7-9 % with CVA as the complication documented in most cases. The micro vascular complication in most cases was neuropathy. Both these types of complications were statistically significantly associated with the levels of HbA1c. Out of all, 122 had hypertension as well with the majority not taking any drug therapy. The macro vascular complications of diabetes were also found to have statistically significant association with hypertension. In conclusion, although most studies negate the impact of strict glycemic control on the macro vascular complications but this effect in turn is indirectly influenced by micro complications, thus, good glycemic control is imperative to prevent the chronic complications of diabetes. The use of HbA1c as a single value may have limited benefit but can be enhanced by keeping an eye on the variability pattern over months or years.

Keywords: Diabetic complications, Micro vascular, Macro vascular, HbA1c

INTRODUCTION

Diabetes mellitus is a syndrome of faulty insulin secretion, action or both with heterogeneity in terms of etiology. This disease is characterized by increased risk of cardiovascular disease by up to four times compared to the non diabetic patients (Bogdan and Oana Albai, 2012). The incidence of this condition is influenced by disease duration, gender and other associated medical conditions. Therefore, good glycemic control is necessary to prevent complications. Besides fasting glucose level, levels of glycated hemoglobin can be calculated to estimate the level of glucose in the blood over a period of 2-3 months (Lind et al., 2009). These glycated hemoglobins are hemoglobins with an attached sugar moiety constituting the HbA1 fraction of the adult hemoglobin. This HbA1c is the predominant fraction of HbA1, the higher levels of which are associated with micro vascular complications (Nitin, 2010). Other than the average levels of HbA1c, the values of HbA1c at different

points in time have possible implications for the clinicians as well as for the researchers (Lind et al., 2009).

The complications of diabetes affecting the eyes, kidneys and peripheral nervous system are collectively called the microvascular complications in contrast to the less diabetes-specific macrovascular complications. Microvascular disease ultimately causes blindness, renal failure and amputation whereas the culmination point for macrovascular disease is, mainly, myocardial infarction and stroke (Nathan, 2014). Multiple studies in different countries confirm that a higher HbA1c level is an independent risk factor for the development of diabetic complications (Marcus et al., 2019). However, this correlation is not statistically significant in most studies in case of macrovascular complications which seem to be, in part, influenced by the vascular diseases. Therefore, the goal of glucose in these patients is moderated by the control of hypertension. The factors that actually influence the glycemic control in most cases are unknown and the research studies in most cases are lagging as well. These determinants of glucose levels are dependent on many factors including religion, culture, behavior, education and income. Thus, the generalization of factors affecting glucose levels in the west is not possible (Kranenburg et al., 2015).

Multiple studies have demonstrated the relationship between glycemia and the complications of diabetes but these studies measured glycemia as just high or low and one occasion mostly limiting the usefulness of the data. Therefore, instead of a single measurement of HbA1c multiple measurements over several years would be more informative. The existence of a threshold of glucose above which complications are inevitable have not been studied in patients with type 2 diabetes. This threshold reference has its significance as the chances of microvascular complications are increased with a significant increase in glycemia whereas that of myocardial infarction increases with any increase in level of glucose in blood above normal (Stratton et al., 2000).

Thus, the aim of this study is to find out the correlation of HbA1c values with diabetic complications which would serve to solidify the already established associations and to give clues as to the ways in which diabetic complications, especially the macro complications, may be predicted. This would ensure steps taken to reduce the risks of developing diabetic complications.

RESEARCH METHODOLOGY

Study Design: *Descriptive cross-sectional study*.

Study Sample: *194 patients*.

Study Duration: *Three months from 20th Aug to 20th Nov 2020*.

Study Population

All the diabetic patients presented to the medical ward in Ayub Teaching Hospital Abbottabad in the previous three months.

Sampling Tool: *Structured questionnaire.*

Sampling Technique: *Non probability sampling (consecutive sampling)*

Sampling Procedure:

Three team members were given the responsibility to collect the data from the medical ward from the admitted patients as well as from the previous records. A Performa was filled with this data which was used for data analysis.

