Chapter 2

Literature review

This chapter explains the narration of the various studies conducted in the field of glycemic control and diabetes management. The review was primarily aimed to summarize the factors addressed by the studies conducted on people with type 2 diabetes mellitus and glycemic control.

2.1. Characteristics of diabetics with high HbA1c who achieved good control

Michal S, et.al. (2008)\textsuperscript{25} conducted a study to find out the characteristics of diabetics with poor control who became well controlled and compared with the subjects with poor control that remained poorly controlled.

The subjects with, age 40 years and older, from the Central district of Clalit Health Service in Israel, with at least one HbA1c measure greater than 9.5 % during 2001 were the study population. Subjects were divided into two categories based on their HbA1c levels in 2003: well controlled (HbA1c < 7.5 %), and poorly controlled (HbA1c > 9.5 %). Subjects with HbA1c 7.5 to 9.5 were excluded.

Four thousand five hundred four diabetics older than 40 years of age had at least one measure of HbA1c > 9.5 % in 2001. Of these, 1542 were excluded because of their HbA1c measure in 2003 was between 7.5 and 9.5 %. A total of 2962 subjects were included in the study. Of these, 1232 (41.6\%) got well-controlled, and 1760 (58.4\%) had poorly controlled diabetes.
Men were more likely than women to achieve well-controlled diabetes (52% vs 43.6%; P < 0.001). The average age of those who achieved well-controlled diabetes was younger than that of those who were in poorly controlled diabetes (63.2% vs 64.5%; P < 0.001). There was no difference between the groups relating to origin, the number of other chronic diseases, or mortality rate.

Well-controlled group had fewer subjects with low socioeconomic status (30.3% vs 41.9%; P < 0.001), and more men (52% vs 43.8%; P < 0.001). The primary care clinic in which the subject belonged was correlated with good glycemic control (P < 0.001). Poorly controlled diabetes were more likely to change their primary care physicians than subjects from the group with well-controlled diabetes (31.1% vs 27.7%; P = 0.044).

Among the poorly controlled diabetics in 2003, 59.6% visited the ophthalmologist vs 55.5% of the group with well-controlled diabetics (P = 0.025); micro-albumin was 72.6% vs 68.2%; P = 0.009.

LDL cholesterol was done in 87.3% vs 82.8%; P < 0.001, average LDL cholesterol was lower in the well-controlled group (103.1 vs 109.8; P < 0.001). Study concluded that primary care physician who takes care of diabetic patient has an important role in their chances of achieving glycemic control.

2.2. Factors associated with glycaemic control in type 2 diabetics

Panarotto D, et.al. (2008) evaluated the factors influencing blood glucose control of type 2 diabetics who attended a tertiary health care center.
A retrospective study by review of medical records of subjects who attended the Diabetes Clinic at the University of Caxias do Sul was carried out. The subjects were evaluated for glycaemic and metabolic control and divided according to glycated hemoglobin level, as compensated (HbA1c ≤ 7%), and not compensated (HbA1c > 7%).

During the study period, 155 type 2 diabetics, whose medical records were analyzed. Of these, 73 subjects (47.09 %) had at least six months of follow-up in the clinic. The average time of follow-up was 20.78 ± 10.05 months, the average number of visits was 5.8 ± 2.23, and the average frequency of consultations was 3.74 ± 1.12 per year.

In the beginning of the follow-up period, 25% of the subjects had HbA1c < 7%; 22.7% had LDL cholesterol < 100 mg/dl, 8.7% had SBP < 130 mmHg, and DBP < 80 mmHg. At the last visit the percentages were, 42.3%, 37.5%, 30.2% and 9.6% respectively.

Younger age, higher levels of LDL cholesterol, and insulin use were associated with poor blood glucose control.

2.3. Poor glycemic control and chronic kidney disease

Bash LD, et.al. (2008)\textsuperscript{19} evaluated the extent at which an elevated glycated hemoglobin (HbA1c) concentration was associated with increased risk of chronic kidney disease in the absence of albuminuria and retinopathy.

HbA1c was measured in 1871 adults with diabetes mellitus followed up for 11 years and categorized into 4 categories: < 6%, 6-7%, 7-8%, ≥ 8%. Baseline characteristics of the population were compared across CKD status and HbA1c categories using chi-squared and t tests.
Incidence rates of CKD during follow-up were compared across HbA1c categories. Follow-up time was calculated from the time of the second ARIC examination to the first date of CKD diagnosis, defined as the earliest of either the fourth examination (if GFR decline was indicated), or the discharge date of a CKD-related hospitalization. Participants were censored at the earliest time of either death, withdrawal, or on December 31, 2004.

Adjusted hazard ratios and their 95% confidence intervals for the time to development of CKD were computed using Cox proportional hazards models after first testing the assumption of proportionality of hazards over time. Models were developed comparing participants by HbA1c category as well as by continuous HbA1c. Multivariable models included age, race, gender, study center, BMI, hypertension, use of anti hypertensive drugs, prevalent coronary heart disease, smoking status, LDL- and HDL cholesterol, and triglyceride concentrations.

HbA1c < 6% (hazard ratio = 1.4; 95% C.I = 0.97 to 1.91), HbA1c = 6% to 7% (HR = 2.5; 95% C.I = 1.70 to 3.66), HbA1c = 7% to 8% (HR = 3.7; 95% C.I = 2.76 to 4.90), and greater than 8% were associated with chronic kidney diseases. Study found that higher HbA1c concentrations were associated with risk of chronic kidney diseases.

Risk of the disease was higher in individuals with albuminuria and retinopathy, and the association between HbA1c concentration and incident of the kidney disease was observed even in subjects without either abnormality: adjusted relative hazards (95% C.I): 1.46 (0.80 to 2.65); 1.17 (0.43 to 3.19); and 3.51 (1.67 to 7.40), respectively.
The study observed a positive association between HbA1c and incident of chronic
diseases and it presented even in the absence of albuminuria and retinopathy.
Hyperglycemia was an important indicator of risk of both diabetic nephropathies with
albuminuria or retinopathy and of less specific forms of chronic kidney diseases.
Glycemic control was a significant modifiable risk factor in the pathology of kidney
disease among individuals with diabetes, both in the presence and absence of other
micro-vascular damages.

2.4. Aspirin resistance associated with HbA1c levels

Cohen HW, et.al. (2008)\textsuperscript{31} examined a hypothesis that aspirin resistance may be
associated with both high HbA1c and depressive symptoms, and assessed other potential
determinants of aspirin resistance in diabetics.

A whole-blood desktop platelet function analyzer (PFA-100) with an epinephrine agonist
was used to assess aspirin resistance among the subjects with type 2 diabetes. It was
defined as PFA closure times ≤ 192 seconds. Subjects being treated for type 2 diabetes (n = 48),
who took aspirin within the past 24 hours, in an outpatient endocrinology clinic
with age ≥ 40 years constituted the study population. It comprised of: 58% females,
median age 68 years, smokers (10%), obese (38%).

Aspirin resistance was observed in 11 subjects (23%), and was not associated with: age,
gender, or race, and it was associated with HbA1c ≥ 8% (P = 0.002), and obesity (BMI ≥
30 kg/m\textsuperscript{2}; P = 0.01). There were no associations of aspirin resistance with: age, gender,
race, plasma glucose, blood pressure, cholesterol, or smoking was observed.
Subjects with HbA1c ≥ 8% had an odds of 11 (95% C.I = 2 to 5.4) of being aspirin resistant compared to subjects with HbA1c < 8%. The principal finding of this study was: a substantial proportion (23%) of the subjects being treated for type 2 diabetes, who were reported, taking aspirin within the previous 24 hours, did not have the platelet inhibition that would be expected for subjects on aspirin therapy. The study concluded that aspirin resistance was associated with poor glycemic control, and suggested that it may be of special concern for diabetics with poor glucose control, and obesity.

2.5. The relationship between glycemic control and platelet activity


Seventy subjects with type 2 diabetes mellitus and ≥ 40 age- and gender-matched healthy individuals were enrolled in the study. They were evaluated for metabolic regulation of diabetes, nephropathy, retinopathy, neuropathy, and CAD. Twenty (29%) had known proliferative diabetic retinopathy treated by photocoagulation, 22 (7.58%) of them had micro-albuminuria, 24 (34%) had poly-neuropathy, and 9 (13%) had CHD.

After baseline evaluation, the subjects were grouped into two: those with HbA1c ≤ 7% (Group A, n = 35), and those with HbA1c > 7% (Group B, n = 35). Initially, both groups were compared according to mean platelet volume, HbA1c, serum lipid levels, coronary artery disease, retinopathy, neuropathy, and nephropathy. Thereafter, Group B was called to monthly visits to obtain the improvement in glycemic control, which was defined as achievement of HbA1c ≤ 7%. At the end of three months of follow-up, Group B was reevaluated.
Mean platelet volume was higher in subjects with diabetes mellitus than in the healthy individuals (8.7 ± 0.8 vs. 8.2 ± 0.7; P = 0.002). There was a positive correlation between mean platelet volume and HbA1c levels (r = 0.39, P = 0.001) but not diabetic vascular complications.

Group B had higher mean platelet volume than Group A (9.0 ± 0.7 vs. 8.4 ± 0.8; P = 0.01). Thirty subjects (86%) of Group B achieved improved glycemic control at the end of the three months. Mean platelet volume of the subjects with improved glycemic control were decreased compared to baseline mean (8.4 ± 0.8 vs. 9.0 ± 0.7; P = 0.003).

Mean platelet volume was associated with HbA1c > 7% (O.R = 0.32; 95% C.I = 0.14 to 0.74). Total cholesterol (O.R = 0.98; 95% C.I = 0.96 to 0.99), triglycerides (O.R = 0.98; 96% C.I = 0.98 to 1.00), and albuminuria (O.R = 1.0; 95% C.I = 0.99 to 1.00) were not associated with HbA1c > 7%.

