Print ISSN: 2321-6379
Online ISSN: 2321-595X

Original Article

A Comparative Evaluation of Blood Sugar and Glycosylated Hemoglobin in Clinically Manifested Diabetic Neuropathy

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Abstract

Introduction: According to the International Diabetes Federation (IDF), the worldwide prevalence of diabetes mellitus (DM) has risen dramatically over the past two decades from an estimated 30 million cases in 1985 to 415 million in 2017. Based on current trends, the IDF projects that 642 million individuals will have diabetes by the year 2040.

Aims and Objectives of the Study: The aims of the study were to assess the efficacy of metabolic control of diabetes in the development of diabetic neuropathy and to identify the predisposing factors for the development of diabetic neuropathy.

Materials and Methods: The present study was conducted at Mahatma Gandhi Memorial Hospital, Warangal. The study was undertaken between June'2019 and May'2020, both in inpatient and outpatient department.

Results: Symptoms of sensory system involvement were the most common in 47 (78.3%) patients followed by motor symptoms 20 (33%) cases. Autonomic symptoms 10 cases and cranial nerve symptoms 2 cases. Distal symmetric sensory neuropathy was the most common type of clinical neuropathy.

Conclusion: Longstanding diabetes and poor glycemic control are particularly associated with an increased risk of neuropathy in DM. It also provides a conceptual framework for the pathogenesis of the long-term complications of diabetes.

Key words: Blood sugar, Diabetes, Glycosylated hemoglobin

INTRODUCTION

According to the International Diabetes Federation (IDF), the worldwide prevalence of diabetes mellitus (DM) has risen dramatically over the past two decades from an estimated 30 million cases in 1985 to 415 million in 2017. Based on current trends, the IDF projects that 642 million individuals will have diabetes by the year 2040. Although the prevalence of both type 1 and type 2 DM is increasing worldwide, the prevalence of type 2 DM is rising much more rapidly because of increasing obesity, reduced activity levels as countries become more industrialized, and the aging of the population. In 2015, the prevalence of diabetes in individuals aged 20–79 ranged from 7.2% to 11.4%. The countries with the greatest number of individuals with diabetes in 2015 are China (109.6 million), India (73 million), United States (30.3 million), Brazil (14 million), and the Russian Federation (9 million). The prevalence of DM increases with age.

The spreading diabetes epidemic is a major health concern for India and a great threat to the nation. According to recent estimates presently, India has 62 million diabetic subjects, and this is projected to increase to 100 million, that is, rise by 250% by the year 2035.

In the urban population study, 12% of individuals above age of 20 years in Chennai were found to be diabetic in the year 1997. The prevalence of diabetes is increasing rapidly and it is estimated that the number of diabetics in worldwide will double by the year 2020 projection published. In the year 1997, International Diabetes Institute stated that there will be more than 400 million people with diabetes by 2020, with the majority of them suffering with

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www.ijss-sn.com

Month of Submission : 01-2021
Month of Peer Review : 01-2021
Month of Acceptance : 02-2021
Month of Publishing : 03-2021

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Type-2 Diabetes.[1] More than 95–97% of elderly diabetics are of Type II disease.

The metabolic syndrome is a deadly combination of hypertension, diabetes, heart disease, and dyslipidemia due to abdominal obesity. The causes are due to both bad genes and bad environment. Vascular complications of both micro- and macro-vascular predominate the features of Indian diabetes due to delayed diagnosis and late presentation of the syndrome. Diabetic foot accounts for one of the largest in-patient admissions in India. Diabetic nerve-related disorders directly or indirectly contribute to morbidity and mortality in a big way. Simple measures such as good glycemic control and neuroadjuvants, visual inspection of feet, and foot care can save and salvage feet at risk. Diabetic neuropathy is one of the most common troublesome complications of DM.

The prevalence of neuropathy is related to age, duration of diabetes, and the quality of metabolic control. By the time a diabetic patient has severe neuropathy, retinopathy and albuminuria are also usually present. It is the most common form of neuropathy in the developed countries of the world and accounts for more hospitalization than all the other diabetic complications and accounts for 50–70% of non-traumatic amputation.