Study Analysis

Done using SPSS 21, frequencies were obtained, presented in the form of tables and crosstabs were used to establish associations. Chi-square test was used for calculation of statistical significance

RESULTS

Of all 194 patients, 90 were above 60 years of age and 93 were in the age range of 40-60 years. Only 9 were <40 years old. Similarly, the data consisted of 105 females and 85 males. Age of onset of diabetes for the vast majority of the patients was between 20 and 60 whereas only 4 patients had onset <20 years of age. Those who developed the disease in old age i.e. >60 years were 49. For the duration of the disease, the vast majority had it for the past fifteen years with a few around one fourth who had the disease for more than 15 years. (Tables.1, 2, 3, 4)

Trend of HbA1c and the complications of diabetes

Overall, the majority of the patients had HbA1c in the range of 7-9% followed by those between 9-11%. However a similar number of patients i.e. 32 and 30 had HbA1c between 6.5-7% and >11%, respectively. Most of the patients in this study had no history of any macro vascular complication related to diabetes whereas about one third i.e. 68 patients had a history of CVA (cerebro-vascular accident). Only 11(5.7%) of the patients had a history of PAD (peripheral arterial disease) while 28 had CAD (coronary artery disease) in the past. In micro-complications, a similar percentage of patients i.e. around 30% had neuropathy and nephropathy whereas only 13%

Table 1. Shows age of the patients

Age	Frequency	Percent	Valid Percent	Cumulative Percent
<40	11	5.7	5.7	5.7
>60	90	46.4	46.4	52.1
40-60	93	47.9	47.9	100.0
Total	194	100.0	100.0	

Table 2. Shows gender of the patients

Gender	Frequency	Percent	Valid Percent	Cumulative Percent
Female	105	54.1	54.1	54.1
Male	89	45.9	45.9	100.0
Total	194	100.0	100.0	

Table 3. Shows age of onset of the diabetic patients

Age of onset of diabetes	Frequency	Percent	Valid Percent	Cumulative Percent
<20	4	2.1	2.1	2.1
>60	49	25.3	25.3	27.3
20-60	141	72.7	72.7	100.0
Total	194	100.0	100.0	

Table 4. Shows duration of the diabetes

Duration of diabetes	Frequency	Percent	Valid Percent	Cumulative Percent
<5 yr	75	38.7	38.7	38.7
>15 yrs	31	16.0	16.0	54.6
5-15yrs	88	45.4	45.4	100.0
Total	194	100.0	100.0	

Table 5. Shows HbA1c of diabetic patients

HbA1c	Frequency	Percent	Valid Percent	Cumulative Percent
>11	30	15.5	15.5	15.5
6.5-7	32	16.5	16.5	32.0
7-9	80	41.2	41.2	73.2
9-11	52	26.8	26.8	100.0
Total	194	100.0	100.0	

Table 6. Shows macro-complication associated with diabetes.

Macro-complications	Frequency	Percent	Valid Percent	Cumulative Percent
CAD	28	14.4	14.4	14.4
CVA	68	35.1	35.1	49.5
None	87	44.8	44.8	94.3
PAD	11	5.7	5.7	100.0
Total	194	100.0	100.0	

Table 7. Shows micro-complication associated with diabetes.

Micro-complications	Frequency	Percent	Valid Percent	Cumulative Percent
Nephropathy	56	28.9	28.9	28.9
Neuropathy	63	32.5	32.5	61.3
None	49	25.3	25.3	86.6
Retinopathy	26	13.4	13.4	100.0
Total	194	100.0	100.0	

Table 8. Shows hypertension associated with diabetes.

Hypertension	Frequency	Percent	Valid Percent	Cumulative Percent
No	72	37.1	37.1	37.1
Yes	122	62.9	62.9	100.0
Total	194	100.0	100.0	

Table 9. Shows drugs used for hypertension

Drugs used for hypertension	Frequency	Percent	Valid Percent	Cumulative Percent
More	5	2.6	2.6	2.6
None	83	42.8	42.8	45.4
One	64	33.0	33.0	78.4
Two	42	21.6	21.6	100.0
Total	194	100.0	100.0	

Table 10. Shows Duration of hypertension

Duration of hypertension	Frequency	Percent	Valid Percent	Cumulative Percent
>15	14	7.2	7.2	7.2
5 yrs	61	31.4	31.4	38.7
5-15	44	22.7	22.7	61.3
None	75	38.7	38.7	100.0
Total	194	100.0	100.0	

had retinopathy. Those patients who had no micro vascular complication were 25%.
(Tables 5, 6, 7)