The study found a relationship between poor glycemic control and increased platelet activity in subjects with type 2 diabetes mellitus. Platelet activity recovered through improved glycemic control, which may prevent the possible role of platelets in cardiovascular events among the diabetics.

2.6. Association of HbA1c with diabetic complications


A total of 676 subjects with type 2 diabetes were investigated. The subjects were divided into two groups: HbA1c > 7% as poorly controlled, and HbA1c ≤ 7% as disease well
controlled, and the relation of HbA1c with the complications were analyzed. Study characteristics included were: nephropathy, neuropathy, retinopathy, diabetes feet, fatty liver, hypertension, and coronary heart diseases.

The 676 diabetics comprised of: 304 males and 372 females, 34 (5.0%) were in the age group 30 to 39 years, 82 (12.1%) aged 40 to 49, 121 (17.9%) in 50 to 59 years, 187 (27.7%) in 60 to 69 years, 252 (37.3%) were over 70 years of old. The subjects were divided into two groups: HbA1c > 7% (n = 439), and HbA1c ≤ 7% (n = 237).

Rate of well controlled was 35.1% (237/676) and 64.9% (439/676) of the subjects had the disease poorly controlled. The rates of hypertension, and cerebrovascular complications were higher in subjects with poorly controlled diabetes than in those with well controlled (69.9% vs 55.7%, and 21.8% vs 8.9%; P < 0.001). Coronary heart disease among the two groups was: 18.7% vs 17.3%; P > 0.05.

Subjects with poor glycemic control had higher incidences of diabetic peripheral neuropathy, and fatty liver than those with well controlled (46.0% vs 35.0%, and 36.9% vs 25.3%; P < 0.01). There was no differences in the incidences of diabetic nephropathy (18.7% vs 16.5%), diabetic retinopathy (30.8% vs 27.4%), or diabetic feet (5.0% vs 3.8%) between the groups (P > 0.05).

Type 2 diabetics had generally low rate of successful glycemic control, which was associated with the occurrence of diabetic complications. The study suggested that there was a need for more rigorous diabetic health education, and HbA1c monitoring measures among the poorly controlled diabetics.
2.7. The potentially poor response to outpatient diabetes care

Curtiss BC, et.al. (2001)\textsuperscript{20} studied the reasons underlying differences in HbA1c outcome, in an outpatient diabetes clinic.

African-Americans with type 2 diabetes were categorized as responders, intermediate responders or poor responders according to their HbA1c level after one year of care. Subjects were classified into three groups: responders (HbA1c $\leq 7\%$), intermediate responders (HbA1c $> 7$ to $\leq 9\%$), and poor responders (HbA1c $> 9\%$).

The 447 subjects had a mean age and disease duration of 58 and 5 years, respectively, and BMI of 32 kg/m\textsuperscript{2}. Overall, the mean HbA1c level fell from 9.6 to 8.1\% after 12 months. Mean HbA1c levels improved from 8.8 to 6.2\% in responders, and from 9.5 to 7.9\% in intermediate responders.

Age, self-reported duration of diabetes, BMI, SBP, DBP, total cholesterol, and triglycerides were different between the groups. In poor responders ($n = 123$), the average HbA1c level was 10.8\% on presentation and 10.9\% at one year. C-Peptide levels were the lowest among poor responders.

In comparing responders ($n = 166$) with intermediate responders ($n = 158$) the study found that self-reported duration of disease, baseline HbA1c, and BMI were the predictors of the change in glycemic control. The odds of being a poor responder were increased with longer disease duration, higher HbA1c level, and greater BMI.
In addition, the odds of being a poor responder decreased with increasing C-Peptide levels (O.R = 0.74; 95% C.I = 0.57 to 0.95). Although doses of oral agents and insulin were higher among poor responders at most visits, the acceleration of insulin therapy did not occur until late in the follow-up period.

Study concluded that clinical diabetes programs need to devise a method to identify the subjects who were at risk for persistent hyperglycemia. Whereas patient characteristics, explains some heterogeneity of HbA1c outcome. In sufficient intensification of therapy may also be a component underlying the failure to achieve glycemic goals.

2.8. Executive cognitive impairment and poor glycaemic control

Hayley W, et.al. (2007) determined whether impaired executive function as detected by a battery of simple bedside cognitive tests of executive function was associated with inadequate glycaemic control or not.

Subjects with type 2 diabetes attended a tertiary referral diabetic clinic, who consented to participate in the study, underwent a brief battery of cognitive testing (the Bedside Executive Screening Test) designed to detect executive function impairment. Glycaemic control was determined by using blood glycated hemoglobin levels (HbA1c). Inadequate glycaemic control was defined as: HbA1c ≥ 7%.

Of the one hundred and seven subjects recruited, 98 consented to participate in the study. The mean age was 57.7 ± 10.4; ranged between 31 to 85 years. Mean education level was 8.2 ± 2.5; ranged between 3 to 16 years.
Executive function impairment was detected in 51 (52%) of the 98 subjects. The presence of executive function impairment was associated with poor glycaemic control (O.R = 4.9; 95 % C.I = 1.3 to 18.8). There were no differences between subjects with and without executive function impairment according to age, target organ damage, patient reported adherence, and hypoglycemic therapy.

Subjects with a lower educational level were more likely to demonstrate executive impairment when glycaemic control was poor (P = 0.013). Executive function impairment was common in a population of people with difficult-to-manage type 2 diabetes. The presence of executive impairment was associated with poor glycaemic control.

2.9. Adherence to regimens and glycemic control

Howteerakul N, et.al. (2007) conducted a cross-sectional study to measure the prevalence of patient adherence to treatment regimens, and factors affecting glycemic control among type 2 diabetics.

Two hundred and forty three subjects who have been seeking care at a tertiary diabetic clinic hospital in Bangkok, Thailand were interviewed. HbA1c was used as an index of glycemic control.

The inclusion criteria were type 2 diabetes with a clinical diagnosis for at least one year, treated with diabetes drugs, and received a HbA1c test at the diabetes clinic of the hospital during the study period. Pregnant, disabled or diabetics with acute renal failure, sever heart disease, and used insulin were excluded.
The proportions of cases with good adherence to physical exercise and diet regimen were 31.7 and 54.3%, respectively. Forty seven percent were reported receiving good social support for diabetes from his/her family. The median HbA1c was 8%. Thirty three percentage were achieved good glycemic control (HbA1c ≤ 7%), while 50.2% had poorly controlled diabetes, HbA1c ≥ 8%.

Subjects with good adherence to taking medication were more likely to have better glycemic control than those who did not (O.R = 4.63; 95% C.I = 1.04 to 20.60). Those subjects who had good family members and friends support for their diabetes tended to have better control than those who did not (O.R = 1.32; 95% C.I = 0.74 to 2.36).

This study identified two variables, which were associated with glycemic control: adherence to diet control, and exercise. The study concluded that Interactive health education should be introduced to increase patient adherence to treatment regimens. Family members should be informed about their important roles in encouraging patients' glycemic control.

**2.10. Effect of self-management practices on glycaemic control**

Javier EG, et.al. (2006) examined the relative impact of self-management activities on glycaemic control in a population at high risk for developing diabetic complications.

Subjects diagnosed with diabetes mellitus of at least one year in duration at 30 years of age or older were sampled from the Instituto de Mexico Seguro Social (IMSS) Family Medicine Clinics in Guadalajara, Mexico (n = 800). Demographic, clinical and health behavior variables were used to predict good/poor HbA1c.
The age of the subjects ranged from 33 to 95 years, with an average of 60 years. Those who were pregnant, had gestational diabetes or had type 1 diabetes were excluded. The average HbA1c was 8.6%, 27.76% had good control (HbA1c ≤ 7.0%) and 72.24% had poor control (HbA1c > 7.0%).

Following a special diet has a protective effect, as those who did so were half as likely to have poor control (O.R = 0.49; 95% C.I = 0.32 to 0.76). Those with poor control were more likely to test their blood glucose (O.R = 1.60; 95% C.I = 1.00 to 2.56).

Having a first degree relative with diabetes increased the likelihood of poor glycaemic control (O.R = 1.52; 95% C.I = 1.06 to 2.19). Longer duration of disease was associated with poor glycaemic control. Those with a disease duration of 10 to 15 years were more than twice as likely to have poor control (O.R = 2.40; 95% C.I = 1.40 to 4.14).

Those who did not take medications for their diabetes were less likely to have poor control than those who took only oral medications (O.R = 0.18; 95% C.I = 0.10 to 0.33), and those on insulin were more likely to have poor control than those who took pills only (O.R = 7.88; 95% C.I = 2.42 to 25.63).

Hyperglycemia was associated with: having diabetes for a longer time (O.R = 2.40; 95% C.I = 1.39 to 4.14), having a first-degree relative with diabetes (O.R = 1.52; 95% C.I = 1.06 to 2.19), and being prescribed anti-diabetic medications, e.g. insulin (O.R = 7.88; 95% C.I = 2.42 to 25.63). After controlling for these variables, the only self-management variable that reduced the likelihood of hyperglycemia was: following a special diet (O.R = 0.49; 95% C.I 0.32 to 0.76).
Depression had an important effect on self-management, as those with lower levels of depressive symptoms were more likely to follow a diet and exercise. While subjects in this study have little control over many factors associated with glycaemic control, an important exception was diet. However, because of the adverse effect of depression on dieting, both depression management, and dietary education were important for diabetics.

2.11. Factors associated with glycemic control in type 2 diabetics

Abdelaziz B, et.al. (2005)\(^{17}\) determined the factors associated with poor glycemic control in type 2 diabetics followed in primary care units in Sousse, Tunisia. This was a cross-sectional study, conducted on a representative sample of type 2 diabetics followed at least two years. Data were gathered from three sources: a self-administrated questionnaire, analysis of patient files, and HbA1c level. Subjects were considered well-controlled if glycated hemoglobin was less than 7%.