The introduction of Insulin in the year 1922 by BANTING and BEST seemed to offer the ideal therapy for the treatment of DM and replacement of the missing hormone. Indeed in the past 50 years, the judicious use of Insulin has made it possible to control the symptoms of hyperglycemia and to avoid death from Diabetic Ketoacidosis. However, despite the continuous use of Insulin many pathological changes (e.g., retinopathy, angiopathy, nephropathy, and neuropathy) can develop and now account for the major morbidity and mortality associated with the disease.

One of the main difficulties to establish whether there is a relation between the degree of hyperglycemia and long-term complications of diabetes is the lack of reliable and objective method for assessing diabetic control. The clinician at present has no quick and simple way of ascertaining whether his patient is well controlled or not. Whether the modification of therapeutic regimen has altered control for better or worse.

Blood and urine glucose testing and urine ketone testing provide useful information for the day-to-day management of diabetes. However, these tests cannot provide the patient and healthcare team with a quantitative and reliable measure of glycemia over an extended period of time and these tests have a drawback in the demands of patient's compliance or frequent measurement.

Measurements of glycated proteins such as primary hemoglobin and serum proteins have added new dimensions in the assessment of glycemia. With a single measurement of each of these tests can quantitate the average glycemia over weeks and months, thereby complementing day-to-day testing. Expert opinion recommends glycosylated hemoglobin (HbA1c) testing at least 2 times a year in patients who have stable glycemic control.[2]

Lately, KEONTG and GABBAY and their coworkers have suggested measurement of HbA1C as an indicator of diabetic control. HbA1C is formed by the post-transcriptional glycosylation of HbA at the amino terminal valine of beta chain. This is a slow irreversible chemical reaction which occurs throughout the life span of the RBC, the prevailing plasma glucose concentration being the most important factor governing the quantity of HbA1C formed. HbA1C can be separated from the major hemoglobin fraction by virtue of its fast movement through action exchange resin.

When properly assayed, HbA1C level in a blood sample gives an estimate of diabetic control for the preceding 3–4 month period (i.e., life span of RBC).[2,3]

Diabetic control and complications trial study proved that allocated hemoglobin (HbA1c) reduction from 9% to 7% for a mean follow-up of 6.5 years was able both to reduce the onset of diabetic neuropathy (from 9.6% to 2.8%) and to slow its progression.[4,5] Euglycemia is only able to halt the progression, rather than reverse it, once the nerve damage has been established.[6,7]

Diabetic neuropathy has been defined by the consensus conference of San Antonio as peripheral neuropathy either clinically evident or sub-clinically that occurs in the setting of DM without other causes.[8] The present combination of the triad of neuropathy, retinopathy, and nephropathy in the course of the lifelong disease regarded this "Triopathy" as consequences rather than complication.[9]

Diabetic neuropathy is one of the most common long-term complication of DM and is clinically present in 30–50% of all diabetes patients.[10,11]

The primary pathological role of hyperglycemia in diabetic complications is well established. With the increasing knowledge that maintenance of euglycemia greatly reduces, if not prevents, the risk of diabetic complications and at times helps even in regression of such complications, monitoring the control of diabetes is essential for the successful management of diabetes. The responsibility of the patient and his physician in close monitoring control of diabetes and tailoring the various components in their management have assumed greater significance.[12]

The present study has been undertaken to monitor the levels of blood sugar and HbA1C in diabetic neuropathy. The study of diabetic neuropathy has been undertaken for many reasons. Diabetes is a frequent cause of peripheral neuropathy. It affects almost every part of nervous system and produces, various type of neuropathy. It has significant morbidity and mortality. Its incidence increases when the control of diabetes is poor.[13]

It is very well established that tight control of diabetes reduces, if not prevents, the risk of neuropathy. The benefit of other modes of therapy like myo-inositol supplementation and all doses of reductive inhibitors remain to be established. Until then, the clinician should monitor the patient's neurological status by routine methods and assess the control of diabetes by the available parameters and give practical advice that may save a limb and life.

Aims and Objectives of the Study

The aims of the study were as follows:

1. To assess the efficacy of metabolic control of diabetes in the development of diabetic neuropathy
2. To compare the value of estimation of blood sugar and HbA1c in monitoring the control of diabetes in diabetic neuropathy
3. To identify the predisposing factors for the development of diabetic neuropathy.