History, duration and control of Hypertension

In this study sample, 122 patients had hypertension as well, out of whom, 83(43%) were not using any medication. One drug for the treatment of hypertension was being used by 33% of the patients whereas the rest were using a combination of two or more drugs. Out of all the patients who had hypertension 31% had it for less than 5 years while only 7% had the duration of hypertension of more than 15 years. However, quite a significant number had a duration of 5-15 years i.e. 22 %. (Tables 8, 9, 10)

Treatment of diabetes and associated conditions

The majority of the patients in this study were on insulin making up 42% of the patients. The second most used drug was from a group sulfonylurea used by 27% of the patients followed by metformin at 22%. SGLT2 (sodium glucose transporter 2) inhibitors and DPP4 (dipeptidyl peptidase 4) inhibitors were not being consumed by many, comprising a total of 3% and 6% patients, respectively. The vast majority of the diabetic patients in this study had other medical conditions as well mostly infections which made up 63% of the total. However, 12% of patients had none other condition. (Tables 11, 12)

Table 11. Shows diabetes treatment

Diabetes treatment	Frequency	Percent	Valid Percent	Cumulative Percent
Biguanides (metformin)	43	22.2	22.2	22.2
DPP4 inhibitors (sitagliptin)	11	5.7	5.7	27.8
Insulin	83	42.8	42.8	70.6
SGLT2 inhibitors (dapaglifalozin)	5	2.6	2.6	73.2
Sulfonylureas	52	26.8	26.8	100.0
Total	194	100.0	100.0	

Table 12. Shows Associated conditions with diabetes.

Associated conditions	Frequency	Percent	Valid Percent	Cumulative Percent
CHF	10	5.2	5.2	5.2
CKD	31	16.0	16.0	21.1
CLD	8	4.1	4.1	25.3
Infections	122	62.9	62.9	88.1
None	23	11.9	11.9	100.0
Total	194	100.0	100.0	

Table 13. Shows Age* duration of diabetes Cross tabulation

		Duration of diabetes			Total
		<5 yr	>15 yrs	5-15yrs	
Age	<40	8	0	3	11
	>60	27	17	46	90
	40-60	40	14	39	93
Total		75	31	88	194

Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	9.478[a]	4	.050
Likelihood Ratio	10.768	4	.029
N of Valid Cases	194		

Correlation between HbA1c and macro and micro vascular complications

The findings in this study suggested a significant association between the range of HbA1c and the macro vascular complications of the disease with a p value of 0.01. Majority of the patients who had a history of CVA and CAD had HbA1c between 7 and 9 comprising 30 and 12 patients, respectively. The patients who had PAD had an HbA1c value of 9-11 making up a total of 7 cases. However the big majority of the diabetic patients had no macro vascular complication comprising 87 patients. Similarly, the maximum number of patients who had neuropathy and retinopathy had HbA1c in the range of 9-11% making up 21 and 11 cases, respectively. Nephropathy was seen mostly in patients with HbA1c between 7 and 9 whereas nearly one fourth i.e. 49, patients had no micro vascular complication. This association proved statistically significant (p value 0.000). (Tables 14, 15)

Correlation between age of onset of diabetes and duration of diabetes with the value of HbA1c

The data showed that patients with HbA1c of >11 had diagnosis of disease between 20 and 60 years of age. This pattern was followed in all ranges of HbA1c making 54 cases with HbA1c range of 7-9 and 39 cases in the range of 9-11. However, this variation in findings was not found significantly associated with a p value of 0.61. Similarly, there was no statistically significant association between the duration and HbA1c with a p value of 0.12. The majority of the patients with HbA1c >11 had the

Table 14. Shows HbA1c * Macro-complications Cross tabulation

HbA1c * Macro-complications Cross tabulation						
Count		Macro-complications				Total
		CAD	CVA	None	PAD	
HbA1c	>11	5	11	14	0	30
	6.5-7	1	8	23	0	32
	7-9	12	30	34	4	80
	9-11	10	19	16	7	52
Total		28	68	87	11	194

Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	21.678[a]	9	.010
Likelihood Ratio	24.462	9	.004
N of Valid Cases	194		

Table 15. HbA1c * Micro-complications Cross tabulation

HbA1c * Micro-complications Cross tabulation						
Count		Micro-complications				Total
		Nephropathy	Neuropathy	None	Retinopathy	
HbA1c	>11	6	16	2	6	30
	6.5-7	10	6	15	1	32
	7-9	25	20	27	8	80
	9-11	15	21	5	11	52
Total		56	63	49	26	194

Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	33.157[a]	9	.000
Likelihood Ratio	35.573	9	.000
N of Valid Cases	194		

Table 16. HbA1c * age of onset of diabetes Cross tabulation

HbA1c * age of onset of diabetes Cross tabulation					
Count		Age of onset of diabetes			Total
		<20	>60	20-60	
HbA1c	>11	1	6	23	30
	6.5-7	0	7	25	32
	7-9	3	23	54	80
	9-11	0	13	39	52
Total		4	49	141	194

Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	4.464[a]	6	.614
Likelihood Ratio	5.959	6	.428
N of Valid Cases	194		

Table 17. Shows HbA1c * duration of diabetes Cross tabulation

HbA1c * duration of diabetes Cross tabulation					
Count		**Duration of diabetes**			**Total**
		<5 yr	**>15 yrs**	**5-15yrs**	
HbA1c	>11	12	7	11	30
	6.5-7	17	2	13	32
	7-9	33	11	36	80
	9-11	13	11	28	52
Total		75	31	88	194

Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	9.911[a]	6	.128
Likelihood Ratio	10.462	6	.107
N of Valid Cases	194		

Table.18. HbA1c* Age Cross tabulation

HbA1c * Age Cross tabulation					
Count					
		Age			**Total**
		<40	**>60**	**40-60**	
HbA1c	>11	2	12	16	30
	6.5-7	7	14	11	32
	7-9	2	34	44	80
	9-11	0	30	22	52
Total		11	90	93	194

Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	23.830a	6	.001
Likelihood Ratio	20.888	6	.002
N of Valid Cases	194		

disease for <5 years whereas those who had HbA1c between 6.5 and 7 had the duration of 5 years as well. A total of 28 patients had had HbA1c in the range of 9-11 with the duration of diabetes between 5 and 15 years. (Tables 16, 17)

Age of the patient associated with HbA1c value

According to the results of this study, the age of the patient had a statistically significant association with the value of HbA1c. In detail, sixteen patients in the age range 40-60 had HbA1c >11 that number was more than the figures in other two age groups. The patients with HbA1c between 7 and 9 mostly were in the age range of >60 whereas those between 7 and 9 were maximum in the range of 40-60. (Table 18)

Associated medical conditions and HbA1c

There were a total of four medical conditions that were looked for in these diabetic patients namely, congestive cardiac failure, chronic kidney disease, chronic liver disease and infections. The results showed a statistically significant association between the levels of HbA1c and the other illnesses giving a p value of 0.04. To elaborate, the maximum number of patients with HbA1c >11 predominantly had infections as other medical conditions. The same holds true in other HbA1c ranges, however, there were a total of 23 cases with no other medical condition besides diabetes. (Table 19)

Hypertension and macro vascular complications

A total of 122 patients had hypertension in addition to

Table.19. HbA1c * associated conditions Cross tabulation

HbA1c * associated conditions Cross tabulation							
Count		Associated conditions					Total
		CHF	CKD	CLD	Infections	None	
HbA1c	>11	0	1	3	24	2	30
	6.5-7	1	8	1	17	5	32
	7-9	6	11	0	50	13	80
	9-11	3	11	4	31	3	52
Total		10	31	8	122	23	194

Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	21.905a	12	.039
Likelihood Ratio	27.039	12	.008
N of Valid Cases	194		

Table 20. HbA1c * Hypertension Cross tabulation

HbA1c * Hypertension Cross tabulation				
Count		Hypertension		Total
		No	Yes	
HbA1c	>11	9	21	30
	6.5-7	13	19	32
	7-9	33	47	80
	9-11	17	35	52
Total		72	122	194

Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	1.841a	3	.606
Likelihood Ratio	1.860	3	.602
N of Valid Cases	194		