The study enrolled 404 type 2 diabetics. The mean age was 60.5 ± 10.89 years, sex-ratio was 0.5, and mean disease duration 8.7 ± 6.1 years. Poor geographic access to the health care center (O.R = 1.89; P = 0.009), and BMI < 30 kg/m\(^2\) (O.R = 2.21, P = 0.034) were associated with poor glycemic control of diabetes. The study concluded that glycemic control in type 2 diabetics was poor and it depends strongly on geographic access to health care.


Cynthia CJ, et.al. (2006)\(^{34}\) evaluated anti-diabetic drug treatment patterns and glycemic control among type 2 diabetics.
Study population consisted of subjects ≥ 18 years of age with diagnosed type 2 diabetes mellitus from 1st January, 2002 to 31st December, 2002. The proportion of subjects, who had optimal glycemic control (HbA1c < 7%) during the six months after the initial documentation of the disease during the year were obtained.

Of the 4282 subjects, who met the inclusion criteria were: 1050 (25%) received one oral agent, 486 (11%) received two oral agents, 56 (1%) received ≥ 3 oral agents, 84 (2%) received insulin and an oral agent, and 107 (2%) received insulin exclusively within 90 days.

Among the 1075 subjects received anti diabetic drug therapy who had a laboratory test result documented, 414 (39%) had optimal glycemic control. Optimal glycemic control was most frequent among the subjects who have been receiving one oral agent (47%), and least frequent among the subjects who receiving ≥ 3 oral agents (13%; P < 0.01).

People with prior history of suboptimal glycemic control were less likely to have optimal glycemic control. Subjects with a prior history of suboptimal glycemic control were less likely than subjects whose HbA1c < 7% to have optimal glycemic control (O.R = 0.08; 95% C.I = 0.05 to 0.14, for those who’s HbA1c ≥ 8% to < 9%; O.R = 0.08; 95% C.I = 0.04 to 0.15, for those who’s HbA1C ≥ 9%).

Majority of subjects treated with multiple oral anti-diabetic agents had suboptimal glycemic control and suggested that there was a need for intensified efforts to treat this particular group of subjects to achieve good glycemic control.
2.13. Factors that influenced improvement in poorly controlled diabetics

Arthur H, et.al. (2006) were assessed the reasons for improved control for subjects with initially poorly controlled diabetes.

Subjects from seven practices with type 2 diabetes mellitus were selected, if within a six month period they had two HbA1c values of at least 8.0%. Patient factors that may influence glycemic control were compared, and the subjects were grouped according to their last two HbA1c levels.

Review of 643 medical records of diabetics treated by 29 physicians identified 69 subjects. After at least one year of follow-up 26 subjects got disease well controlled, 14 had intermediate control, and 29 remained in poorly controlled. Getting well controlled was not associated with: gender, age, duration of diabetes, and BMI.

It was inversely associated with greater use of medications (P = 0.04), and positively associated with understanding of diabetes (P = 0.03), adherence to recommendations for meal plan (P = 0.001), and glucose monitoring (P = 0.02). Thirty-one percent of the subjects who got disease well controlled had a change in life style.

Controlled and uncontrolled subjects did not differ with respect to: gender, age, duration of diabetes, BMI or HbA1c levels prior to base line. The study suggested that differences between the subjects who gain control and those who do not may not be primarily due to basic physiologic factors measured by age or BMI or even measures of diabetes status such as duration or severity of disease.
It also did not seem to be due to medication use; subjects who gained control generally used lower medication doses than those who did not. There was evidence that patient factors such as understanding of diabetes and adherence to recommended behaviors were of primary importance. The study concluded that improved glycemic control depends largely on subject’s self-care behaviors.

2.14. Predictors of glycemic control among type 2 diabetics

Stephen RB, et.al. (2005) determined what demographic, health status, treatment, access/quality of care, and behavioral factors were associated with poor glycemic control in type 2 diabetics.

Longitudinal observational data was collected on subjects with type 2 diabetes from Project Dulce, a program in San Diego County designed to care for an underserved diabetic population. The study sample included 573 subjects with a racial/ethnic mix of 53% Hispanic, 7% Black, 18% Asian, 20% White, and 2% other.

Mixed effects models were used to determine the factors associated with poor glycemic control by using HbA1c as the outcome of interest. HbA1c was measured over a period of 2 to 3 months and HbA1c < 7% was considered as well controlled.

Subjects had mean age of 55 years, 69% were female, the mean duration of diabetes was 7.1 years, 31% were treated with insulin, and 57% were obese. The factors associated with glycemic control were: disease duration, insurance status, pharmacotherapy, and cholesterol level. Those subjects who had diabetes over ten years had a 15.3% higher HbA1c level compared to those who had diabetes less than one year.
The subjects who were diabetic for six to ten years had higher HbA1c values compared to those with diabetes less than one year. Those who required insulin had a 22.4% higher HbA1c and those who required more than one oral medication had 12.0% compared to those who used one oral medication or no medication at all. On average every 0.65 unit increase in total cholesterol, the HbA1c value was 2.6% higher.

Study concluded that that subjects who were uninsured, had diabetes for a longer period of time, used insulin or multiple oral agents, or had high cholesterol had higher HbA1c values over time indicating poorer glycemic control.

2.15. Pharmacist-led, primary care-based disease management improves HbA1c

Russell R, et.al. (2003) developed and evaluated a comprehensive pharmacist-led, primary care-based diabetes management program for subjects with poorly controlled type 2 diabetes mellitus. The primary goal of this program was to improve glucose control, as measured by hemoglobin levels (HbA1c).

Clinic-based pharmacists offered support to subjects with diabetes through direct teaching about diabetes, frequent phone follow-up, medication algorithms, and use of a database that tracked the outcomes and actively identified opportunities to improve care. Adult (≥18 years) subjects with a diagnosis of type 2 diabetes, who were followed up for primary care, in the UNC General Internal Medicine practice were eligible for the study. Subjects were excluded if they identified an outside practitioner as the main provider of their diabetes management. From September 1999, to May 2000, 159 subjects had HbA1c ≥ 8% and they were enrolled into the study.
Baseline HbA1c averaged 10.8%, and after an average of six months of intervention, the mean reduction in HbA1c was 1.9%. HbA1c and new onset of diabetes were associated with the improvements in HbA1c.

Age, race, gender, educational level, and provider status were not the predictors of improvement. The study concluded that, pharmacist-based diabetes care program integrated into primary care practice were causes for reduced HbA1c among the subjects with diabetes that was poorly controlled.

2.16. Food habits were related to glycemic control of type 2 diabetics

Savoca MR, et.al. (2004) investigated the food habits of people with type 2 diabetes and identified how those habits related to glycemic control among the diabetics.

The purposive sampling plan targeted at people (40 to 65 years old) living in two urban communities of the Southeastern United States with type 2- diabetes, for more than one year (60% women, 50% African Americans, and low-income individuals). In-depth interview was conducted to identify their habits.

A four-factor solution derived from 15 food habits explained 51.5% of the total variance in HbA1c values. High factor scores for three factors (basic eating practices, meal planning, and carbohydrate/ vegetable strategies), and low factor scores for a fourth factor (challenges of dining out) were related to lower HbA1c levels. Based on similar patterns across the 15 food habits, subjects were clustered into four groups: The clusters differing on HbA1c were healthful eating lifestyle (6.25 ± 0.25), disciplined eating approach (7.31 ± 0.35), limited dietary focus (8.28 ± 0.33), and poor dietary management (9.05 ± 0.24).
The study concluded that, Knowledge of the specific food habits of people with diabetes can offer a way to structure a meaningful dialog with clients about dietary self-management and guide the collaborative development of relevant dietary goals.

2.17. Patient characteristics which do not predict poor glycaemic control

Alex NG, et.al. (2004) assessed which characteristics of type 2 diabetics treated in a primary care center will predict poor glycaemic control (HbA1c ≥ 7%).

This study was carried out in the Utrecht region between July 1999 and October 2000. Of the 110 general practices invited to take part, 52 (67 doctors) were willing to participate. Twenty seven practices (52%) were connected to the Utrecht Diabetes Project. The practices covered 131,000 people and included 2140 subjects who were type 2 diabetics. Of the 2140 participants, 1641 subjects had HbA1c 7.1 ± 1.7%, and 42% had HbA1c ≥ 7%.

Age, longer duration of diabetes, higher levels of blood glucose at diagnosis, most recent fasting blood glucose (FBG), total cholesterol, and triglyceride, higher body mass index (BMI), treatment with oral hypoglycemic agents (OHA), treatment with insulin, and lower educational level were associated with poorly controlled diabetes.

Higher levels of FBG (O.R = 1.6; 95% C.I = 1.49 to 1.70), treated with OHA (O.R = 2.1; 95% C.I = 1.41 to 3.04), treated with insulin (O.R = 7.2; 95% C.I = 4.18 to 12.52), and lower educational level (O.R = 1.26; 95% C.I = 1.01 to 1.56) were associated with poor levels of HbA1c.
When FBG levels were excluded from the model, higher blood glucose at diagnosis, higher values for triglyceride, total cholesterol, and younger age predicted poor glycaemic control, but these variables explained only 15% of the variation in HbA1c. The study concluded that prediction of poor glycaemic control from patient characteristics in diabetic subjects in general practice is hardly possible.

2.18. A probabilistic model for predicting hypoglycemia

Glen HM, et.al. (2004)\textsuperscript{40} developed, and validated a method for estimating hypoglycemia risk in stable, insulin-treated subjects with type 2 diabetes mellitus.

Subjects (n = 195) monitored their blood glucose levels 4 times daily for 8 weeks. An 8-week mean blood glucose value (GLUMEAN) with standard deviation (GLUSD) was obtained for each subject. They were randomly allocated to a derivation or validation set. For the derivation set, a logistic function was developed, based on GLUMEAN and GLUSD to describe the 8-week risk of hypoglycemia (blood glucose \( \leq 60 \) mg/dl). Subjects were assigned to risk quartiles and followed up for up to 52 weeks.

