CHAPTER I
INTRODUCTION

Background and Rationale

Type 2 diabetes mellitus is a progressive chronic illness that has a great impact on health care system. Obesity and fat distribution are well-recognized risk factor for the development of type 2 diabetes.[1-3] Current World Health Organization (WHO) cut-off point for overweight is body mass index (BMI) $\geq$ 23 kg/m^2.[4] Treatment regimen for this type of diabetes is usually consists of oral antidiabetic agents. They can be divided into five categories according to their actions: 1) enhances insulin secretion, sulfonylurea ; 2) targets insulin resistance, thiazolidinedione; 3) decreases hepatic glucose output, decrease intestinal glucose absorption, metformin; 4) slows intestinal carbohydrate absorption, acarbose; and 5) inhibits dipeptidylpeptidase-4 (DPP-4) activity, increases incretin hormones, sitagliptin.[2'5-8,25] Sulfonylureas and metformin are equally effective[5-8] however, nowadays using metformin along with lifestyle interventions is recommended unless metformin is contraindicated.[2] If monotherapy fails to achieve the desired level of glycemic control over 3-6 months, the second oral agent , a GLP-1 receptor agonist, or insulin should be added.[2]

Glycemic control is fundamental to the management of diabetes. Glycosylated hemoglobin A_{1C} (A1C) is a test that measures a patient's average glycemia over the preceding 2-3 months.[1,10] It is used to assess treatment efficacy and it is the best predictor of glycemic control in diabetic patients. It correlates well with mean daily blood glucose concentration. It means that A1C is a function of both fasting and postprandial hyperglycemia.[11,12] However there is some disagreement among researchers as to the level of significance of either pre- or postprandial glucose in affecting and/or predicting overall glycemic control, as measured by A1C.[13-18]

In order to study the effect of both fasting and postprandial glucose levels on the A1C and to be able to suggest the best time point for monitoring blood glucose

level one needs to look at glucose profile. Measuring blood glucose levels of patients at different time of day and look at the area under the curve of glucose seems to answer the question. However, only few studies have looked at the relationship between the area under the curve of glucose (AUC glucose) and A1C in type 2 diabetes patients. Monnier et al [19] looked at the diurnal glucose profile and found that pre-lunch glucose concentration (11 A.M.) were significantly highest during the day. The relative contributions of postprandial and fasting glucose to the total glucose increment were similar from the calculation of AUC of glucose. Next year they reported that all plasma glucose values both at fasting and during postprandial periods of type 2 diabetes patients were increasing significantly and progressively from the lowest (A1C <7.3%) to the highest quintiles A1C (>10.2%).[20] Fasting hyperglycemia appeared as main contributor to the overall diurnal hyperglycemia in poorly controlled diabetic patients, whereas the role of postprandial glucose elevations decreased as patients progressed toward poor diabetic control.

The main purpose of this research is to study the relationship between AUC of glucose as calculated from the blood glucose levels obtain at different time point by self-monitoring blood glucose (SMBG) and the A1C which is an indicator of glucose control in type 2 diabetic patients in real clinical setting.

Objectives

1. To study the relationship between the average area under the curve (AUC) of glucose after 3 main meals and hemoglobin A_{1C} (A1C) in type 2 diabetic patients.

2. To study the relationship between the area under the curve (AUC) of glucose of each main meal and hemoglobin A_{1C} (A1C) in type 2 diabetic patients.

3. To study the relationship between glucose concentration at each time point (preprandial/postprandial) of each meal and hemoglobin A_{1C} (A1C) in type 2 diabetic patients.

4. To study the relationship of aforementioned objectives 1-4 between normal and overweight diabetic patients.

Scope of the study

1. Samples of this study are the outpatients at Police General Hospital who were willing to participate in the study.

2. Samples were type 2 diabetic patients who used hyperglycemic agent as mono- or combination therapy and /or combined with insulin

Conceptual framework

Conceptual framework is shown in Figure 1.

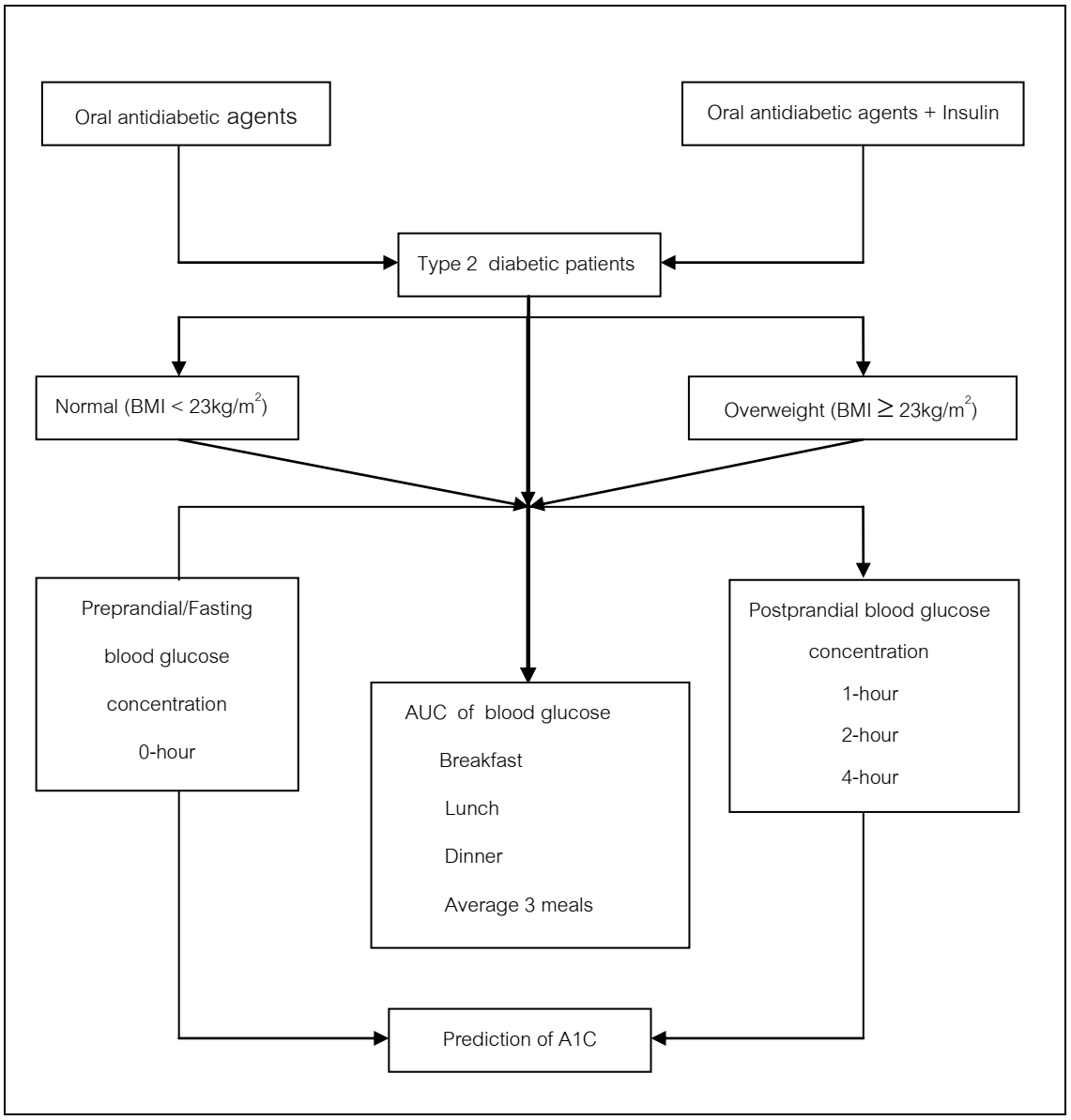

Figure 1: Conceptual framework

Expected Benefits

1. The relationship between the average AUC of glucose after 3 main meals in type 2 diabetic patients and A1C will be known.