Table 21. Shows Hypertension * Macro-complications Cross tabulation

Hypertension * Macro-complications Cross tabulation						
Count		Macro-complications				Total
		CAD	CVA	None	PAD	
Hypertension	No	7	16	44	5	72
	Yes	21	52	43	6	122
Total		28	68	87	11	194

Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	14.219a	3	.003
Likelihood Ratio	14.462	3	.002
N of Valid Cases	194		

diabetes. Of these, 52 patients had a history of CVA and 21 had CAD with only 6 patients having a history of PAD. There were about one third patients with no macro vascular complications. This variation in result was proved significant statistically with a p value of 0.003. However there was no association between the micro vascular complications of diabetes and hypertension. The p value for this correlation was 0.155. (Table 21)

Table 22. Shows Hypertension * Micro-complications Cross tabulation

Hypertension * Micro-complications Cross tabulation						
Count		Micro-complications				Total
		Nephropathy	Neuropathy	None	Retinopathy	
Hypertension	No	17	24	24	7	72
	Yes	39	39	25	19	122
Total		56	63	49	26	194

Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	5.234[a]	3	.155
Likelihood Ratio	5.227	3	.156
N of Valid Cases	194		

Table 23. Shows duration of diabetes * Micro-complications Cross tabulation

Duration of diabetes * Micro-complications Cross tabulation						
Count		Micro-complications				Total
		Nephropathy	Neuropathy	None	Retinopathy	
Duration of diabetes	<5 yr	20	22	26	7	75
	>15 yrs	10	9	4	8	31
	5-15yrs	26	32	19	11	88
Total		56	63	49	26	194

Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	10.524[a]	6	.104
Likelihood Ratio	10.026	6	.124
N of Valid Cases	194		

Table 24. Shows Duration of diabetes * Macro-complications Cross tabulation

Duration of diabetes * Macro-complications Cross tabulation						
Count		Macro-complications				Total
		CAD	CVA	None	PAD	
Duration of diabetes	<5 yr	11	25	35	4	75
	>15 yrs	2	12	14	3	31
	5-15yrs	15	31	38	4	88
Total		28	68	87	11	194

Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	3.169[a]	6	.787
Likelihood Ratio	3.363	6	.762
N of Valid Cases	194		

Duration of diabetes and complications

The analysis of the results showed no statistical association between the duration of diabetes and the macro or micro vascular complications. Overall, the majority of the patients with diabetes for a duration of >5 years to > 15 years had no complication whereas in micro vascular complications, the majority of the patients with disease duration of 5-15 years had neuropathy or nephropathy. (Tables 23, 24)

DISCUSSION

Recent studies have shown the lesser benefit of mean HbA1c while demonstrating higher utility of glycemic variability particularly over a period of 24 months which was found to be a better predictor of all chronic diabetic complications except for retinopathy and peripheral neuropathy (Cardoso et al., 2018). Moreover, studies have shown that higher levels of HbA1c, one year after diagnosis, were associated with higher risk of diabetes related mortality and morbidity. The increased value of HbA1c during the first six years of diagnosis have been shown to be linked to higher incidence of micro vascular complications (Jeon et al., 2013). One other study has shown association between platelet dysfunction, and HbA1c and diabetic neuropathy, nephropathy and retinopathy (Walinjkar et al., 2019). This decreased utility of HbA1c has been shown in on more study where three glycemic measures were studied namely, mean updated HbA1c, incremental area under the curve (iAUC) and the total area under the curve(tAUC). The results showed both iAUC and tAUC to be better predictors of micro vascular complications than mean updated HbA1c (Maple-Brown et al., 2013).

However, studies also show that HbA1c predicts some adverse outcomes of diabetes better than others. For example, the correlation between risk of infection and penile implant surgery is backed by studies. Therefore, an HbA1c threshold of 8% is given for clinicians to consider for increased risk of infections (Habous et al., 2018). This is further supported by a study done on > 8000 patients showing an increase in incidence of micro vascular complications with HbA1c of >7% and that rises by 30 to 40% per 1% increase in HbA1c. In addition, these complications are affected more than macro vascular complications by age, duration and glycemic control. These micro complications, although, can be minimized by effective glycemic control but cannot be reversed once developed (Ismail-Beigi et al., 2010).