Among 195 subjects, 95% of them were men and 69% were non-Hispanic white. For 72 derivation subjects, GLUMEAN and GLUSD were the determinants of hypoglycemia during intensified monitoring. The 123 validation subjects were followed up for 39.7 \( \pm \) 7.1 weeks. Hypoglycemia was detected in 36 subjects. The median number of events among the hypoglycemic subjects was 2.5 (IQR = 2 to 5). The number of events detected during the intensified monitoring was different (P = 0.07) across the groups. Subjects who became hypoglycemic had a lower 8 week mean blood glucose level (P = 0.001).
The occurrence of long-term hypoglycemia differed across risk quartiles (19.4%, 36.7%, 61.3%, and 77.4%; P < 0.001). GLUMEAN was negatively correlated with the number of blood glucose readings taken during intensified monitoring (r = -0.388; P = 0.002) and there was no relationship for GLUSD.

Receiver operating characteristic curve analysis showed that the area for the probability function (0.746 ± 0.046) was higher than the area for HbA1c (0.549 ± 0.052). The function also identified subjects who developed long-term hypoglycemia at a rate exceeding the median frequency.

The study concluded that, Self-monitoring of blood glucose was superior to HbA1c measurement in predicting long-term hypoglycemia in subjects with type 2 diabetes. The risk of hypoglycemia associated with treatment intensification may be offset by strategies that reduce glucose variability.

2.19. Influence of psychosocial factors on glycemic control


The study population comprised of 193 (75%) men and 63 (25%) women, with a mean age of 62.3 ± 8.8 years. Of these 250 subjects were followed for a period of 12 months. There was a positive correlation between HbA1c and: psychosocial scores (r = 0.21; P < 0.001), life events impact (r = 0.19; P < 0.001), and daily burden (r = 0.12; P < 0.05).

There was a negative correlation between HbA1c and: adherence to: diet (r = -0.16; P < 0.01), exercise (r = -0.16; P < 0.05), and diabetes related self efficacy (r = -0.26; P <
0.01). Self-efficacy directly reinforced adherence, and adherence had a direct association with future HbA1c. Other psychosocial factors, including social support, diabetes-related distress, daily burden, and emotion-focused coping prospectively influenced HbA1c indirectly through self-efficacy.

**2.20. Predictors of glycemic control in insulin-using adults with type 2 diabetes**

Nichols GA, et.al. (2000)\(^{62}\) determined the characteristics that influence glycemic control among insulin dependent adults with type 2 diabetes.

The study population comprised of 1,333 eligible members of a large not-for-profit health maintenance organization who responded to a 1997 survey. Associations among the: demographic, treatment, and psychometric variables with mean HbA1c values were assessed.

The Problem Areas in Diabetes (PAID) instrument was used to assess the emotional effect of living with diabetes, and the short form 12 physical function scale was used to assess the effect of physical limitations on daily activities.

Based on differences between and within treatment groups, model was built to predict glycemic control for subgroups of subjects who were using insulin alone and those who were using insulin in combination with an oral hypoglycemic agent.

This study regressed HbA1c against demographic and treatment and psychometric variables in a relatively well controlled population of 1178 subjects with type 2 diabetes who were using insulin. Separate models have been constructed for subjects receiving insulin alone (n = 931), receiving combination therapy (n = 247), and for HbA1c > 8%.
Younger age, lower BMI, and increased emotional distress about diabetes were the predictors (P < 0.05) of poorly controlled diabetes. However, individuals with HbA1c level of > 8.0% who were receiving combination therapy, only approximately 10% of the variance in glycemic control could be predicted by demographic, treatment, or psychometric characteristics.

Personal characteristics explain little of the variation in glycemic control in insulin-using adults with type 2 diabetes. The reduced complexity of control in type 2 diabetes makes the disease less sensitive to personal factors, that health-related behavior was less driven by personal and environmental characteristics among elders, or that, in populations exposed to aggressive glycemic control with oral hypoglycemic agents.

2.2.1. Personality correlates of glycemic control in type 2 diabetics

James DL, et.al. (2000) conducted a longitudinal cohort study by using data from 105 type 2 diabetics in a clinical trial of a stress management intervention.

Before treatment assignment, subjects completed the NEO Personality Inventory, which was a questionnaire inventory measuring five major domains of normal personality and 30 important traits that define these domains. Glycemic control was assessed by HbA1c and average blood glucose levels based on seven days of self-monitoring at baseline and at 6 and 12 months. Relationships between personality traits and measures of glycemic control were examined.

A total of 99 of the 105 subjects completed the self-monitoring of blood glucose. The HbA1c ranged from 5.2 to 15.7% (7.8 ± 1.9%).
Average blood glucose values at baseline were associated with higher scores for the personality domain of neuroticism and several specific traits including anxiety, anger and hostility, depression, self-consciousness, and vulnerability were associated with higher levels of HbA1c.

There was a correlation between the measures of short and long term blood glucose control. The study concluded that common personality traits may help to explain variation in glycemic control achieved by subjects with type 2 diabetes under conditions of standard diabetes management. Poor glycemic control was associated with lower scores for neuroticism and the associated personality facets of anxiety, anger and hostility, depression, self-consciousness, and vulnerability. Higher altruism scores were linked to poorer glycemic control.

2.22. Insulin refusal in subjects with poorly controlled diabetics

Khan H, et.al. (2007) determined the prevalence and reasons for refusal to commence insulin in Bangladeshi subjects with type 2 diabetes.

A survey was conducted among Bangladeshi subjects (n = 212), with poorly controlled diabetes (HbA1c ≥ 8.0%) on maximum oral glucose-lowering therapy, in whom insulin was deemed necessary. Subjects who refused insulin were invited to attend focus groups.

Of the 212 subjects offered insulin, 122 (57.5%) commenced insulin immediately, 47 (22.1%) started insulin within six months and 43 (20.3%) refused to commence insulin despite repeated counseling. Thirty-six (83.7%) of those who refused insulin agreed to participate in focus groups.
There were no differences in the demographic or clinical characteristics of those who refused insulin compared with the subjects who were willing to commence insulin.

Reasons for insulin refusal included: disease severity--perceptions that requirement for insulin was an indicator of a more serious stage of their condition; insulin leading to premature death--common suggestion that commencing insulin led to early death; loss of control--including fear of hypoglycemia, weight gain, loss of independence and reliance on others to give insulin or look for signs of hypoglycemia; lack of perception of benefits--poor perception of the benefits of improved glycaemic control on quality of life and cardiovascular risk.

2.23. Effects of sulphonylurea or metformin on glycemic control

Gregorio F, et.al. (1999) assessed the effects and safety of increasing sulphonylurea dosages or adding metformin among poorly controlled type 2 diabetics.

An 18-month multi-centre clinical study was performed on sulphonylurea-treated diabetics over 70 years of age with well-preserved renal function, FBS $\geq$ 200 mg/dl and HbA1c $\geq$ 9%. Subjects were randomly assigned to sulphonylurea increased up to its maximum dosage (1$^{st}$ group, n = 85) or in addition to of metformin (2$^{nd}$ group, n = 89).

Glycaemic control, lipid pattern, haemostatic status, and safety were monitored, at baseline and at scheduled intervals for 18 months. Similar improvements in glycaemic levels were observed with both treatments within the first month and a similar decrease in HbA1c within the third month. No further changes occurred in glycaemic control.
In the 1st group, fasting glucose (mmol/l, mean ± SE) decreased from 14.21 ± 0.49 to 9.88 ± 0.21, average day-long glucose from 14.87 ± 0.27 to 10.69 ± 0.19 and HbA1c (%) from 10.32 ± 0.13 to 8.66 ± 0.13. In the 2nd group fasting glucose decreased from 14.59 ± 0.61 to 9.05 ± 37.28, average day-long glucose from 15.09 ± 0.29 to 10.32 ± 0.21, and HbA1c from 10.33 ± 0.13 to 8.77 ± 0.12 (for all P < 0.0005).

In the 2nd group, a decrease in LDL-cholesterol (P < 0.05) and an increase in HDL-cholesterol levels (P < 0.02), reductions in markers of platelet function (P < 0.01), thrombin generation (P < 0.01), and fibrinolysis inhibition (P < 0.001) were observed. Fasting lactate concentrations were unchanged in the metformin-treated group.

The results suggested that either high sulphonylurea dosages or a therapy combining lower sulphonylurea dosage with metformin were effective and safe in an aged but healthy population.

2.24. Multidisciplinary care plans and its benefits for poorly controlled diabetics

Zwar N, et.al. (2008) examined whether, the care plans were more likely to be implemented and have greater benefit for the subjects with poor metabolic control.

Retrospective before and after medical record audit of 230 type 2 diabetics with care plans were conducted. The study cohort was divided into two groups: pre care plan level (HbA1c > 7%) and Post care plan level (HbA1c ≤7%). There was an increase in the mean HbA1c from 6.2% pre-care plan to 6.5% post-care plan (p = 0.039; mean difference = -0.25, 95% C.I = -0.48 to -0.01). Among the subjects who had a pre-care plan HbA1c >7% the mean HbA1c level fell from 8.2 to 7.9%.
Those who had pre-care plan were more likely to receive multidisciplinary care than those who had pre-care plan (P < 0.001). Care plans were beneficial and more often implemented for the subjects with poor metabolic control. If this positive impact was due to the implementation of multidisciplinary care, questions were raised about the relative effectiveness of general practitioner management plans and team care arrangements.

2.25. Diabetic complications and glycaemic control


This was a prospective cohort study. Over a six week period, all subjects attending the diabetic clinic at Mekelle Hospital in northern Ethiopia were assessed. HbA1c lipid profile, serum creatinine, and urinary albumin–creatinine ratio were measured.