2. The relationship between the AUC of glucose of each main meal in type 2 diabetic patients and A1C will be known.

3. The relationship between the glucose level at each point of time during the day in type 2 diabetic patients and A1C will be known.

4. The relationships between the AUC of glucose after 3 main meals, after each meal and at each point of time in type 2 diabetic patients who are normal and overweight will be known.

5. To be able to suggest the best time of day to monitor blood glucose in order to achieve good glycemic control in type 2 diabetic patients.

CHAPTER II
LITERATURE REVIEWS

Diabetes

Diabetes is a chronic illness that has a great impact on health system. Estimated prevalence of diabetes worldwide in the year 2030 is 366 million.[1,21] Based on the International Collaborative Study of Cardiovascular Disease in Asia, in 2000 there were 2.4 million with diabetes and the WHO South-East Asia Region estimation for Thailand in year 2030 there will increase to 2,739,000 people [22-23] Diabetes is an illness that requires continuing medical care and patient self-management education to prevent acute complications and to reduce the risk of long-term complications. Diabetes complications include cardiovascular disease (CVD), nephropathy, retinopathy, and neuropathy.[2,3] CVD is the major cause of mortality (between 50-80%) for individuals with diabetes.[2] Type 2 diabetes is an independent risk factor for macrovascular disease, and its common coexisting conditions such as hypertension and dyslipidemia are also risk factors. Diabetic nephropathy occurs in 20-40% of patients with diabetes and is the single leading cause of end-stage renal disease (ESRD). Diabetic retinopathy is a highly specific vascular complication of both type 1 and type 2 diabetes and is estimated to be the most frequent cause of new cases of blindness among adults aged 20-74 years. Amputation and foot ulceration are the most common consequences of diabetic neuropathy and major causes of morbidity and disability in people with diabetes. [2]

Classification and Treatment of Diabetes

The American Diabetic Association (ADA) has classified diabetes into four clinical classes[2]

- Type 1 diabetes results from β-cell destruction, usually leading to absolute insulin deficiency.

- Type 2 diabetes results from a progressive insulin secretory defect on the background of insulin resistance.
- Other specific types of diabetes due to other causes, e.g., genetic defects in β-cell function, genetic defects in insulin action, diseases of the exocrine pancreas, and drug or chemical induced.
- Gestational diabetes mellitus (GDM) diagnosed during pregnancy.

However 90-95% of those with diabetes are type 2 diabetes.

Type 2 diabetes mellitus is a progressive disorder. Obesity and fat distribution are well-recognized risk factor for the development of type 2 diabetes.[1-3] Current WHO cut-off point for overweight is body mass index (BMI) $\geq$ 23 kg/m^2.[4] However there was increasing evidence of the high prevalence of type 2 diabetes and increased cardiovascular risk factors in parts of Asia where the average BMI is below the cut-off point of 23 kg/m^2. For Asian countries suggested categories are as follows: less than 18.5 kg/m^2 underweight ; 23 –27.5 kg/m^2 increased risk; and 27.5 kg/m2 or higher high risk. [4] Treatment regimen for this type of diabetes is usually consists of oral antidiabetic agents. They can be divided into five broad categories according to their mechanism of action: 1) enhances insulin secretion, sulfonylurea ; 2) targets insulin resistance, thiazolidinedione; 3) decreases hepatic glucose output,decrease intestinal glucose absorption, metformin; 4) slows intestinal carbohydrate absorption, acarbose; and 5) inhibits DPP-4 activity, increases incretin hormones, sitagliptin. [2'5-8] Sulfonylureas and metformin are equally effective[5-8 Sulfonylureas stimulate the production and release of insulin by binding to a receptor site on the membrane of the pancreatic β cells through hydrophobic anchoring. [5,8] Metformin, on the other hand, suppresses hepatic glucose output. It also improves glucose transport and utilization by skeletal muscle due to improvements in non-oxidative glucose disposal and glycogen synthesis. These actions result in enhanced insulin-stimulated glucose uptake.[6,7,24] Thiazolidinediones increases peripheral insulin sensitivity. DPP-4 inhibitors increases active GLP-1, and GIP concentrations, increase insulin secretion and decrease glucagon secretion. [2]

α-glucosidase inhibitors inhibit intestinal α-glucosidase so they slow intestinal carbohydrate digestion and absorption. [2] Nowadays metformin has been recommended as first-line therapy as long as no contraindications are presented.[2,25] Metformin and sulfonylureas are equally effective in decreasing plasma glucose levels when used as a monotherapy. If monotherapy at maximal tolerated dose fails to achieve the desired level of glycemic control, the second oral agent, a GLP-1 receptor agonist, or insulin should be added. [2] The rationale for combination therapy is to use two different classes of agents with different mechanisms of action that target the likely defects seen in type 2 diabetic patients.

Glycemic control

Glycemic control is fundamental to the management of diabetes. The prospective randomized clinical trials such as the Diabetes Control and Complications Trial (DCCT) [26], the U.K. Prospective Diabetes Study (UKPDS) [27,28] and the Kumamoto Study [29] presented glycated hemoglobin (HbA_{1c} or A1C) goal of < 7%, preprandial plasma glucose 90-130 mg/dl (5.0 – 7.2 mmol/L) and postprandial plasma glucose <180 mg/dl (<10.0 mmol/L). This goal of A1C level was associated with fewer long-term microvascular complications (30-35% reduction per 1% absolute reduction of glycated hemoglobin). Epidemiological data from the United Kingdom Prospective Diabetes Study (UKPDS) [28] also showed a 14-16% decrease in macrovascular complications for every 1% absolute reduction in glycated hemoglobin. This aggressive A1C level is also true for the glycemic control in type 2 diabetes. Current recommendations of the American Diabetes Association (ADA) 2012 [2] and the American Association of Clinical Endocrinologists (AACE)[3] on glycemic control are shown in Table 1.