Of all the macro vascular complications, coronary artery disease is the one most influenced by glycemic control and is significant for the fact that CAD as the cause of death has decreased generally except for diabetic patients (Gu et al., 1999). This not only is an important cause of death in diabetic patients but is also a cause of significant economic burden (Kim et al., 2011). Even though, microvascular complications of diabetes are mainly, neuropathy, nephropathy and retinopathy but these have been shown to cause to coronary artery disease. This retinopathy is not directly associated with atherosclerotic plaque but with intima-media thickness which in turn is associated with atherosclerotic plaque formation. Similarly, microalbuminuria and low GFR are both linked to overall increased mortality from major cardiovascular accidents (Gerstein et al., 2001).

U.K prospective diabetes study (UKPDS) showed the decrease incidence of diabetic retinopathy, neuropathy and nephropathy in patients with strict glycemic control compared to the conventional treatment. In addition, the findings of ACCORD (action to control cardiovascular risk in diabetes) study showed reduced 5 year non-fatal myocardial infarction but was associated with a 22% increase in overall mortality. However, a recent meta analysis found out that the all cause mortality and deaths from cardiovascular diseases in diabetic patients were not significantly lowered by intensive glycemic control (Gerstein et al., 2008).

Although strict gylcemic therapy has beneficial effect as far as micro vascular complications are concerned but the pros must be weighed against the cons of increasing the all-cause mortality, weight gain and increased chances of inducing hypoglycemic events (Ismail-Beigi et al., 2010). The better approach seems to incorporate multiple factors targeting the lipid levels and decreasing the chances of plaque formations. This means, an approach consisting of good glycemic control with lipid lowering therapy and aspirin which would safely help lower the risk of non-fatal cardiovascular disease (van Wijngaarden et al., 2017). Furthermore, the use of one baseline value of HbA1c underestimates the importance of HbA1c as a risk factor for glucose control thus a mean of values at different times is calculated called updated mean HbA1c. This updated mean has better predictive ability to estimate the risk of diabetic complications, mainly, the micro vascular complications (The relationship of glycemic exposure (HbA1c) to the risk of development and progression of retinopathy in the diabetes control and complications trial, 1995). In addition, studies have shown hypertension to be associated with both the macro and micro vascular complications of diabetes (Yamazaki et al., 2018). This conforms, partly, to the findings in this study where hypertension was found to have significant association with the macro vascular complications and not with the micro vascular complications. Studies have shown association between the duration of diabetes and the diabetic complications particularly the micro vascular complications; however, this study did not find any statistically significant association between the duration of the disease and the ultimate complications (Akhter et al., 2017).

Moreover, a study has found out that the visit to visit variability in glucose level calculated as coefficient of variation of glucose as a better predictor of the complications of diabetes compared to HbA1c values. They showed that the people who had higher FG-CV in the first five years of diagnosis of diabetes had increased risk of early insulin initiation, diabetic retinopathy and overall mortality which was independent of mean glycemia, classical risk factors and medication use (Slieker et al., 2019).

CONCLUSION

The relationship between the values of HbA1c and the diabetic complications is well documented especially for microvascular complications. Although most studies negate the impact of strict glycemic control on the macro vascular complications but this effect in turn is indirectly influenced by micro complications, thus, good glycemic control is imperative. Secondly, diabetic patients with hypertension have a higher chance of complications i.e. macrovascular complications. Therefore, tight hypertension control alongside good diabetes control is must. Furthermore, the use of HbA1c as a single value has limited benefit which can be enhanced by keeping an eye on the variability pattern over months or years to get a better idea. Although, there are certain better predictors of the future risk of complications in these patients e.g. variation coefficient of diabetes but HbA1c is simpler and cheaper and gives a reasonably accurate estimate of the future risks of the complications; thus, should be a part of routine care of diabetic patients.

REFERENCES

Akhter J, Ahmed A, Mawani M, Lakhani L, Kalsekar A, Tabassum S, Islam N (2017). Patterns, control and complications of diabetes from a hospital based registry established in a low income country. BMC Endocr Disord. Jun 5;17(1):30. doi: 10.1186/s12902-017-0179-1. PMID: 28583113; PMCID: PMC5460467.