Study population comprised of 105 diabetics with age 41 ± 16 years and diabetes duration 7 ± 6 years. There were 74 (70%) males, and 69 (66%) on insulin. Median body mass index was low at 20.6 kg/m², mean HbA1c was 11.3 ± 2.8% (68% had an HbA1c >10.0%).

The presence of complications were: Cataract (12%), retinopathy (21%), neuropathy (41%) and micro-albuminuria (51%), nephropathy (2%), and 6% had peripheral vascular disease. The study concluded that in several resource-limited area of North Africa, glycaemic control among the diabetics was very poor. Neuropathy, retinopathy and micro-albuminuria were common; but large vessel disease risk factors were beneficial, and macro-angiopathy prevalence was low.
2.26. Patient’s knowledge about HbA1c improves glycaemic control

Iqbal N, et al. (2008)\textsuperscript{46} examined the impact of improving patients' interpretation of a given HbA1c value on glycaemic control.

A questionnaire survey among 111 subjects attending in a hospital was conducted. They were provided with information relating to the association between HbA1c and mean plasma glucose levels.

Of the respondents, 40.5\% (45/111) were familiar (F) (31 type 1, 14 type 2) and 59.5\% (66/111) were unfamiliar (U) (23 type 1, 43 type 2) with the term HbA1c. Subjects with poorly controlled diabetes (HbA1c > 9\%) showed reduction in HbA1c levels if they were from group U (10.7\% vs. 9.5\%, \( P = 0.04 \)) but not from group F (10.5 vs. 9.8, \( P = 0.28 \)). Subjects with moderately poor glycaemic control (HbA1c 7.5-9\%) showed no change in HbA1c levels following intervention (8.3\% vs. 8.2\%, \( P = 0.57 \) group U; 8.3\% vs. 8.2\%, \( P = 0.79 \) group F).

The study concluded that patient’s knowledge about HbA1c was poor, among type 2 diabetics. Improvement in patients' understanding of HbA1c, particularly among those with very poorly controlled diabetes with no prior knowledge of HbA1c was associated with improvement in their glycaemic control.

2.27. Future improvement in glycaemic control

Singh R, et al. (2008)\textsuperscript{71} determined the factors responsible for poor glycaemic control among the diabetics and assessed whether any such factors were associated with improvement in glycaemic control or not.
A group of 130 diabetic subjects having poor glycaemic control (HbA1c ≥ 10.0%) with one year of follow-up in a teaching hospital were the study population. Changes in HbA1c were measured after one year of follow up. Poor glycaemic control was attributed to one of the 15 possible causes.

Subjects with low mood or alcohol excess, inadequate blood glucose monitoring, poor exercise/sedentary lifestyle, refusal to take tablets or under dosing, and refusal to take insulin or to increase the dose were associated with poor glycaemic control.

Among the subjects with poor glycaemic control, it was possible by simple features identified at the clinic to predict which individuals were likely to show improvement in disease control and which will not. Findings of this study suggested that, about half of the individuals with poorly controlled will improve within the current diabetes clinic practice. Additional strategies will be required to address those individuals who were not likely to respond.

2.28. The relationship between alcohol consumption and glycemic control

Ahmed AT, et.al. (2008) evaluated the association between alcohol consumption and glycemic control among the diabetics.

This was a follow-up study, 1994-1997, among Kaiser Permanente Northern California members (38,564 adult diabetics). Self-reported alcohol consumption, and HbA1c, was assessed within one year of survey date. Linear regression of HbA1c by alcohol consumption was performed, adjusted for socio demographic variables, clinical variables, and diabetes disease severity.
The subjects were grouped into seven categories of alcohol consumption: lifetime abstainers, former drinkers, and consumers of < 0.1, 0.1 to 0.9, 1.0 to 1.9, 2 to 2.9, and ≥ 3 drinks/days.

The factors associated with alcohol consumption and glycemic control were: diabetes duration, use of oral diabetes medications, self-monitoring of blood glucose, use of diet and exercise to control diabetes, and obesity.

Alcohol consumption was associated with HbA1c values (P = 0.001); were 8.88 (lifetime abstainers), 8.79 (former drinkers), 8.90 (< 0.1 drink/day), 8.71 (0.1-0.9 drink/day), 8.51 (1-1.9 drinks/day), 8.39 (2-2.9 drinks/day), and 8.47 (≥ 3 drinks/day). Alcohol consumption was linearly (p < 0.001) and inversely (P = 0.001) associated with HbA1c.

Study concluded that, alcohol consumption was inversely associated with glycemic control among the diabetics. As glycemic control affects incidence of complications of diabetes, the lower HbA1c levels were associated with moderate alcohol consumption and it may translate into lower risk for complications.

2.29. Association of younger age with poor glycemic control

Imad ME, et.al. (2003) studied the relationship of age to glycemic control in a predominantly urban African American population with type 2 diabetes.

Subjects with type 2 diabetes who were enrolled in the Grady Diabetes Clinic, Atlanta, between 1st April, 1991, and 31st December, 1998, and had a HbA1c level measured at their initial visit and at follow-up 5 to 12 months later (n = 2539) were the study population.
Subjects were divided into four age categories: less than 30 years, 30 to 49 years, 50 to 69 years, and more than 69 years old. At baseline, average HbA1c levels were 9.9%, 9.5%, 9.2%, and 8.8% in the four groups ranked in increasing age, respectively (P < 0.001), and body mass indexes were 37.8, 33.9, 31.6, and 29.2, respectively (P < 0.001). On follow-up, HbA1c level improved in all the groups (P < 0.001).

The prevalence of having HbA1c level > 8.0% at baseline increased from 54% to 75% with decreasing age (P = 0.001). 19% to 23% of the subjects had an HbA1c < 7%, increasing to 33% to 41% at 8 months. The proportion of subjects having HbA1c > 8% at follow up increased from 31% to 48% with decreasing age (P = 0.001).

Younger age, longer diabetes duration, higher body mass index, less frequent interval visits, and treatment with oral agents or insulin were associated with a higher HbA1c level at follow-up. HbA1c level and body mass index were negatively correlated with age (P < 0.001). The study concluded that there was a high prevalence of obesity and poor glycemic control in young adult urban African Americans with diabetes.

2.30. Association between glycaemic control and serum lipids profile

Khan HA, et.al. (2007) examined the impact of glycaemic control on the lipid profile of diabetics. They also determined the ability of glycated hemoglobin (HbA1c) as an indirect marker of dyslipidemia.

A total of 1011 type 2 diabetics (males, 574; females, 437; mean age, 59.76 years) who visited the clinics of Armed Forces Hospital, Riyadh were included in this study. The mean age of males and females were 62.72 ± 10.24, and 55.86 ± 12.08 years respectively.
The effect of glycaemic control on various parameters was evaluated. Venous blood samples were collected from all the subjects after at least eight hours of fasting. The sera were analyzed for HbA1c, fasting blood glucose (FBG), total cholesterol, triglycerides (TG), high-density lipoprotein cholesterol (HDL), and low-density lipoprotein cholesterol (LDL).

The levels of HbA1c, FBG and LDL did not differ between males and females. Female showed higher serum cholesterol levels, and HDL as compared to males. There was a correlation between HbA1c and FBG. Both HbA1c and FBG exhibited direct correlations with cholesterol, TG and LDL had an inverse correlation with HDL.

There was a linear relationship between HbA1c and dyslipidemia. The levels of serum cholesterol and TG were higher and HDL lower in subjects with poor glycaemic control as compared to well controlled. The age of the subjects was inversely correlated with cholesterol, HDL and LDL whereas it was not correlated with TG.

The impact of glycemic control on various parameters was evaluated by categorizing all the subjects into three groups on the basis of HbA1c levels: group 1, good glycemic control (HbA1c < 6%); group 2, poor glycemic control (HbA1c > 6 to 9%); groups 3, worst glycaemic control (HbA1c ≥ 9%).

The concentration of FBG was higher in group 3 (P < 0.001) and group 2 than group 3. The findings of this study indicated that HbA1c was not only a useful biomarker of long-term glycaemic control but also a good predictor of lipid profile.
2.31. Co-morbidity and glycemic control

Imad ME, et.al. (2001) determined the impact of co-morbidity on glycemic control of type 2 diabetes. The sample size was 654.

Study population was comprised of 654 subjects, from a diabetes clinic in 1997. Co-morbidity was rated using the Chronic Disease Score (CDS) index, weighted score that takes into account the subject's age, gender, and classes of medications.

Univariate and multivariate linear regressions were performed to determine the contribution of age, body mass index, and diabetes duration, type of therapy, and CDS to HbA1c level.

The subjects were: 90% African-American, of whom 66% were female, with an average age of 53 years. Average diabetes duration was 5 years and HbA1c level was 8.8%. At presentation, subjects with higher CDSs tended to be older and to have a lower HbA1c level.

Those subjects receiving pharmacological therapy, younger aged subjects, and having a lower C-peptide level were the contributors to HbA1c level. Of the 169 subjects followed up, presenting characteristics were not different from those of the full cohort: average baseline HbA1c level was 8.8%; CDS, 1073. Their HbA1c level at 6 months averaged 7.5% and the CDS had no impact on their follow-up HbA1c level. The study concluded that co-morbidity does not appear to limit achievement of good glycemic control in subjects with type 2 diabetes.
2.32. Patterns of glycaemic control among type 2 diabetics

Maclsaac RJ, et.al. (2009) described the patterns of glycaemic control in subjects who participated in the national evaluation of the frequency of renal impairment co-existing with non-insulin dependent diabetes mellitus.

Expressions of interest were invited from all registered general practitioners in Australia, from which 500 investigators were randomly selected and asked to provide data on 10-15 consecutive adults with type 2 diabetes presenting in their practice. Just less than half of the 3893 enrolled had HbA1c \( \leq 7.0\% \) (47.7%) and quarter had an HbA1c \( \leq 8.0\% \) (24.3%).