MATERIALS AND METHODS

The present study was conducted at Government Medical College, Suryapet, Telangana State , Study period June 2019- May 2020, both in inpatient and outpatient department. Diabetic patients seeking consultation for the symptoms suggestive of neuropathy were screened and labeled as suffering from diabetic neuropathy based on the inclusion and exclusion criteria described by PIRAR.

Inclusion Criteria

The following criteria were included in the study:

1. Loss of knee/ankle jerk
2. Sensory deficits
3. Other neurological abnormalities.

Exclusion Criteria

The following criteria were excluded from the study:

1. Other causes of neuropathy, especially alcoholism
2. Generalized areflexia without signs of neuropathy, and
3. Unilateral reflex loss.

Among those diagnosed to be suffering from diabetic neuropathy, further exclusion of the factors which would lead to falsely abnormal values for HbA1C was done before proceeding further.

1. Anemia (Hb <10 g%)
2. Acute metabolic complications
3. Ingestion of antibiotics and aspirin
4. Alcohol intake
5. Uremia
6. Hemoglobinopathies
7. Recent Blood Transfusion
8. Hyperlipidemia.

In all, 60 patients of diabetic neuropathy who satisfied the above criteria were selected and were subjected to a thorough evaluation as per working pro forma A battery of tests of cardiovascular autonomic function as described in Hutchison's clinical method was performed in all patients normal and abnormal values in tests were described by Ewing and Clarke (1982) given below.

Laboratory Investigations Done in all Patients Include

1. Urine – Sugars and Ketone bodies
   - Albumin
   - Microscopy
2. Fasting blood sugar (FBS) and postprandial blood sugar test (Folin-Wu method).
3. Blood
   - Hb%
   - Urea
   - Creatinine
   - Cholesterol
4. HbA1C by ion exchanges chromatographic method.
5. Electrocardiogram, X-ray chest, and other investigations whenever necessary were done. HbA1C was estimated in blood sample taken for FBS estimation.

Ion Exchange Resin Chromatographic Method of Estimation of HbA1C

(GlycoHb) (KYNOCK and LEHMANN 1977)

It is a rapid and simple method; total time required is <30 min.

Principle

Whole blood is mixed with a lysing reagent to prepare a hemolysate. This is then mixed with a weakly binding cation exchange resin. The non-glycosylated hemoglobin bind stores in, leaving HbA1C free in the supernatant. The HbA1C is determined by measuring the absorbance of the HbA1C fraction and of the total Hb.

Reagents and Apparatus

1. Ion exchange Resin (Bio-Rex 70)
2. Hemolyzing Reagent
   - 0.3 g white saponin
   - 0.5 g potassium cyanide

   Dissolved in a buffer pH 6.7 to make 1 L.

3. Control (lyophilized)
4. Apparatus – plastic tubes and resin separators.

Specimen

Whole blood collected in EDTA bulb. Heparin may also be used. HbA1C in blood is found to be stable for 1 week at 2–8°C.

Equipment Required

1. Spectrophotometer/photocolorimeter
2. Cuvettes
3. Test tubes
4. Vortex mixer
5. Pipettes and micropipette.

Reagent Preparation

Reagents 1 and 2 are ready to use. HbA1C control (3) is dissolved in 1 ml of deionized water by inverting/swirling. Reconstituted control is stable for 30 min only at room temp or 15 days at −20°C.

Procedure

Assay temperature: 23 ± 2°C.

Wavelength: 415 nm (Hg 405 nm).

Step 1: Hemolysate preparation

1. 0.5 ml of lysing reagent (2) was pipetted into a test tube
2. To it, 0.1 ml of well-mixed whole blood sample was added
3. Mixed and allowed to stand at room temperature for 5 min.

Step 2: Hb A1C separation and assay

1. 3.0 ml of ion exchange resin (1) was pipetted into the plastic tube. Mixed well before use.
2. 1.0 ml of the hemolysate was added (from step 1)
3. The resin separates or was positioned in the plastic tube so that the rubber sleeve was approximately 2 cm above the liquid level.
4. Plastic tube was placed on vortex mixer and was mixed for 5 min
5. The resin separator was pushed down in the plastic tube until therein was firmly packed
6. The supernatant was poured directly into a cuvette and absorbance was measured against deionized water within 60 min.