Binsaleh AS, Ralph D, Mulhall J (2018). Defining a glycated haemoglobin (HbA1c) level that predicts increased risk of penile implant infection. BJU Int. Feb;121(2):293-300. doi: 10.1111/bju.14076. Epub 2017 Dec 1. PMID: 29124870; PMCID: PMC7478354.

Cardoso CRL, Leite NC, Moram CBM, Salles GF (2018). Long-term visit-to-visit glycemic variability as predictor of micro- and macrovascular complications in patients with type 2 diabetes: The Rio de Janeiro Type 2 Diabetes Cohort Study. Cardiovasc Diabetol. Feb 24;17(1):33. doi: 10.118 6/s12933-018-0677-0.PMID: 29477146; PMCID: PMC638 9075

Gerstein HC, Mann JF, Yi Q, Zinman B, Dinneen SF, Hoogwerf B, Hallé JP, Young J, Rashkow A, Joyce C, Nawaz S, Yusuf S (2001). HOPE Study Investigators. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. JAMA. Jul 25;286(4):421-6. doi: 10.1001/jama.286.4.421. PMID: 11466120.

Gerstein HC, Miller ME, Byington RP, Goff DC Jr, Bigger JT, Buse JB, Cushman WC, Genuth S, Ismail-Beigi F, Grimm RH Jr, Probstfield JL, Simons-Morton DG, Friedewald WT (2008). Action to Control Cardiovascular Risk in Diabetes Study Group, Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. Jun 12;358(24):2545-59. doi: 10.1056/NEJMoa0802743. Epub 2008 Jun 6. PMID: 18539917; PMCID: PMC4551392.]

Gu K, Cowie CC, Harris MI (1999). Diabetes and decline in heart disease mortality in US adults. JAMA. Apr 14;281(14):1291-7. doi: 10.1001/jama.281.14.1291. PMID: 10208144.

Habous M, Tal R, Tealab A, Soliman T, Nassar M, Mekawi Z, Mahmoud S, Abdelwahab O, Elkhouly M, Kamr H, Remeah Ismail-Beigi F, Craven T, Banerji MA, Basile J, Calles J, Cohen RM, Cuddihy R, Cushman WC, Genuth S, Grimm RH Jr, Hamilton BP, Hoogwerf B, Karl D, Katz L, Krikorian A, O'Connor P, Pop-Busui R, Schubart U, Simmons D, Taylor H, Thomas A, Weiss D, Hramiak I (2010). ACCORD trial group. Effect of intensive treatment of hyperglycaemia on microvascular outcomes in type 2 diabetes: an analysis of the ACCORD randomised trial. Lancet. 2010 Aug 7;376(9739):419-30. doi: 10.1016/S0140-6736(10)60576-4. Epub Jun 30. Erratum in: Lancet. 2010 Oct 30;376(9751): 1466. PMID: 20594588; PMCID: PMC4123233

Ismail-Beigi F, Craven T, Banerji MA, Basile J, Calles J, Cohen RM, Cuddihy R, Cushman WC, Genuth S, Grimm RH Jr, Hamilton BP, Hoogwerf B, Karl D, Katz L, Krikorian A, O'Connor P, Pop-Busui R, Schubart U, Simmons D, Taylor H, Thomas A, Weiss D, Hramiak I (2010). ACCORD trial group. Effect of intensive treatment of hyperglycaemia on microvascular outcomes in type 2 diabetes: an analysis of the ACCORD randomised trial. Lancet. Aug 7;376(9739):419-30. doi: 10.1016/S0140-6736(10)60576-4. Epub 2010 Jun 30. Erratum in: Lancet. 2010 Oct 30;376(9751):1466. PMID: 20594588; PMCID: PMC412 3233

Jeon WS, Park JW, Lee N, Park SE, Rhee EJ, Lee WY, Oh KW, Park SW, Park CY, Youn BS (2013). Urinary adiponectin concentration is positively associated with micro- and macro-vascular complications. Cardiovasc Diabetol. Sep 28;12:137. doi: 10.1186/1475-2840-12-137. PMID: 24073643; PMCID: PMC3849544.