Table 1 ADA Glycemic recommendations for nonpregnant adults with diabetes

Parameter	value
A1C	<7.0 %*
Preprandial capillary plasma glucose	3.9-7.2 mmol/L(70-130mg/dl)*
Peak postprandial capillary plasma glucose¶	<10.0mmol/L(<180mg/dL)*

¶ Postprandial glucose measurements should be made 1-2 h after the beginning of the meal, generally peak levels in patients with diabetes

- Goals should be individualized based on
    - duration of diabetes
    - age/life expectancy
    - comorbid conditions
    - known CVD or advanced microvascular complications
    - hypoglycemia unawareness
    - individual patient considerations
- More or less stringent glycemic goals may be appropriate for individual patients
- Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals

In assessing glycemic control, there are two ways to do it : self-monitoring of blood glucose(SMBG) and A1C measurement.[2,30] A1C is a test that measures a patient's average glycemia over the preceding 2-3 months. It is used to assess treatment efficacy. A1C testing should be performed routinely in all patients with diabetes, first to document the degree of glycemic control at initial assessment and then as part of continuing care. Measurement approximately every 3 months is required to determine whether a patient's metabolic control has been reached and maintained within the target range [2] on the other hand SMBG provides a real-time measurement of blood glucose. It helps in detecting hypoglycemia or post-prandial hyperglycemia.[30,31]

Patients who used insulin are recommended to do self-monitoring of blood glucose more often than type 2 diabetic who do not use insulin while it is useful as a guide in management in patients who are not using insulin. [2] However SMBG as part of the management strategy showed a statistically significant decrease in A1C of approximately 0.4% in patients with type 2 diabetes who are not taking insulin [30] and patients who use glucose meter at home exhibit significant improvement in fasting blood glucose level and A1C after they started using the meter.[32]

Since A1C which is the best predictor of glycemic control in diabetic patients correlates well with mean daily blood glucose concentration. It means that A1C is a function of both fasting and postprandial hyperglycemia.[14] However in type 2 diabetes the first-phase insulin response which is the rise and fall of postprandial glucose level in which large amounts of endogenous insulin are released, usually within 10 minutes in response to nutrient intake is severely diminished or absent. It results in persistently elevated postprandial glucose throughout most of the day. There is some disagreement among researchers as to the level of significance of postprandial glucose in affecting and/or predicting overall glycemic control, as measured by A1C.

Many researchers are interested in whether pre- post prandial blood glucose can predict A1C. Bouma et al [17] studied type 2 diabetic patients treating with diet or oral antidiabetic agents to find association between A1c and fasting plasma glucose (FPG). Pearsons correlation coefficient for A1C and FPG was 0.77($p = 0.001$) for patients on oral antidiabetic agents. Bonara et al .[14] Showed that A1C levels are more closely related to preprandial than postprandial glucose levels, even though majority of patients studied had extremely elevated glucose excursions with meals and extended periods of postprandial hyperglycemia. Hoffman et al [15] showed that in stable insulin-treated type 2 diabetes, the mean blood glucose for each of the four once-daily testing strategies (prebreakfast, prelunch, predinner, and at bedtime) were significantly correlated with A1C ($r= 0.65$-0.70, $p <0.0001$) as were mean blood glucose values for the twice-daily testing strategies($r =0.73$-0.75, $p <0.0001$). Relimpio et al [33] found that A1C values had a stronger correlation with pre-breakfast SMBG ($r = 0.53$, $p<0.001$) than

with 1-hour post breakfast ($r = 0.39$, $p<0.001$) in 227 type 2 diabetic patients. They also found that A1C value correlated stronger with pre-breakfast level in patients not using insulin. Koga et al [34] studied 209 Japanese diabetic patients (both types) and found positive correlation between FPG and A1C levels ($r = 0.485$, $p < 0.0001$). In contrast Avignon et al [16] found that post-lunch and extended post-lunch plasma glucose was better correlated to A1C than fasting values. Soonthornpun et al [18] demonstrated that postprandial hyperglycemia, specifically the 2-h postprandial glucose level, is associated with high A1C levels($r = 0.51$, $p<0.05$). The study done by Shimizu et al [35] suggested that postprandial breakfast and dinner were important in improving glycemic control in insulin treated patient while Nakazaki et al [36] suggested that pre-and post-breakfast blood glucose levels are the most reliable predictors of 1- month later A1C in type 2 diabetic outpatients who visit clinic every month.

Many researchers studied relationship between A1C and SMBG levels. Rohlfling et al [12] studied 1439 patients from the Diabetes Control and Complications Trial (DCCT) who had regular glucose measurements 7 times per day. Their regression equation was glucose (mg/dl) = 35.6 HbA1c - 77.3 , with $r^2 = 0.67$. Hoffman et al [15] studied insulin treated type 2 diabetic patients who self-monitored blood glucose four times daily (premeal and bedtime). Overall correlation of glucose and A1C was 0.79 ($p<0.0001$). Mean blood glucose values for each of the pre-meal testing were significantly correlated with A1C ($r = 0.65$-0.70, $p <0.0001$). Peter et al [37] studied newly diagnose treatment naïve type 2 diabetic patients. They found that A1C was more strongly correlated with FPG ($r = 0.85$, $p<0.001$) than the overall postprandial glucose level ($r = 0.539$, $p = 0.003$). Sarwat et al [38] studied the relationship between A1C and SMBG mearsures in type 2 diabetic treated with different type of insulin. Seven point SMBG profiles three times in a 2 -week period prior to each A1C measurement. Correlation between A1C and among individual SMBG measurement ranged from 0.34-0.49 and were similar for both regimens.

Rather than pinpoint whether only pre-or post -blood glucose levels are more contributed to the correlation of A1C, there are many studies that investigated both

points. In order to study the effect of both fasting and postprandial glucose levels on the A1C, one needs to look at glucose profile. Measuring blood glucose levels of patients at different time of day and look at the area under the curve of glucose seems to answer the question. However, only few studies have looked at the relationship between the area under the curve of glucose (AUC glucose) and A1C in type 2 diabetes patients. Monnier et al [19] studied the diurnal glucose profiles at different levels of diabetic control. The diurnal glucose profiles were determined at pre-breakfast at 8.00 A.M., at 2-h post-lunch at 2.00 P.M., at 3-h time interval between blood samplings at 11.00 A.M., and the 5-h post-lunch value at 5.00 P.M. They found that pre-lunch glucose concentrations (11.00 A.M.) were significantly higher than fasting (at 8.00 A.M.), and post-lunch (2.00 P.M. and 5.00 P.M.) plasma glucose values. The relative contributions of postprandial and fasting glucose to the total glucose increment were similar from the calculation of AUC of glucose. Monnier et al [20] analyzed the diurnal glycemic profiles (obtained 4 points) of type 2 diabetic patients at different levels of A1C and calculated the AUC of glucose for further evaluation of relative contributions of postprandial and fasting plasma glucose increments to overall diurnal hyperglycemia. All plasma glucose values both at fasting and during postprandial periods were increasing significantly and progressively from the lowest (A1C <7.3%) to the highest quintiles A1C (>10.2%). Fasting hyperglycemia appeared as main contributor to the overall diurnal hyperglycemia in poorly controlled diabetic patients (A1C>9.3%), whereas postprandial glucose levels made the highest contribution in patients with good to moderate glycemic control (A1C <8.5%).[24,39]