Step: 3 total hemoglobin (THB) assay

1. 5.0 ml of deionized water was pipetted into test tube
2. 0.02 ml of hemolysate (from step 1) was pipetted into it
3. Mixed and absorbance was read against deionized water within 60 min.

Good: 6–8 g%

Fair: 8–10 g% Calculations

$$\text{HbA1C\%} = \frac{\text{Absorbance of}}{\text{Absorbance of THb}} \times 10\text{X Temp.factor}\left(\text{Ff}\right)$$

Tf for assay at 23± 20°C=1.0 Tf for assay at 300°C= 0.7.

The pooled information was analyzed using appropriate statistical methods. HbA1C estimation done by ion exchanges chromatographic method.

The interpretation of GlycoHb test in our study is as follows:
Normal: <6. g%
Poor: >10 g%.

RESULTS

History

Of the 60 cases studied, 36 (62.6%) were male and 24 (38%) were female.

Average age group was 52.18 years.

Diabetic neuropathy was common in the age group of 56–65 years in both male and female (33.3%).

Average duration of diabetes was 8.7 years. NIDDM was more common (58 out of 60).

Ten patients were not on any treatment at the time of evaluation. Out of these, 6 patients were detected to be diabetic when they were admitted to this hospital for evaluation of neuropathy. Diabetic neuropathy was commonly observed in those patients with irregular treatment.

None of the patients had previous medical records documenting their diabetic status (urine sugar, blood sugar, and HbA1C estimation) before this evaluation except 5 patients who had previous admission record and record documenting glycemic status. Hence, diabetic control status could be assessed as either good or poor depending on symptoms of diabetes, regularity or otherwise of treatment and previous hospital admissions for their complications of diabetes, excluding the 6 patients who were detected on admission 46 patients were classified as "poor" controlled diabetics either because of failure to take treatment or persistence of symptoms in spite of treatment. Remaining 8 patients were judged to be "good" controlled with minimal parameters. Out of 60 patients, 26 patients were smokers and 34 were non-smokers.

Degree of control	Blood sugar (No of cases)	Glycosylated hemoglobin (No of cases)
Normal	9 (15%)	1 (1.9%)
Good control	14 (23.3%)	6 (20%)
Fair control	25 (41.6%)	14 (23%)
Poor control	12 (20%)	39 (68%)

P<0.001 Highly significant

Thus HbA1C showed evidence of poor control more frequently than blood sugar estimation in these patients. The difference between this parameter as a measure of poor control of diabetic was statistically significant.

When these patients were evaluated for their diabetic control status depending on the presence of symptoms of diabetes, regularity or otherwise of the treatment, history of the previous hospitalization for the complications, only 8 patients were judged to be under good control.

When these patients were analyzed for control status based on blood sugar and HbA1C, following observation was made. When 46 patients, thought to be "poorly" controlled diabetics using the same criteria, were further analyzed, taking blood sugar and HbA1C criteria into consideration, following observation was obtained.

Thus, it can be seen that in those patients who were on regular treatment and asymptomatic for glycosuria, HbA1C estimation revealed evidence of poor control in 6 patients. In contrast, blood sugar estimation revealed acceptable levels for diabetic control in these patients.

Even in those patients who were designated to be "poorly" controlled diabetics (n = 46), estimation of HbA1C revealed supportive evidence of the same more frequently (n = 30) than blood sugar estimation (n = 7). This difference was highly statistically significant ($P < 0.001$).

Patients with both retinopathy and neuropathy in this study had DM for periods 2 months–20 years (Mean 8.2 years). Whereas, patients with neuropathy alone had DM which was either detected on admission or was there for periods up to 10 years (Mean 8.2 years).

Thus, it is clear that the longer the duration of diabetes, more is the chance for the development of complications of diabetes.

Sixteen patients had abnormal autonomic nervous system function as per the criteria laid down by Ewing and Clarke and two patients showed evidence of diabetic gastroparesis. Out of these 18, only 2 (11%) patients had blood sugar in the "poorly" controlled category as compared to 11 (61%) patients in whom the HbA1C showed evidence of poor control. This difference was statically significant.