Kim JH, Kim DJ, Jang HC, Choi SH (2011). Epidemiology of micro- and macrovascular complications of type 2 diabetes in Korea. Diabetes Metab J. 2011 Dec;35(6):571-7. doi: 10.4093/dmj.2011.35.6.571. Epub Dec 26. PMID: 22247898; PMCID: PMC3253966.

Kranenburg G, van der Graaf Y, van der Leeuw J, Nathoe HM, de Borst GJ, Kappelle LJ, Visseren FL, Westerink J (2015). SMART Study Group. The relation between HbA1c and cardiovascular events in patients with type 2 diabetes with and without vascular disease. Diabetes Care. Oct;38(10):1930-6. doi: 10.2337/dc15-0493. Epub 2015 Aug 25. PMID: 26307606..

Lind M, Odén A, Fahlén M, Eliasson B (2009). The true value of HbA1c as a predictor of diabetic complications: simulations of HbA1c variables. PLoS One.;4(2):e4412. doi: 10.1371/journal.pone.0004412. Epub 2009 Feb 11. PMID: 19209233; PMCID: PMC2636883

Maple-Brown LJ, Ye C, Retnakaran R (2013). Area-under-the-HbA1c-curve above the normal range and the prediction of microvascular outcomes: an analysis of data from the Diabetes Control and Complications Trial. Diabet Med. Jan;30(1):95-9. doi: 10.1111/dme.12004. PMID: 22937915; PMCID: PMC3843010.

Marcus L, Aldina P, Ann-Marie S, Arndis FÓ, Hans W, Johnny L (2019). HbA_{1c} level as a risk factor for retinopathy and nephropathy in children and adults with type 1 diabetes: Swedish population based cohort study BMJ ;366:l4894

Nathan DM (2014). DCCT/EDIC Research Group. The diabetes control and complications trial/epidemiology of diabetes interventions and complications study at 30 years: overview. Diabetes Care. 37(1):9-16. doi: 10.2337/dc13-2112. PMID: 24356592; PMCID: PMC3867999.

Nitin S (2010). HbA1c and factors other than diabetes mellitus affecting it. Singapore Med J. Aug;51(8):616-22. PMID: 20848057.

Slieker RC, van der Heijden AAWH, Nijpels G, Elders PJM, 't Hart LM, Beulens JWJ (2019). Visit-to-visit variability of glycemia and vascular complications: the Hoorn Diabetes Care System cohort. Cardiovasc Diabetol. Dec 12;18(1):170. doi: 10.1186/s12933-019-0975-1. PMID: 31830993; PMCID: PMC6909524.

Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, Hadden D, Turner RC, Holman RR (2000). Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ. Aug 12;321(7258):405-12. doi: 10.1136/bmj.321.7258.405. PMID: 10938048; PMCID: PMC27454

The relationship of glycemic exposure (HbA1c) to the risk of development and progression of retinopathy in the diabetes control and complications trial (1995). Diabetes. Aug;44(8):968-83. PMID: 7622004

Timar B, Albai O (2012). The relationship between hemoglobin a1c and chronic complications in diabetes mellitus. Romanian J. Diabetes Nutrition and Metabolic Diseases Jun 1;19(2):115-22.

van Wijngaarden RPT, Overbeek JA, Heintjes EM, Schubert A, Diels J, Straatman H, Steyerberg EW, Herings RMC. (2017). Relation Between Different Measures of Glycemic Exposure and Microvascular and Macrovascular Complications in Patients with Type 2 Diabetes Mellitus: An Observational Cohort Study. Diabetes Ther. Oct;8(5):1097-1109. doi: 10.1007/s13300-017-0301-4. Epub 2017 Sep 18. PMID: 28921256; PMCID: PMC5630557.

Walinjkar RS, Khadse S, Kumar S, Bawankule S, Acharya S (2019). Platelet Indices as a Predictor of Microvascular Complications in Type 2 Diabetes. Indian J Endocrinol Metab. 2019 Mar-Apr;23(2):206-210. doi: 10.4103/ijem.IJEM_13_19. PMID: 31161104; PMCID: PMC6540898

Yamazaki D, Hitomi H, Nishiyama A (2018). Hypertension with diabetes mellitus complications. Hypertens Res. 2018 Mar;41(3):147-156. doi: 10.1038/s41440-017-0008-y. Epub Jan 22. PMID: 29353881.