Many studies suggested that mean blood glucose (MBG) levels correlate better with A1C. Ozmen et al [40] performed study in type 2 diabetic patients treated with diet alone(9.9%), oral antidiabetic agents(72.7%) and insulin(17.4%). Pearson's correlation coefficient for A1C and FPG was 0.723 ($p < 0.0001$) and 0.734 for A1C and postprandial plasma glucose (PPG).The strongest correlation was between mean plasma glucose (MPG) and A1C ($r = 0.761$, $p < 0.0001$). While for non-insulin using group, correlation for A1C, and FPG, PPG and MPG were 0.751, 0.760, 0.787, respectively. Murata et al [41]

evaluated the weekly contribution of glucose readings to A1C during an 8-week period of intensified self-monitored blood glucose testing. Regression correlation between A1C and mean glucose was 0.77, $p<0.001$ and the mean blood glucose values from weeks 4, 6 and 8 significantly and equally influenced A1C. Pupillo et al [42] studied type 2 diabetic patients who performed SMBG and found statistically significant relationship between MBG and A1C (A1C = 4.049+0.443x MBG, $r = 0.70$, $p <0.0001$). Another study on the relationship between mean blood glucose and A1C done by Makis et al [43] also showed strong correlation between MBG and A1C in type 2 diabetic patients ($r = 0.93$, $p<0.05$) and got the model which was MBG (mg/dl) = (34.74x A1C) – 79.21. Borg et al [44] on the behalf of the ADAG Study Group studied relationship among features of glucose exposure and A1C such as average blood glucose, pre-post prandial SMBG. Blood glucose measurements were done using continuous glucose monitoring (CGM) and the seven-point SMBG (pre-prandial, 90 minutes postprandial, and bedtime). Patients were type 1 diabetic, type 2 diabetic and nondiabetic.
The result showed that the area under the glucose curve calculated from CGM 2 h after meal correlated well with 90 min SMBG postprandial measurements ($r = 0.92$).
Fasting blood glucose were moderately correlated with index of hyperglycemia (AUC>11mmol/L) and average or postprandial glucose levels (correlation coefficients were between 0.60 and 0.70). A1C correlated well with average blood glucose from CMG and SMBG combined ($r = 0.89$). From SMBG preprandial glucose levels had a larger effect on A1C than postprandial levels. Chubb et al [45] tried to determine how well SMBG correlates with A1C and fasting serum glucose. Relationships for pre-and post - prandial SMBG were similar ($R^2 = 0.275$ and 0.244, $p<0.001$,respectively) from all patients with the weakest associations in insulin treated patients ($R^2 = 0.152$ for pre-prandial and = 0.094 for post-prandial).

Most studies mention earlier, blood glucose levels were done in a controlled laboratory setting such as at clinic or inpatient. Not too many studies can be generalizable to clinical care setting because they used the SMBG and were able to demonstrate associations between glycemic control and multiple glucose

measurements. Since there is still a controversial discussion whether fasting or postprandial glucose values have more impact on metabolic control, in order to understand this, the blood glucose level must be measured frequently. The concept behind what point in time to choose bases on the fact that the blood glucose draws immediately before meal will represent the fasting/preprandial glucose level. Blood glucose levels measure at 1,2, and 4 hour after meal represent the blood glucose concentrations peak at 60-90 minutes after meal and return to preprandial values within 3 hour. [20] There is also lack of strong correlations between A1C and glucose levels in a single day [14] and the differences in carbohydrate intake seems of little relevance compared with other potential pathophysiological mechanisms in type 2 diabetes.[19] Therefore, several glucose determinations over several days may yield a better correlation to A1C.

CHAPTER III
MATERIALS AND METHOD

1. Study design

This study was a prospective study. The main purpose of the study was to study relationship between area under the curve of glucose (AUC) as calculated from the blood glucose levels obtain at different time point by self-monitoring blood glucose (SMBG) and hemoglobin A_{1C} (A!C) which is an indicator of glucose control in type 2 diabetic patients in real clinical setting. This study was conducted during August 2007-April 2012.

2. Patients population

Type 2 diabetic patients who attended the hospital as the outpatients at the Diabetic clinic Police General Hospital were recruited.

2.1 Inclusion criteria:

Patients eligible for this study were type 2 diabetic outpatients aged 18- year or more who had the following characteristics

- Had been diagnosed as having type 2 diabetes for at least three months using the American Diabetes Association criteria [2]
- Treated with the stable dose of oral antidiabetic agents and/or combined with insulin
- Had stable glycemic control define as having either A1C level changes not more than 1% or having postprandial plasma glucose level changes not more than 80 mg/dl on 2 consecutive tests
- If use any other medications, they had to be stable at least 2 month before the study
- Willing to have SMBG done themselves or allow caretakers to do
- Consented to enroll in the study

2.2 Exclusion criteria:

The exclusion criteria were as follow

- Planning to become pregnant, pregnancy or breast–feeding
- Having acute or chronic liver/pancreatic diseases
- Having acute or chronic renal failure; Having chronic infectious disease;
- Having comorbidity other than hypertension, dyslipidemia, ischemic heart disease
- Taking drugs that would affect glucose profile such as corticosteroids
- Having oral antidiabetic drugs change during the study period;
- Having endocrinopathies other diabetes that affected glucose homeostasis
- Consider not appropriate to be recruited into the study by physician

3. Sample size determination

From the study of Monnier et al [20] , the AUC of glucose in 290 patients whose venous blood glucose values were obtained at 4 points (fasting and postprandial) was significantly correlated to A1C, $r^2 = 0.48$.

Sample size (n*) is obtained by using Cohen's Table (Table 6.2) n* to detect r by t Test at $\alpha = .05$ (two tailed) [46.]

Since $\sqrt{0.48}$ is 0.693, the number of sample size need for power to be .80 α .05 and r = 0 .60 was 18 and for r = 0.70 was 12. Including an extra 10% dropout rate the number of sample size in this study was determined to be at least 20 patients for each of the regression analysis.

4. Study site

Since the estimated overall prevalence of diabetes in Thai adults aged $\geq$ 35 years was 9.6 $\pm$ 0.7 (mean $\pm$ SE) and the proportion of diabetes that was diagnosed did not significantly differ between urban and rural areas, and between men and women.[22] Therefore, the Police General Hospital which is a 770 bed governmental hospital was selected as the study site.