After establishing the efficacy of the estimation of HbA1C, the influence of the other parameters such as age, sex, duration, and mode of therapy on its estimation was analyzed. The following observations were made:

There were 19 patients aged <45 years and 41 patients aged more than 45 years.

HbA1C estimation indicated poor control in 12 patients in the former group as compared to 27 patients in the later. This difference was not statistically significant ($P > 0.05$).

Twenty-four out of the 36 male patients had evidence of poor control of diabetes; similarly, 15 out of the 24 females had evidence of poor control. There was no statistically significant difference between the value of HbA1c ($P > 0.05$) [Tables 1-3].

DISCUSSION

The exact mechanism in the development of neuropathy in diabetes is uncertain. Whether a poor control of the diabetic state hastens the progression of neuropathy is a question that yet to be answered, one of the earlier studies to establish relationship between glycemic control and neuropathy performed by Pirart, which showed that poor control was associated with a higher incidence of neuropathy. Intensive glycemic control in the DCCT study showed decreased incidence of diabetic neuropathy to 3% in intensively treated patients compared to 10% in the group that received conventional treatment.[4] Holman *et al.* concluded that tight control of diabetes retarded or reversed the progression of neuropathy.

On the other hand, Service *et al.* found no such correlations. However, majority of the authorities, Dyck *et al.* favor the view that poor control of diabetes is associated with an increased risk of neuropathy.

In the present study, the accurate classification regarding control of the diabetic state as laid down by the recommendations of the American Diabetes Association (1988) could not be done. There as on, has been elaborated earlier. However, patients who could be grossly classified as having poor metabolic control outnumbered those who could be classified as having good control (46 vs. 8) in this study.

Although considerable controversy exists regarding the etiopathogenes is of neuropathy in diabetes. It has been conclusively shown by Pirart that the incidence of neuropathy increases with the duration of diabetes. Heal so showed that there was a positive correlation between the occurrence of neuropathy and retinopathy. Tesfaye *et al.* showed a significant or relationship between diabetic neuropathy, age, duration of diabetes, diabetic retinopathy,

cigarette smoking, and prevalence of cardiovascular disease in IDDM patient.[14] This fact was brought out in this study.

In the present study, 33 (55%) neuropathy patients had retinopathy and the duration of diabetes was long. Furthermore, 16 neuropathy patients showed evidence of myocardial infarction and smoking habit observed in 26 neuropathy patients.

As noted by various authors (Thomas and Brown) as well as various (Holzer *et al.*) studies shown that symmetric distal sensory polyneuropathy is the most common form of diabetic neuropathy; this is supported by our study where the incidence of is more than any other type (61.2%); as documented by many workers earlier, the sensory disturbances follow a "Length related pattern" with the lower limb fibers being involved earlier than upper limb fibers.

This has been observed in our study. All patients who exhibited sensory changes did so in lower limbs. No patients showed sensory loss to touch (large fiber neuropathy) and yet to be firmly established. The existence of sensorimotor polyneuropathy was doubted by Thomas and Brown (1984), who feel that it is just a variation of the sensory neuropathy with minor motorabnormalities. However, Dycketal (1985) tends to classify this as a separate entity and the incidence of this particular form of neuropathy in our study is 40.8% (24 cases).

Prepared from pig and cattle pancreases and human insulin, synthesized by recombinant DNA technology, are now available which are superseding the older preparations. They are less likely to cause insulin allergy and lipodystrophy which prevent the potential hazards of patients non-compliance. Example includes Humulin S, Humulin I, actrapid MC, Actrapid HM, Neusilin, etc.

In summary, better method of soft treatment such as better delivery system and better insulin offers the hope of better control of diabetes and thereby better quality of life.

A recent study by MALIK suggested that the ACE inhibitor quinapril shows improvement in autonomic neuropathy. In 12 month's study of trandolapril treatment showed significant improvement in peripheral nerve function; however, this role of angiotensin-converting enzyme inhibitors as neuroprotective agents remains to be clearly delineated.

A recent meta-analysis by Nicoluccietal of randomized control trial involving acute respiratory infections demonstrated a modest benefit of treatment in only one aspect, improving the median nerve motor conduction velocity.