On an average, subjects with poor HbA1c were: younger, more obese, had a longer duration of diabetes, with more micro and macro-vascular complications and higher lipid levels than those who achieved adequate levels of glycemic control. In subjects on mono therapy, more than half (55%) achieved an HbA1c < 7%.

There were no difference in the number of subjects achieved HbA1c < 7% for taking either metformin or a sulfonylurea. The targets for glycaemic control in type 2 diabetes have generally been followed in Australian general practice, but there was a gap in the achievement of recommended glycaemic goals. A quarter of the subjects had poor glycaemic control.

The immediate steps that can be taken to improve glycaemic control include the early use of a combination of oral glucose-lowering therapies and the increased use of insulin.
2.33. Insulin resistance is a poor predictor of type 2 diabetes in subjects with no family history of disease

Goldfine AB, et al. (2003)²¹ determined whether low insulin sensitivity, low glucose effectiveness or low acute insulin response to glucose were the predictive of diabetes in a population at low genetic risk for diabetes.

The study population included was: normal glycemic individuals (n = 181) with no family history of diabetes (FH-), and 150 normal glycemic offspring (n = 150) of type 2 diabetic parents (FH+) who underwent glucose tolerance testing between the years 1964-82. During 25 ± 6 years of follow-up, comprising 2,758 person years, the FH- cohort (54 ± 9 years) had an age-adjusted incidence rate of type 2 diabetes of 1.8 per 1,000 person years, similar to that in other population-based studies.

The acute insulin response to glucose was not predictive of the development of diabetes when considered independently or when assessed as a function of glucose disposition. Hence the low glucose disposal rates were associated with the development of diabetes in the FH+ individuals and insulin resistance was not sufficient for the development of poorly controlled diabetes in individuals without a family history of diabetes.

2.34. Impact of body weight, β-cell function, and patient education on HbA1c

Chan WB, et al. (2000)³³ examined the determinants of glycaemic control in a consecutive cohort of 562 newly-referred Chinese type 2 diabetics (57% women) during a 12-month period. All subjects underwent a structured assessment with documentation of clinical and biochemical characteristics.
Pancreatic $\beta$-cell function was assessed by fasting plasma C-peptide concentration. Insulin deficiency was defined as fasting plasma C-peptide $< 0.2 \text{ mol/ml}$. Insulin resistance (IR) was calculated by using the homeostasis model assessment based on a product of fasting plasma glucose and insulin concentrations. Treatment was considered appropriate when insulin-deficient subjects were treated with insulin and non-insulin-deficient subjects were treated with oral agents or diet.

The characteristics included were: age, $54.3 \pm 13.8$ years (range 17 to 87 years); and disease duration, $5.0 \pm 5.9$ years. At the time of referral, 70.5\% ($n = 396$) were on drug therapy (9\% on insulin and 62.8\% on oral agents), 20.6\% ($n = 116$) were on diet and 9\% ($n = 50$) had not received any form of treatment. The mean HbA1c was $8.4 \pm 2.3\%$.

Glycated hemoglobin was positively correlated with age ($P = 0.013$), disease duration ($P < 0.001$), insulin resistance ($P < 0.001$), and negatively with BMI ($P < 0.001$). Glycated hemoglobin was lower in subjects who had seen a dietitian (7.9\% vs. 8.7\%; $P < 0.001$) or diabetes nurse (7.8\% vs. 8.7\%; $P < 0.001$) or who performed self blood glucose monitoring (7.9\% vs. 8.6\%; $P = 0.001$) and higher among smokers (8.9\% vs. 8.2\%; $P = 0.003$).

Compared to insulin-deficient subjects ($n = 118$), non-insulin-deficient ($n = 413$) had features resembling that of Metabolic syndrome with increased waist hip ratio ($P = 0.005$), blood pressure ($P < 0.001$), BMI ($P = 0.001$) and were older ($P = 0.04$). Amongst the insulin-deficient subjects, 27\% were treated with oral agents or diet.
Subjects receiving appropriate therapy \( (n = 362) \) had a lower HbA1c than those treated inappropriately \( (n = 173) \) (8.2\% vs. 8.7\%, \( P = 0.02 \)). On multivariate analysis, short disease duration \( (P < 0.001) \), low insulin resistance \( (P < 0.001) \), higher BMI \( (P = 0.001) \), diabetes education \( (P < 0.001) \), lack of smoking \( (P = 0.014) \) and choice of appropriate treatment \( (P = 0.009) \) were the independent determinants of good glycaemic control.

### 2.35. Socio-demographic determinants of glycaemic control

Ismail IS, et.al. (2000)\(^47\) observed the glycaemic control in subjects from different centers in Peninsular Malaysia and the factors that determine it. The subjects \( (n = 926) \) were diagnosed before age 40 years from seven different centers, with proportionate representation from the three main ethnic groups. Clinical history and physical examination were done and blood sample were taken for measuring HbA1c and FBS.

Glycaemic control in subjects with type 2 diabetes varied between the various centers and ethnic groups, with the best control obtained in Chinese subjects. The predictors of HbA1c included were: access to nurse educators, ethnic background, and waist hip ratio. Insulin use and household income were the predictors of glycemic control. Socioeconomic status had an effect in type 2 diabetes.

There were no differences in the glycaemic control in subjects with different educational status. The study concluded that, glycaemic control was related to the availability of diabetes care facilities and ethnic group, rather than socioeconomic status.

### 2.36. Factors influencing disease self-management in poorly controlled diabetics

Karin MN, et.al. (2007)\(^50\) assessed the factors influencing diabetes self-management among poorly controlled diabetes.
A questionnaire was mailed to the subjects with type 2 diabetes and HbA1c of 8% or greater who attended the Medical Centers in Washington State (n = 1,286). The survey instruments assessed readiness to change, self-efficacy, provider advice, and diabetes self-care practices.

The response rate was 56% (n = 717). Most respondents reported appropriate advice from physicians regarding physical activity, nutrition, and glucose monitoring (73%, 92%, and 98%), but many were not ready to change self-management behaviors. Forty-five percent reported non-adherence to medications, 42% ate a high-fat diet, and only 28% obtained either moderate or vigorous physical activity.

The mean self-efficacy score for diabetes self-care was low, and half of the sample reported readiness to change nutrition (52%) or physical activity (51%). Individuals with higher self-efficacy scores were more likely to: adhere to medications, follow a diabetic meal plan, eat a lower fat diet, have higher levels of physical activity, and monitor their blood sugar levels (P < 0.001).

The study concluded that although subjects with poor diabetes control receive appropriate medical advice, many were not sufficiently confident or motivated to make and maintain self-management changes.

2.37. Insulin resistance in elderly subjects with poorly controlled diabetics

Kastuki A, et.al. (2002) studied whether homeostasis model assessment (HOMA IR) and quantitative insulin sensitivity check index (QUICKI) was an indicator of insulin resistance in elderly subjects with type 2 diabetes mellitus
This study comprised of 56 Japanese subjects with type 2 diabetes mellitus; of these, 28 were ≥ 70 years of age (group 1) and 28 were < 70 years of age (group 2). Their blood sugar levels were in poor control (fasting plasma glucose levels: group 1, 9.0 ± 2.6 mmol/liter; group 2, 8.9 ± 2.3 mmol/liter; HbA1c: group 1, 9.5 ± 2.0%; group 2, 9.2 ± 1.7%).

Subjects with HbA1c ≤ 6.5% were considered as well controlled diabetics. There was a positive correlation between QUICKI and infusion rate in group 2 subjects (r = 0.50, P < 0.01). No correlation was observed between QUICKI and glucose infusion rate in group 1 subjects (r = 0.31, P = 0.12).

Study concluded that, neither HOMA IR nor QUICKI should be used as an index of insulin resistance in elderly subjects with poorly controlled type 2 diabetes mellitus. The results of this study suggested the need for developing a new noninvasive method for evaluating insulin resistance in poorly controlled diabetics.

2.38. The effects of ageing on glycaemic control

Kilpatrick ES, et.al. (1996) investigated the discrepancy in the assessment of glycaemic control by using glycated hemoglobin (HbA1c), and glycated proteins, the effect of age on these variables was measured in diabetic individuals.

The subjects (n = 128, median age 63 years) were classified according to European guidelines into good or poor glycaemic control by using both an age-matched (n = 101) and a younger (n = 108, median age 37 years) non-diabetic reference population, fewer
subjects were in good control (14% vs. 25%; P < 0.05) and more in poor control (73% vs. 53%; P < 0.05).

In a subgroup of 126 non-diabetic subjects, HbA1c rose with age (r = 0.48), but glycated protein and fasting glucose were not associated (r = 0.07, r = 0.009, P > 0.05). There was a linear relationship between HbA1c and age among the subjects (r = 0.49, P < 0.001).

Age-associated differences in non-diabetic HbA1c values may affect the assessment of glycaemic control in diabetics. Age-related HbA1c reference intervals may therefore be required for the treatment and the accurate auditing of clinic performance.


Patric JL, et.al. (2007) determined whether both short- and long term treatment were associated with improvement in glycemic control or not.

Ninety-three type 2 diabetics with major depressive disorder received bupropion hydrochloride in a two-phase, open-label treatment trial were the study population. Those who completed the acute phase (10 weeks; n = 75) and whose depression remitted (n = 63) continued bupropion at the remission dose and were followed in the maintenance phase (24 weeks) until attrition (n = 8) or relapse of the disorder (n = 0).

Self-report scales were used to measure depression symptom severity and diabetes self-care behaviors. Body composition and glycemic control were determined by using dual-energy X-ray absorptiometry and serial determinations of HbA1c.
BMI, total fat mass, and HbA1c decreased and composite diabetes self-care improved over the acute phase (P < 0.01), effects that persisted through the maintenance phase for BMI, HbA1c, and self-care (P ≤ 0.01).