5. Ethical consideration

All studied participants provided informed consent . Study protocol was submitted and approved by the Police General Hospital. Ethic Review Boards

6. Methodology

Flow chart of the study protocol was shown in Figure 2

6.1 Patients who met the inclusion and exclusion criteria would be recruited from the outpatient medical records.

6.2 At the outpatient clinic the researcher explained about the study protocol to the selected patients or their legal representatives. Patients or their legal representatives signed the consent forms.

6.3 Demographic data, socioeconomic status, medical and drug histories, current medication usage, physical examination and any laboratory workup available such as fasting blood glucose (FBG), postprandial blood glucose, A1C, height , weight serum creatinine, liver function test, blood pressure, etc of the subjects were collected at the beginning of the study as the baseline information.

6.4 Individual patient and /or caretaker was trained about the usage of the self-monitoring blood glucose (SMBG) meter, accuracy in obtaining SMBG reading would be observed.

6.5 Every patient and /or caretaker was instructed to test his/her blood glucose at home four times a day rotating the meal tested; immediately before meal ("0" hr), 1, 2 and 4 hour after meal. Glucose level of each meal would be collected twice on different days using Accu-Check Advantage glucose meter (Roche Diagnostics, Thailand). The glucose meter strip is calibrated by hexokinase method. Capillary blood samples are measured using the hexokinase method on an automatic analyzer (reference). The mean imprecision is <4.0% for repeatability and <2.6% for reproducibility. The glucose measurement range is 10-600 mg/dl (0.6-33.3 mmol/L). [47] The test kit (glucose meter, glucose strips, softclick lancets, alcohol, cotton ball) for SMBG testing were provided by the researcher.

Example of the collection was as follow:

Day 1 , 7 at 0,1,2,4 hr. after breakfast

Day 3, 9 at 0,1,2,4 hr. after lunch

Day 5, 11 at 0,1,2,4 hr. after dinner

6.6 After setting the testing date with the patient, the researcher then marked them on the printout calendar which was given to each patient.

6.7 Patients were asked to follow their usual treatments and consumed their usual diets during the entire studied period. Patients had to record diet, the time they measured their blood glucose level, and the result of each blood glucose tested in the forms provided by the researcher.

6.8 The researcher telephoned to remind the patients to test their blood glucose within 1-2 day of their scheduled testing.

6.9 Patients were requested to return the following two weeks with the results of their SMBG reading, if possible.

6.10 The researcher checked the patients' record of blood glucose levels by comparing with the one in the memory of the meter.

6.11 AUC of glucose will be calculated using the trapezoidal rule [48] :

$$[AUC]_0^{t_x} = \Sigma[AUC]_{t_{n-1}}^{t_n} \quad , \quad [AUC]_{t_{n-1}}^{t_n} = \frac{C_{n-1} + C_n}{2}(t_n - t_{n-1})$$

AUC = area under the blood glucose concentration-time curve

C_x = last observed blood glucose concentration on the terminal phase

t_x = time corresponding to the last observed blood glucose concentration on the terminal phase

C_n = blood glucose concentration at time n

t_n = time corresponding to the blood glucose concentration at time n

C_{n-1} = blood glucose concentration at time n-1

t_{n-1} = time corresponding to the blood glucose concentration at time n-1

6.12 A1C level for each patient was measured at the end of the study, 2 months after starting on the SMBG reading. A1C was measured by high performance liquid chromatography assay (D-10 Hemoglobin Testing System, Bio-Rad™, Thailand) at central laboratory of the Police General hospital.

7. Data analysis

Statiscal analysis was performed using the Statistical Package for Social Sciences (SPSS) software version 17.0. (SPSS Co., Ltd., Bangkok Thailand).
The trapezoidal method was used to calculate areas under the glucose curves (AUC).

Data on patient characteristics would be assessed using descriptive statistics (mean $\pm$ SD).

SMBG levels were calculated as follows:

1. For each time point, blood glucose level was the average of two values obtained from the same time point at different days.

2. For each meal, blood glucose level was the sum of average blood glucose level 4 points (at pre-meal, 1-,2-, and 4- hour post meal) divided by 4.

3. For 3 meals, blood glucose level was the sum of blood level each meal divided by 3 or the average of all 24 points.

Areas under the curve (AUC) of glucose were calculated as follows:

1. For each time interval, AUC of glucose was the average AUC of blood glucose levels obtained twice at different days.

2. For each meal, AUC of glucose was the sum of average AUC of blood glucose levels obtained during 0-1 hour post meal, 1-2 hour post meal, and 2-4 hour post meal.

3. For 3 meals, AUC of glucose was the sum of AUC of glucose each meal.

Relationships between AUC of glucose and A1C were evaluated using linear regression with Pearson's correlation coefficients. These included mean AUC of

glucose for all meals measurement, mean of each meal, and mean of AUC glucose at pre-and 1, 2- and 4 hour post meals for all patients, for patients who used oral antidiabetic agents and who used insulin combined with oral antidiabetic agents Statistical significant will be assumed when $p < .05$.

Relationships between glucose levels obtained from SMBG and A1C were evaluated using linear regression with Pearson's correlation coefficients. These included mean blood glucose for all meals measurement, mean of each meal, and mean of glucose at pre-and 1, 2- and 4 hour post meals for patients who used oral antidiabetic agents and who used insulin combined with oral antidiabetic agents . Statistical significant will be assumed when $p < .05$.

Relationships between AUC of glucose and A1C and between glucose levels obtained from SMBG and A1C in normal and overweight patients were also evaluated using linear regression with Pearson's correlation coefficients. Statistical significant will be assumed when $p < .05$.

Relationships between glucose levels obtained from SMBG of normal and overweight patients and A1C were evaluated using linear regression with Pearson's correlation coefficients. These included mean blood glucose for all meals measurement, mean of each meal, and mean of glucose at pre-and 1, 2- and 4 hour post meals. Statistical significant will be assumed when $p < .05$.

Equations for prediction of A1C from SMBG level and AUC of glucose for all patients, for patients who treated with oral antidiabetic agents only, for patients treated with insulin combined with oral agents, for normal and overweight patients were analyzed using multiple linear regression analysis.