A recent 1 year multicentre trial of GLA administration to patients with diabetic neuropathy reported improvement in clinical and electrophysiological nerve function. Clinical trials regarding, use of alpha-lipoic acid in diabetic neuropathy is undergoing in the USA. The role of recombinant NGF remains uncertain in the treatment of diabetic neuropathy.

Asbury metal has noted that third nerve palsy is the most common cranial mononeuropathy encountered in diabetics. This feature has been documented in our study also where 2 cases had third nerve involvement. They have also noted that inspite of total paralysis of the extraocular muscles supplied by this nerve; there will be sparing of the pupillary reflex, more frequently in those who were aged above 50 years. Both the suspects were documented significantly in the present study.

Kurezyn suggested that Bell's Palsy (LMN facial Palsy) occurs greater than expected frequency in diabetics; however, only one case was observe in the present study.

In the present study, 30% of neuropathy patients had coexisting autonomic dysfunction. The duration of diabetes was long and level of glycemic control was poor (mean value GlycoHb– 11.05%). Ewing and Clarke have reviewed various series and suggested that the incidence of such abnormalities may vary from 17% to 40% in diabetes. Pfeifer *et al.* and Youne *et al.* (1986) have also documented the occurrence of autonomic abnormalities in patients with somatic neuropathy.

Elevated HbA1C was observed in diabetic neuropathy suggestion hyperglycemia or a related metabolic abnormality as an important factor in establishing neuropathy (Boulton *et al.*, 1982).

Several studies showed a position correlation between HbA1C and retinopathy, neuphropathy, and platelet aggregation. Even in those patients who were thought to have poor metabolic control, levels of HbA1C were more consistent in indicating poor metabolic control than blood sugar levels. This difference was statistically significant ($P < 0.01$). Zonen *et al.* but also a more sensitive and reliable indicator in monitoring the control (Koenig and Gabbay *et al*).

Boulton *et al.* (1982) observed an increased level of HbA1C in patients with diabetic neuropathy. Mcdonal *et al.* (1979) noted elevation level of HbA1C causes a shift of the oxygen dissociation curve to the left resulting in tissue hypoxia and this forms one of the hypothesis for the pathogenesis of neuropathy and other microvascular complication associated with diabetes.

Part of the examination included an assessment of neurological function, including neuropathic symptoms and physical signs, vibration perception threshold, tests of autonomic function, and the prevalence of impotence. The prevalence of diabetic neuropathy across Europe was 28% with no significant geographical differences.

Significant correlations were observed between the presence of diabetic peripheral neuropathy with age ($P < 0.05$), duration of diabetes ($P < 0.001$), quality of metabolic control ($P < 0.001$), height ($P < 0.01$), the presence of background or proliferative diabetic retinopathy ($P < 0.01$), cigarette smoking ($P < 0.001$), high-density lipoprotein cholesterol ($P < 0.001$), and the presence of cardiovascular disease ($P < 0.05$), thus confirming previous associations. New associations have been identified from this study – namely with elevated diastolic blood pressure ($P < 0.05$), the presence of severe ketoacidosis, an increase in the levels of fasting triglyceride ($P < 0.001$), and the presence of microalbuminuria ($P < 0.01$). All the data were adjusted for age, duration of diabetes, and HbA1c. Although alcohol intake correlated with the absence of leg reflexes and autonomic dysfunction, there was no overall association of alcohol consumption and neuropathy.

The reported problems of impotence were extremely variable between centers, suggesting many cultural and attitudinal differences in the collection of such information in different European countries. In conclusion, this study has identified previously known and new potential risk factors for the development of diabetic peripheral neuropathy.

"Matsumoto *et al.* showed the FBS is a major determinant of neuropathy independent of age, body mass index, and duration of diabetes. The fasting hyperglycemia was observed in 83.3% (50) of patients, while post-prandial hyperglycemia was observe in 33.3% of patients in the study. As Perice, Detal 1991 showed, erectile dysfunction was a common complication observed in diabetic men and was related to the many other complication, sexual dysfunction was observed in 72.2% of diabetic men in the study (26 out of 36 diabetic male patients). The duration of diabetes was longer in these patients and the estimated glycosylated hemoglobin clearly showed a poor controlled state.

Elevated levels of HbA1C were observed in most of the patients of diabetic neuropathy in the present study which supports the above outcomes.