Reductions in BMI (P = 0.01) and depression severity (P = 0.046) independently predicted lower HbA1c after acute-phase of treatment, whereas only reduction in depression severity (P = 0.001) predicted HbA1c over the maintenance interval. In the short term, improvement in glycemic control during bupropion treatment was predicted independently by improvements in mood and body composition.

Long-term improvements in glycemic control were predicted primarily by sustained improvement in mood via mechanisms independent of anthropometric and self-care modifications.

2.40. Depression and poor glycemic control

Patric JL (2000) conducted a systematic review to determine whether depression was associated with poor glycemic control or not.

Medline and PsycINFO were used to locate studies published in the period between: 1975 to 1999 that reported the association of depression with HbA1c in adult (age ≥ 18 years) diabetics, databases and published reference lists were used to identify the various studies that measured the association of depression with glycemic control.

The study characteristics were recorded, and the studies were categorized by methodology of the study.
A total of 24 studies qualified for the meta-analysis. Depression was associated with hyperglycemia ($Z = 5.4$, $P < 0.0001$). This study concluded that depression was associated with hyperglycemia in subjects with diabetes.

2.41. Psychosocial factors associated with poor control of diabetes

Lerman I, et.al. (2004)\textsuperscript{58} examined the relationship between demographic, clinical and psychosocial variables and diabetes self-care management in Mexican type 2 diabetics.

This was a cross-sectional study of 176 subjects with type 2 diabetes aged 30-75 years, attended to a tertiary health-care center at Mexico City. The study group consisted of 64 males/112 females; aged $55 \pm 11$ years, mean diabetes duration was $12 \pm 8$ years. HbA1c was $9.0 \pm 2.0\%$, 78.4% followed correct dose of diabetes pills or insulin, 58% ate the recommended diet, and 44.3% did exercise three or more times per week.

A good adherence to these three recommendations was observed in only 26.1% of the subjects. They were considered as a group, characterized by a greater knowledge about the disease ($P < 0.001$), regular home blood glucose monitoring ($P < 0.01$), an inner perception of better diabetes control ($P = 0.007$), good health ($P = 0.004$), and better communication with their physician ($P < 0.02$).

Poor adherence to two or three main diabetes care recommendations was associated with a depressive state (O.R = 2.38; 95% C.I = 1.1 to 4.9) and a history of excessive alcohol intake (O.R = 4.03; 95% C.I = 1.1 to 21.0). Poor adherence to standard diabetes care recommendations was frequently observed in subjects with type 2 diabetes.
2.42. Improvement in glycaemic control with rosiglitazone/metformin

Rosenstock J, et.al. (2006) explored the safety and efficacy of open-label treatment with rosiglitazone and metformin fixed-dose combination therapy in subjects with poorly controlled diabetes, to better characterize the magnitude of HbA1c reduction after 24 weeks of therapy.

In this multicentre, open-label trial, 190 subjects with an HbA1c > 11% or fasting plasma glucose (FPG) > 15 mmol/l were included. Subjects were assessed for efficacy and safety at five visits over a 24-week period.

The primary efficacy end point was change from baseline HbA1c at week 24. Secondary efficacy end points included the proportion of subjects achieving defined HbA1c targets; change from baseline to week 24 in FPG and insulin sensitivity.

The majority of the subjects (78%) completed 24 weeks of open-label treatment. At week 24, there was mean reduction in HbA1c from 11.8 to 7.8%, (4.0 ± 2.2%; p < 0.0001) and mean FPG reduction from 16.9 to 9.2 mmol/l, (7.7 ± 4.4 mmol/l; p < 0.0001) were observed.

Despite a high mean baseline HbA1c of 11.8%, 33% of the subjects achieved HbA1c ≤ 6.5% at week 24, and 44% achieved HbA1c < 7%. RSG/MET fixed-dose combination was well tolerated, with a low incidence of hypoglycemia (2%) and mean increase in weight from baseline of 2.6 ± 5.2 kg, and a few subjects withdrew (2.6%) because of an adverse event.
RSG/MET fixed-dose combination therapy was effective as initial therapy in subjects with type 2 diabetes and very high levels of HbA1c and/or FPG, as demonstrated by robust and relatively rapid improvements in glycaemic control. RSG/MET fixed-dose combination was well tolerated as first-line therapy with no new tolerability issues identified.

2.43. Elevated HbA1c as an independent predictor of clinical behavior

Siddiqui AA, et.al. (2008) studied the association between glycemic control of type 2 diabetes mellitus determined by HbA1c levels, and the outcome of colorectal cancer. This was a retrospective study. Study population comprised of subjects with type 2 diabetes who had colorectal cancer diagnosed between 1997 and 2001. Diabetics with HbA1c < 7.5% was considered as poorly controlled and HbA1c ≥ 7.5% as well controlled. A group of age- and gender-matched subjects who had colorectal cancer without type 2 diabetes were used as controls. Forty clinical factors were reviewed, and those associated with poor clinical outcome in each group were analyzed.

Subjects with poorly controlled type 2 diabetes had more right-sided colorectal cancer (O.R = 2; 95% C.I = 1 to 4.1), more advanced colorectal cancer (O.R = 2.1, 95% C.I = 1 to 4.4), a younger age of presentation (P = 0.05), greater use of exogenous insulin (P = 0.002), and a poorer survival rate over 5 year period (P = 0.001).

This study concluded that poorly controlled type 2 diabetes independently predicted the early onset of colorectal cancer, a more advanced stage at the time of presentation, poorer 5-year survival, and an increased incidence of right-sided colorectal cancer.
Subjects with type 2 diabetes who have colorectal cancer, poor glycemic control was associated with a clinically aggressive course for the cancer.

2.44. Relationship between atherogenic dyslipidemia and HbA1c

Giacomo Z, et.al. (2009) evaluated the relation between BMI and serum gamma-glutamyltransferase (GGT) and their effects on poor HbA1c and co-morbidities.

They assessed whether the association of BMI with poor glycemic control, hypertension, atherogenic dyslipidemia, hypercholesterolemia, and hyperglycemia differed according to serum GGT concentration in a cohort of 3,633 type 2 diabetics.

There was an association between BMI with: atherogenic dyslipidemia (P = 0.01), and glycemic control (P = 0.004). The association of BMI with hypertension, hypercholesterolemia, and hyperglycemia did not change across GGT quartiles.

Within the lowest GGT quartile, BMI was not associated with atherogenic dyslipidemia or poor glycemic control, whereas in the highest GGT quartile, the prevalence rates ranged from 62.3 to 74.7% for dyslipidemia and from 75.3 to 83% for poor glycemic control.

The study concluded that, BMI was associated with atherogenic dyslipidemia and poor glycemic control only when serum GGT activity was in its high-normal range. It was suggested that obesity itself may not be a sufficient risk factor for atherogenic dyslipidemia or poor glycemic control among type 2 diabetes.
2.45. Effectiveness of psychological interventions on glycaemic control

Alam R, et.al. (2009) determined the effectiveness of psychological interventions on HbA1c and psychological status of diabetics and compared the effects when interventions were delivered by generalist physicians compared to psychological specialists.

This was a systematic review. A comprehensive search was done in Cochrane central register of controlled trials, Medline, Embase, PsychLIT, and Google Scholar. Thirty five trials were reviewed, of these 19 trials (n =1431) were qualified for meta-analysis.

Reporting HbA1c found a reduction in HbA1c by 0.54% (-0.32; 95% C.I = -0.47 to -0.16). In nine trials (n = 832) interventions were delivered by diabetes or general physicians reduced HbA1c by 0.51% (-0.27; 95% C.I = -0.50 to 0.04).

Of these, interventions (n = 561) were delivered by psychology specialists reduced HbA1c by 0.57% (-0.36; 95% C.I = -0.61 to 0.12). Meta-analysis of 13 trials revealed that psychological status was lower in the intervention groups -0.56 (95% CI: 1.00 to -0.13).

2.46. Effects of exercise on glycemic control

Normand GB, et.al. (2001) systematically reviewed and quantified the effect of exercise on glycosylated hemoglobin (HbA1c) and body mass in subjects with type 2 diabetes mellitus.

Database searched were: MEDLINE, EMBASE, sport discuss, health star, and the Cochrane Controlled Trials Register. Additional data sources included bibliographies of textbooks and articles identified by the database searches.
Selected studies were evaluated for the effects of exercise interventions (duration ≥8 weeks) in adults with type 2 diabetes.

Fourteen (11 randomized and 3 nonrandomized) controlled trials were included. Studies that included drug co-interventions were excluded from the review. Two reviewers independently extracted baseline and post-intervention means and SDs for the intervention and control groups.

The characteristics of the exercise interventions and the methodological quality of the trials were also extracted. The weighted mean post-intervention HbA1c was lower in the exercise groups compared with the control groups (7.65% vs 8.31%; weighted mean difference, −0.66%; \( P < 0.001 \)).

There was no difference in post-intervention body mass between exercise groups and control groups (83.02 kg vs 82.48 kg; weighted mean difference, 0.54; \( P = 0.76 \)). Exercise training reduces HbA1c by an amount that should decrease the risk of diabetic complications, but no change in body mass index was found when exercise groups were compared with control groups.

**2.47. Moderate alcohol consumption lowers the risk of type 2 diabetes**

Koppes LL, et.al. (2005)\(^5\) conducted a meta-analysis to obtain an insight regarding the shape and strength of the relationship between alcohol consumption and the risk of type 2 diabetes mellitus, the effects of adjustment for confounders.

Among the 15 original prospective cohort studies, which were comprised of 11,959 incident cases of the subjects. Of which 369,862 individuals were followed for 12 years.
Compared with non-consumers, the relative risk (R.R) for type 2 diabetes in those who consumed ≤ 6 g/day alcohol was 0.87; 95% C.I = 0.79 to 0.95.