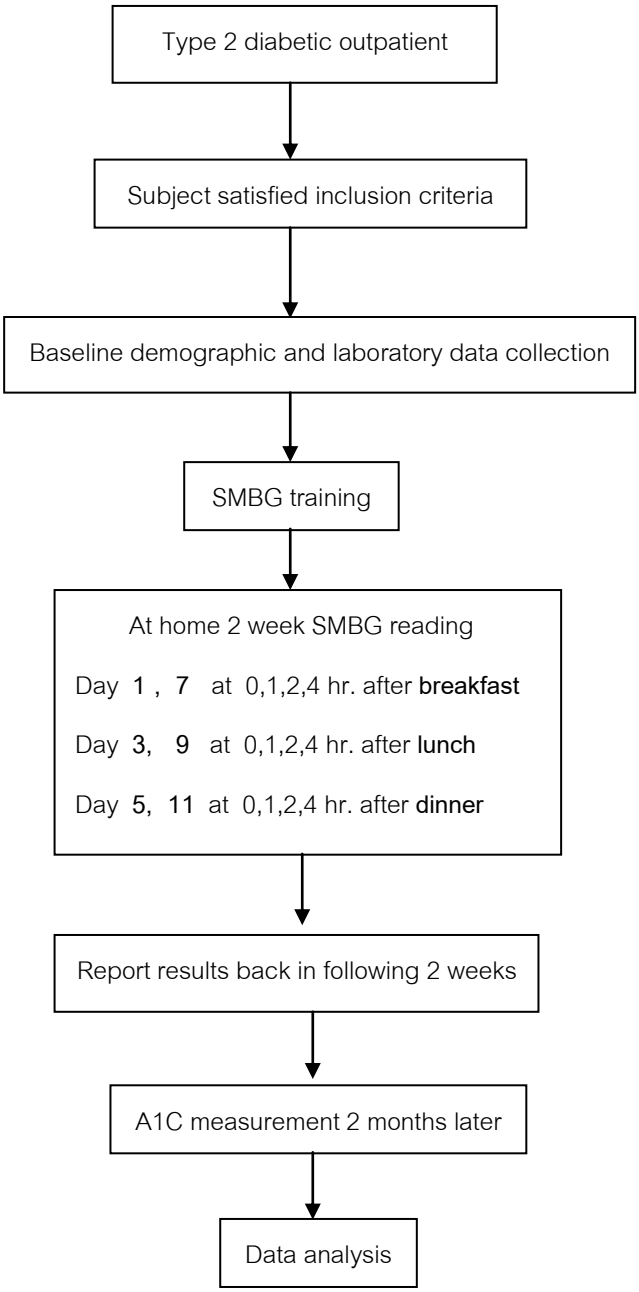

Figure 2 . Flow chart of the study

CHAPTER IV
RESULTS

A total of sixty-four patients were studied. They were willing to complied with the study protocol by getting self-monitoring of blood glucose done and got hemoglobin A_{1c} values. The results were detailed in parts as follow:

1. Patient characteristic
2. Self-monitoring of blood glucose (SMBG) level
3. Area under the curve (AUC) of glucose
4. Hemoglobin A_{1c} (A1C) value
5. Relationship between self-monitoring of blood glucose (SMBG) level and hemoglobin A_{1C} (A1C) in type 2 diabetic patients
6. Relationship between the average area under the curve (AUC) of glucose and hemoglobin A_{1C} (A1C) in type 2 diabetic patients.
7. Relationship between self-monitoring of blood glucose (SMBG) level and hemoglobin A_{1C} (A1C) in different weight group type 2 diabetic patients
8. Relationship between the average area under the curve (AUC) of glucose and hemoglobin A_{1C} (A1C) in different weight group type 2 diabetic patients
9. Model to predict A1C value

1. Patient characteristic

One hundred forty-four patients met the inclusion/exclusion criteria however only sixty-four patients were willing to comply with the study protocol. Patient characteristics were shown in Table 1. They were 37 women (57.8%) and 27 men (42.2%). Age (mean ± SD) was 60.03 ±10.07 years. Forty-three patients (67.2%) were in a group aged between 51-70 year. Body mass index (BMI) of all patients (mean ± SD) was 26.24 ± 3.66 kg/m^2 with the highest at 40.1 kg/m^2 and the lowest at 18.6 kg/m^2. Fifty-two patients (81.3%) had BMI $\geq$ 23.0 kg/m^2. Duration of diabetes (mean ± SD) for all patients was 11.19 ± 7.10 year. Nineteen (29.7%), sixteen (25.0%) and fourteen (21.9%) patients

had been diagnosed with type 2 diabetes for 6-10, 11-15 and up to 5 years, respectively. More than half of patients, 39 (60.9%) were either retiree (over 60 years) or a homemaker. This finding was in accordance with the results shown before that more than half of the patients in this study were women and were between 51-70 years. Payment for treatment of the patients were mostly subsidized by government in 45 patients (70.4%), only 13 patients were self-paid.

Of all patients, 39 (60.9%) had hypertension and dyslipidemia as co-existing diseases, 7 (10.9%) had only hypertension and 13(20.3%) had dyslipidemic problem. Of total of 64 patients, 39 patients (60.9%) were managed with oral antidiabetic agents (n = 7 for sulfonylureas, n = 11 for metformin, n = 1 for thiazolidinedione, n = 11 for combination of two two oral antidiabetic agents, and n = 9 for combination of three oral antidiabetic agents). Twenty-five patients (39.1%) used insulin in combination with oral antidiabetic agents (n = 1 for combination of insulin and one oral antidiabetic agent, n = 7 for combination of insulin and two oral antidiabetic agents, n = 10 for combination of insulin and three oral antidiabetic agents, and n = 7 for combination of insulin and four oral antidiabetic agents).

Table 2 Characteristics of the patients (n=64)

Characteristic	Frequency	Percent
Gender		
Female	37	57.8
Male	27	42.2
Age (year)		
30-40	3	4.7
41-50	8	12.5
51-60	21	32.8
61-70	22	34.3
71-80	9	14.1
>81	1	1.6
BMI(kg/m^2)		
< 23.0	12	18.8
≥ 23.0	52	81.3
Duration of DM (year)		
0-5	14	21.9
6-10	19	29.7
11-15	16	25.0
16-20	8	12.5
21-25	3	4.7
> 26	4	6.2
Employment		
Retiree	22	34.3
Homemaker	17	26.6
Government	13	20.3
Semi-government	1	1.6
Private company	4	6.3
Self-employed	7	10.9

Table 2 Characteristics of the patients (n=64) (continue)

Characteristic	Frequency	Percent
Payment		
Government	44	68.8
Semi-government	2	3.1
Social security	4	6.2
30-Baht	1	1.6
Self-paid	13	20.3
Co-existing disease		
None	1	1.6
Hypertension	7	10.9
Dyslipidemia	13	20.3
Hypertension+ Dyslipidemia	39	60.9
Other	4	6.3
Medication		
Oral agent	39	60.9
One	19	29.7
Two	11	17.1
Three	9	14.1
Insulin plus oral agent	25	39.1
Plus 1 oral agent	1	1.6
Plus 2 oral agents	7	10.9
Plus 3 oral agents	10	15.7
Plus 4 oral agents	7	10.9

2. Self-monitoring of blood glucose levels

Every patient tested his/her blood glucose at home four times a day rotating the meal test. With every meal four blood glucose levels would be recorded at these time points

1. Immediately before meal (“0” hr)
2. 1-hour post meal (1-h post)
3. 2-hour after meal (2-h post)
4. 4-hour after meal (4-h post)

Glucose level of each meal was tested twice on different day. Within two weeks period there were 24 blood glucose values from every patient (2 sets of 4-point blood glucose level for each meal). Blood glucose value for each time point, each meal, and for three meals were averaged. The mean $\pm$ SD values of blood glucose level at each time point include the minimum and maximum were shown in Table 3. Mean blood glucose level of each meal and 3 meals of 64 patients were shown in Table 4. The unit of SMBG was reported as mmol/L. To convert this unit to mg/dl, multiply value in mmol/L with 18. The mean ± SD value of blood glucose level for breakfast, lunch, dinner and 3 meals were not that differ (8.49 ± 1.98, 8.31 ± 2.07, 8.48 ± 1.77 and 8.42 ± 1.77 mmol/l, respectively). The pre-meal blood glucose level of each meal did not differ from each other, however the level at 1 hour post breakfast (10.63 ± 2.86 mmol/L) seemed to increase more than 1 hour post lunch and dinner.