The effect of various other parameters on the efficacy of HbA1C estimation as an indicator of poor metabolic control was also analyzed.

During optimal diabetic control, the blood sugar concentration was 84 mg per deciliter (range, 70–100) and HbAIc concentration 5.8% (range, 4.2–7.6). HbAIc concentration appears to reflect the mean blood sugar concentration best over previous weeks to months.

The periodic monitoring of HbAIc levels provides a useful way of documenting the degree of control of

Table 1: Ormal and abnormal values in tests of autonomic neuropathy

Test	Normal	Borderline	Abnormal
Parasympathetic (heart rate response).			
Valsalva ratio	≥1.21	1.11–1.20	≤1.10
Deep breathing (max: min HR)	≥15 beats/min	11–14 beats/min	≤10 beats/min
Standing 930:15 ratio RR)	≥1.04	1.01–1.03	≤1.00
Sympathetic (blood pressure response)			
Standing (↓systolic)	≥10 mm hg	11–29 mm hg	≥30 mm hg
Exercise (↑diastolic)	≥16 mm hg	11–15 mm hg	≤10 mm hg

Table 2: The age and sex distribution of these cases is as below

Age in years	Male	Female	Total	Percentage
<25 years	0	3	3	5
26–35 years	1	1	2	3.33
36–45 years	11	3	14	23.3
46–55 years	7	4	11	1.6
56–65 years	12	8	20	33.3
66 and above	5	5	10	16.6
Total	36	24	60	100

Table 3: Depicts the duration of diabetes in these patients varied from freshly detected cases to 25 years. Patient with IDDM and NIDDM could be further sub-classified depending upon the duration of diabetes as under

Duration of diabetes in years	No of type 1 DM patients	No of type 2 DM patients	Total no of diabetes	Percentage
<5 years	0	18	18	30
6–10 years	1	23	24	40
11–15 years	0	13	13	21.6
>15 years	1	4	5	8.4
Total	2	58	60	100

glucose metabolism in diabetic patients and provides a means whereby the relation of carbohydrate control to the development of sequelae can be assessed. From the Laboratory of Medical Biochemistry, Rockefeller University, Cornell University Medical College and the Beth Israel Medical Center Ronald J. Koenig at Rockefeller University, 1230 York Ave., New York, NY 10021.

Whereas, in the present study, it has been demonstrated that the sequelae of DM, especially diabetic neuropathy, has been the cornerstone for this study and thus the study indicated that Hba1c levels are directly related to the management of diabetic neuropathy.

The study of Koenig *et al.* was conducted only in the inpatients, whereas the present study was concentrated on both inpatients and outpatients.

Natural Progression of Diabetic Peripheral Neuropathy in the Zenarestat Study Population by Bird *et al.* to report the baseline and natural progression of diabetic peripheral neuropathy over 12 months in a large mild-to-moderate neuropathy population concluded that neurologic decline over 12 months is evident when measured by nerve conduction studies and cool thermal quantitative sensory testing (QST). Other measures, vibration QST, neuropathy rating scores, and monofilament examination, are insensitive to changes over 12 months in a mild-to-moderate affected population of this size.

CONCLUSION

1. Longstanding diabetes and poor glycemic control are particularly associated with an increased risk of neuropathy in DM
2. Estimation of HbA1C is a simple, rapid, and objective procedure to assess diabetic control
3. It serves both as a screening test for uncontrolled diabetes and as an indicator of the efficacy of various therapeutic regimens
4. It also provides a conceptual framework for the pathogenesis of the long-term complications of diabetes.
5. Its estimation gives a relatively precise reflection of the state of diabetic control as compared to blood glucose estimation. Therefore, it is now possible to estimate more accurately and with greater sensitivity the degree of glucose intolerance, particularly in cases associated with diabetic complications. It represents an accurate technique to evaluate new ways of controlling blood glucose.

Thus, as an integral of diabetic control, HbA1C estimation is superior to the conventional measures in the assessment of control.

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How to cite this article: Sudhakar M. A Comparative Evaluation of Blood Sugar and Glycosylated Hemoglobin in Clinically Manifested Diabetic Neuropathy. Int J Sci Stud 2021;8(12):212-219.

Source of Support: Nil, **Conflicts of Interest:** None declared.