For the moderate consumption ranges of 6 to 12 (R.R = 0.70; 95% C.I = 0.61 to 0.79), 12 to 24 (R.R = 0.69; 95% C.I = 0.58 to 0.81), and 24 to 48 g/day (R.R = 0.72; 95% C.I = 0.62 to 0.84). The risk of type 2 diabetes in heavy drinkers (≥ 48 g/day) was equal to that in non-consumers (R.R = 1.04; 95% C.I = 0.84 to 1.29).

A larger RR reduction was associated with moderate alcohol consumption were observed for women compared with men. There was no difference in RR reductions between individuals with low or high BMI.

The evidence from observational studies suggested an approximately 30% reduced risk of type 2 diabetes in moderate alcohol consumers, whereas no risk reduction was observed in consumers of ≥ 48 g/day.

2. 48. Severe periodontitis and risk for poor glycemic control

Taylor GW, et.al. (1996) tested the hypothesis that severe periodontitis in subjects with non-insulin-dependent diabetes mellitus (NIDDM) increases the risk of poor glycemic control.

Data from the longitudinal study of residents of the Gila River Indian Community were analyzed. The study population comprised of subjects aged 18 to 67, who had at least 200 mg/dL plasma glucose after a 2-hour oral glucose tolerance test, with baseline HbA1c < 9%, and who were likely to come for a 2-year follow-up. Medical and dental examinations were conducted at 2-year intervals.
Severe periodontitis was specified two ways for separate analyses: as baseline periodontal attachment loss of 6 mm or more on at least one index tooth, and baseline radiographic bone loss of 50% or more on at least one tooth. Clinical data for loss of periodontal attachment were available for 80 subjects who had at least one follow-up examination, 9 of whom had two follow-up examinations at 2-year intervals after baseline.

Radiographic bone loss data were available for 88 subjects who had at least one follow-up examination, 17 of whom had two follow-up examinations. Poor glycemic control was specified as the presence of HbA1c ≥ 9% at follow-up. To control for non-independence of observations, generalized estimating equations (GEE) were used for regression modeling.

Severe periodontitis at baseline was associated with increased risk of poor glycemic control at follow-up. Other significant covariates in the GEE models were: baseline age, level of glycemic control at baseline, having more severe diabetes at baseline, duration of the diabetes, and smoking at baseline.

The results support considering severe periodontitis as a risk factor for poor glycemic control and suggest that physicians treating subjects with NIDDM should be alert to the signs of severe periodontitis in managing NIDDM.

2.49. Poor glycaemic control and lower quality of life

Kamarul IM, et.al. (2010)\(^4\)\(^9\) compared the quality of life based on the Short Form-36 (SF-36) between two different groups of type 2 diabetics with glycaemic control: those with a HbA1c ≤ 7.5% and those > 7.5%.
This was a cross-sectional study. A generic SF-36 questionnaire was self-administered to subjects with type 2 diabetes mellitus. Based on the HbA1c level, the mean SF-36 scale scores were compared.

The analysis of covariance was used to obtain the adjusted mean scores of the SF-36 scales while controlling for age, and duration of type 2 diabetes mellitus. Subjects with type 2 diabetes mellitus (n = 150) were analyzed. There were 63 (42 %) women and 87 (58 %) men, and their mean HbA1c level was 8.9 ± 2.4 %.

When comparing the two groups of subjects with different HbA1c levels, the adjusted means of four scales: physical health functioning, general health, social functioning and mental health, differed between the groups. The SF-36 scale scores in type 2 diabetes mellitus patients were also lower than those of the SF-36 norms for the Malaysian population.

Type 2 diabetes mellitus subjects with poor glycaemic control had lower mean SF-36 scores in physical functioning, general health, social functioning and mental health, and the SF-36 scores in these subjects were also lower than the SF-36 norms of the Malaysian population.

2.50. Barriers to medication adherence in poorly controlled diabetics

Odegard PS, et.al. (2008)\textsuperscript{59} characterized the adherence and medication management barriers for adults with poorly controlled type 2 diabetes mellitus (HbA1c \geq 9\%) and identified specific adherence characteristics associated with poor control of diabetes.
This was a cross-sectional study of baseline data from a randomized, controlled diabetes intervention conducted at University of Washington Medicine Clinics in the greater Seattle, Washington, area. The goal of the study was to evaluate the effect of a pharmacist intervention on improving diabetes control over 12 months.

Eligible subjects included all adults (older than 18 years of age) with type 2 diabetes, taking at least one oral diabetes medication, and with HbA1c > 9%. Those with unstable psychiatric conditions or with a prognosis deemed to be terminal within six months were excluded. A computerized diabetes registry was used to identify the inclusion and exclusion criteria.

Evaluation measures for medication adherence included self-reported adherence, and medication management challenges using the Morisky question format and difficulty with taking medications for each diabetes medication based on the brief medication questionnaire.

Specific adherence characteristics associated with poor diabetes control (HbA1c ≥ 9%) were identified. Seventy-seven type 2 diabetics (mean HbA1c, 10.4%; mean duration of diabetes mellitus, 7 years) were studied.

A single oral diabetes medication was used by 25 subjects (32.5%) whereas 38 (49.4%) and 12 (15.6%) were using two and three oral diabetic medication. The most common adherence challenges included were paying for medications (34%), remembering doses (31%), reading prescription labels (21%), and obtaining refills (21%). Difficulty with self-reported adherence was noted by 47% of the subjects at baseline (P = 0.37).
Taking more than two doses of diabetes medication daily (beta = 0.78, SE = 0.32, P = 0.02), and difficulty in reading the medication prescription label (beta = 0.76, SE = 0.37, P = 0.04) were associated with higher levels of HbA1c. Self-reported adherence was not related to glycemic control.

The factors that were associated with poor glycemic control of diabetes mellitus: taking medication doses greater than twice daily, and the ability to read the medication prescription labels. It suggests the importance of identifying potential challenges to medication adherence for those with type two diabetes mellitus, and providing support to minimize or resolve these barriers to control the disease.

2.51. Glycemic control and its determinants among subjects with type 2 Diabetes

Akour NA, et.al. (2011) determined the rate of poor glycemic control and its associated factors among the subjects attending a tertiary teaching hospital in the north of Jordan.

This was a cross-sectional study, conducted on subjects with type 2 diabetes mellitus aged 18 years and above, who attended diabetes outpatient clinics at the King Abdullah University Hospital (KAUH) in the north of Jordan in the period between June, 2008 and December, 2008.

A systematic random sample of 533 subjects was selected during the study period. Every third subject attending the clinic in each working day was invited to participate in the study. Only subjects taking a combination of oral hypoglycemic agents and insulin were included in this study.
HbA1c was categorized as good glycemic control if HbA1c < 7% and poor glycemic control if HbA1c ≥ 7%. This study included a total of 533 (203 males and 330 females) subjects with type 2 diabetes mellitus. Their age ranged from 18 to 79 years with mean 50.1 ± 14.1.

The BMI was ranged from 18.9 to 41.2 kg/m² with a mean 27.6 ± 3.5 kg/m². Of the total 533 patients with type 2 diabetes, 51.6% had poor glycemic control. Diabetics with a duration of disease of more than 10 years had higher odds of poor glycemic control (O.R = 1.53; 95% C.I = 1.09 to 2.17) compared to those with duration of 10 years or less.

Increased family and friend support score was associated with decreased odds of poor glycemic control (O.R = 0.96; 95% C.I = 0.93 to 0.98).

### 2.52. Effects of improved HbA1c on complications in type 2 Diabetics

Barak G, et.al. (1998)\(^3\) reviewed the results of the existing epidemiologic and clinical trial studies to understand the effects of improved glycemic control on diabetic complications.

A systematic review was conducted to attempt to retrieve all English language studies published since 1970 that were relevant to the association between glycemic control and complications among the diabetics.

MEDLINE was searched by using the keywords: diabetes, retinopathy, neuropathy, nephropathy, cardiovascular disease, atherosclerosis, weight gain, hypoglycemia, glycemic control, and hyperglycemia.
All prospective cohort studies as well as randomized controlled trials of more than 3 months' duration that assessed diabetic complication rates were selected.

Improved glycemic control was effective at lessening the risks of retinopathy, neuropathy, and nephropathy in type 2 diabetes. The hypoglycemic risk from improved glycemic control was less among the diabetics.

Improved glycemic control was likely to prevent or delay retinopathy, nephropathy, and neuropathy in subject with type 2 diabetes. No convincing evidence existed that improved glycemic control with insulin treatment worsens CHD in subjects with type 2 diabetes.

There was an association between poorly controlled hyperglycemia and increased rates of CHD. The study concluded that neither, hypoglycemia, weight gain, nor changes in quality of life were likely to meaningfully affect the overall risk benefit ratio of improved glycemic control in type 2 diabetics.

2.53. Poorly controlled diabetes with multiple oral hypoglycemic agents/ insulin

Calvert MJ et.al. (2007) examined the extent of monitoring and glycaemic control of subjects with type 2 diabetes prescribed oral agents and/or insulin.

A total of 154 general practices in the UK contributing to the DIN-LINK database between 1995 and 2005 were the study population. People with type 2 diabetes were identified using Read codes and prescribing data.
Outcome measures were: glycaemic monitoring and control on multiple oral agents and/or insulin, and transition to insulin.

Among 14824 people with type 2 diabetes who were prescribed multiple oral agents concurrently, of whom 5064 (34.16%) had HbA1c assessments six months before and following initiation of their last oral therapy.

Mean HbA1c before therapy was 9.07%, which dropped to 8.16% (mean difference 0.91%, 95% C.I = 0.86 to 0.95). Of the subjects with HbA1c assessments, 3153 (62.26%) had evidence of poor glycaemic control following therapy.

Median time for the subjects to not on insulin to be prescribed multiple oral agents was 7.7 years (95% C.I = 7.4 to 8.5 years); 1513 people began insulin during the study. The study concluded that intensive management was required to reduce the risk of microvascular complications among poorly controlled diabetics.