Table 3 Self-monitored blood glucose level (n=64)

Blood glucose	Minimum (mmol/l)	Maximum (mmol/l)	Mean ± SD (mmol/l)
Pre Breakfast	4.0	14.2	7.41 ± 1.99
1-h post Breakfast	6.0	18.7	10.63 ± 2.86
2-h post Breakfast	4.4	16.1	8.84 ± 2.59
4-h post Breakfast	3.7	15.2	7.13 ± 2.54
Breakfast	5.7	15.4	8.49 ± 1.98
Pre Lunch	3.7	15.2	7.52 ± 2.44
1-h post Lunch	4.8	15.0	8.91 ± 2.30
2-h post Lunch	3.3	17.1	8.75 ± 2.52
4-h post Lunch	4.2	17.6	8.01 ± 2.71
Lunch	5.2	15.4	8.31 ± 2.07
Pre Dinner	4.6	14.1	7.79 ± 2.14
1-h post Dinner	5.1	15.4	9.54 ± 2.42
2-h post Dinner	3.1	16.2	9.03 ± 2.55
4-h post Dinner	4.7	14.7	7.62 ± 2.22
Dinner	5.8	14.8	8.48 ± 1.77
3 meals	5.8	13.8	8.42 ± 1.77

Table 4 Mean blood glucose level of each meal and 3 meals (mmol/L) (n=64)

No.	Mean Breakfast	Mean Lunch	Mean Dinner	Mean3 meals
1	7.1	7.6	7.0	7.2
2	7.4	6.2	6.6	6.8
3	7.9	7.0	7.9	7.6
4	7.1	7.3	6.7	7.1
5	7.2	6.8	6.7	6.9
6	8.3	7.5	9.8	8.6
7	8.7	8.1	7.8	8.2
8	7.0	6.5	7.8	7.1
9	7.3	8.0	8.6	8.0
10	7.2	7.0	7.2	7.1
11	7.5	7.7	7.4	7.5
12	6.4	6.9	6.5	6.6
13	8.4	8.3	7.8	8.2
14	8.4	6.6	6.5	7.2
15	8.7	10.3	9.7	9.6
16	6.2	6.4	6.2	6.2
17	5.9	5.8	6.3	6.0
18	8.8	9.1	8.8	8.9
19	5.7	6.3	6.6	6.2
20	8.5	8.6	8.6	8.5
21	12.5	14.1	14.8	13.8
22	10.0	8.1	8.3	8.8
23	11.3	7.7	8.9	9.3
24	7.9	8.5	7.4	8.0
25	12.4	12.0	12.3	12.2

Table 4 Mean blood glucose level of each meal and 3 meals (mmol/L) (n=64) (continue)

No.	Mean Breakfast	Mean Lunch	Mean Dinner	Mean3 meals
26	5.8	7.3	7.1	6.7
27	9.0	11.5	11.8	10.8
28	15.4	15.4	7.5	12.8
29	11.3	10.3	13.6	11.7
30	7.5	7.5	8.1	7.7
31	9.6	7.8	9.8	9.1
32	9.4	10.5	12.4	10.7
33	8.3	8.0	6.4	7.6
34	8.6	10.1	9.0	9.2
35	10.8	9.9	10.7	10.5
36	9.0	11.4	10.3	10.2
37	6.9	6.8	6.9	6.9
38	7.4	9.3	7.3	8.0
39	12.5	12.7	8.7	11.3
40	8.2	8.3	8.3	8.3
41	10.7	9.3	10.1	10.1
42	9.4	8.2	10.7	9.4
43	7.8	7.0	7.1	7.3
44	8.3	9.8	10.2	9.4
45	8.2	7.8	8.7	8.3
46	8.2	12.0	10.4	10.2
47	9.5	9.4	9.2	9.4
48	7.3	5.7	7.5	6.9
49	9.2	9.5	10.0	9.5
50	7.7	5.2	6.3	6.4

Table 4 Mean blood glucose level of each meal and 3 meals (mmol/L) (n=64) (continue)

No.	Mean Breakfast	Mean Lunch	Mean Dinner	Mean3 meals
51	12.1	8.1	10.8	10.3
52	9.8	9.7	8.6	9.4
53	7.7	8.1	7.9	7.9
54	6.3	5.4	5.8	5.8
55	13.3	9.1	10.1	10.8
56	7.5	5.9	6.3	6.5
57	7.7	5.8	8.0	7.2
58	7.2	7.5	6.7	7.1
59	5.7	6.7	6.8	6.4
60	7.5	6.5	7.1	7.0
61	5.8	6.6	6.2	6.2
62	7.5	8.8	8.3	8.2
63	6.9	7.4	11.9	8.7
64	8.5	6.9	8.0	7.8

3. Area under the curve (AUC) of glucose

Area under the curve (AUC) of glucose for each time point of every patient was calculated using the trapezoidal rule. Values were reported as

1. AUC between 0-1 hour was calculated by using average self-monitored blood glucose level immediately before meal and 1 hour post meal (AUC 0-1 h).

2. AUC between 1-2 hour post meal was calculated by using average self-monitored blood glucose level 1 and 2 hour post meal (AUC 1-2 h).

3. AUC between 2-4 hour post meal was calculated by using average self-monitored blood glucose level 2 and 4 hour post meal (AUC 2-4 h).

4. AUC total for each meal was calculated by summing up AUC values from 0-1 hour, 1-2 hour, and 2-4 hour post meal.

Similar to self-monitored blood glucose levels, there were 2 set of AUC values for each time point. The mean ± SD of AUC of glucose include the minimum and maximum were shown in Table 5. The average AUC of glucose between breakfast, lunch and dinner were not that different from each other (34.68 ± 8.44; 33.82 ± 8.59; 34.57 ± 8.28 mmol/L, respectively). The average AUC of glucose each meal and total 3 meals were shown in Table 6

Table 5 AUC of glucose (mmol/L) (n=64)

AUC glucose	Minimum (mmol/l)	Maximum (mmol/l)	Mean ± SD (mmol/l)
0-1 h Breakfast	5.7	16.4	9.02 ± 2.14
1-2 h Breakfast	5.8	17.4	9.72 ± 2.47
2-4 h Breakfast	9.7	29.8	15.94 ±4.68
Breakfast	22.5	62.6	34.68 ± 8.44
0-1 h Lunch	4.7	13.7	8.22 ± 2.08
1-2 h Lunch	4.5	15.7	8.83 ± 2.25
2-4 h Lunch	9.8	34.8	16.78 ±4.88
Lunch	21.1	63.8	33.82 ± 8.59
0-1 h Dinner	6.0	14.2	8.65 ±2.00
1-2 h Dinner	4.1	15.6	9.28 ± 2.34
2-4 h Dinner	10.2	30.9	16.64 ±4.40
Dinner	20.7	60.8	34.57 ± 8.28
3 meals	67.3	168.3	103.05 ± 22.17

Table 6 Mean AUC of glucose each meal and total 3 meals (mmol/L) (n=64)

No.	Mean AUC Breakfast	Mean AUC Lunch	Mean AUC Dinner	Mean AUC 3 meals
1	28.3	33.5	27.6	89.4
2	30.1	25.3	27.8	83.1
3	32.4	29.0	33.6	95.0
4	29.1	30.8	27.5	87.4
5	29.4	29.3	27.4	86.1
6	34.0	31.7	41.2	107.0
7	36.7	34.1	31.1	101.9
8	28.2	28.1	31.5	87.7
9	32.6	34.2	35.3	102.0
10	29.9	28.8	29.8	88.4
11	30.2	31.5	30.3	91.9
12	25.6	28.1	26.3	80.0
13	33.0	35.1	30.2	98.3
14	34.8	26.9	27.5	89.2
15	35.7	44.8	38.6	119.1
16	24.8	25.5	24.6	75.0
17	23.5	23.6	25.5	72.6
18	35.8	36.7	36.0	108.4
19	22.5	23.6	26.4	72.5
20	34.2	35.9	33.8	103.9
21	49.9	57.6	60.8	168.3
22	41.4	32.0	33.5	106.9
23	48.3	29.3	37.9	115.5
24	29.6	33.9	29.5	93.0
25	49.4	48.5	50.1	147.9

Table 6 Mean AUC of glucose each meal and total 3 meals (mmol/L) (n=64) (continue)

No.	Mean AUC Breakfast	Mean AUC Lunch	Mean AUC Dinner	Mean AUC 3 meals
26	22.7	30.3	30.0	82.9
27	35.7	43.2	47.8	126.7
28	62.6	63.8	30.4	156.8
29	49.0	42.8	56.1	147.8
30	29.1	28.8	32.0	90.0
31	37.8	31.9	38.1	107.9
32	38.3	42.2	48.9	129.3
33	34.3	33.9	25.7	93.9
34	36.3	42.2	36.8	115.3
35	44.0	39.0	43.7	126.8
36	36.4	43.3	45.1	124.8
37	27.5	27.3	28.7	83.4
38	29.4	37.1	31.0	97.5
39	52.0	53.0	35.9	140.8
40	34.5	34.0	34.3	102.8
41	45.5	38.1	43.9	127.6
42	37.1	32.9	41.0	111.0
43	30.8	30.4	28.2	89.4
44	36.6	41.0	41.3	118.9
45	33.1	32.5	34.5	100.1
46	32.2	48.7	43.3	124.2
47	37.6	38.2	37.1	112.9
48	29.2	22.9	30.5	82.6
49	39.0	39.0	40.9	118.8
50	30.5	21.4	23.7	75.6

Table 6 Mean AUC of glucose each meal and total 3 meals (mmol/L) (n=64) (continue)

No.	Mean AUC Breakfast	Mean AUC Lunch	Mean AUC Dinner	Mean AUC 3 meals
51	50.7	33.2	46.2	130.2
52	40.9	41.8	34.3	116.9
53	33.0	33.2	32.8	98.9
54	25.5	21.1	20.7	67.3
55	55.8	34.0	40.8	130.5
56	29.4	23.1	25.6	78.1
57	30.2	22.5	32.1	84.8
58	31.1	29.4	26.8	87.3
59	22.6	26.5	27.7	76.9
60	31.2	26.3	30.2	87.7
61	24.5	24.7	24.2	73.4
62	30.9	35.3	32.9	99.1
63	27.3	29.5	50.3	107.1
64	35.6	27.9	35.3	98.8

4. A1C value

A1C level of every patient was obtained at the hospital 2 months later after he/she finished 2-week self-monitored blood glucose. At the end of the study patients had a mean A1C of 7.37± 1.22% with minimum of 5.1% and maximum of 10.6%. Only 27 patients (42.2%) had A1C ≤7.0% (Table 7). Individual A1C values were shown in Table 8

Table 7 Categorized A1C value (%) (n=64)

A1C (%)	Frequency	Percent
5.1-6	8	12.5
6.1-7.0	19	29.7
7.1-8.0	20	31.3
8.1-9.0	13	20.3
9.1-10.0	1	1.6
>10.1	3	4.7
Total	64	100.0

Table 8 Individual A1C value (n=64)

No	A1C	No	A1C	No	A1C
1	6.4	26	5.6	51	8.8
2	6.2	27	8.9	52	7.2
3	7.0	28	10.6	53	8.4
4	6.1	29	8.0	54	7.2
5	5.3	30	8.9	55	8.7
6	7.2	31	7.3	56	7.3
7	7.0	32	8.1	57	7.6
8	8.6	33	5.1	58	7.0
9	7.0	34	8.6	59	5.9
10	6.4	35	8.2	60	6.2
11	6.8	36	8.4	61	6.7
12	6.5	37	6.6	62	7.2
13	7.5	38	6.4	63	7.6
14	6.6	39	10.6	64	7.3
15	7.2	40	7.2		
16	6.0	41	7.2		
17	5.7	42	7.8		
18	7.7	43	7.6		
19	5.7	44	7.2		
20	6.2	45	7.4		
21	10.6	46	8.5		
22	5.7	47	8.7		
23	6.9	48	7.5		
24	6.9	49	8.7		
25	9.6	50	7.0		

5. Relationship between self-monitoring of blood glucose (SMBG) level and hemoglobin A_{1C} (A1C) in type 2 diabetic patients

Relationships between self-monitoring of blood glucose (SMBG) level at each time point, 3 main meals and each main meal and A1C in 64 type 2 diabetic patients were examined using Pearson correlation. Results were in Table 9. SMBG level of total 3 meals moderately-high correlated with A1C ($r = 0.766$, $p < 0.01$). Comparing correlation between meals, glucose level at lunch meal was strongest correlated ($r = 0.713$, $p < 0.01$). For breakfast mean SMBG level before meal had the highest correlation with A1C ($r = 0.689$, $p < 0.01$). For lunch SMBG level before meal and mean 4-hour were moderately correlated with A1C ($r = 0.631$ and $r = 0.671$, $p < 0.01$, respectively). For dinner SMBG level for all points were moderately correlated with A1C.

For thirty-nine patients who used oral antidiabetic agents only whether as mono- or combination therapy, the results of correlation between SMBG and A1C were in Table 9. Comparing SMBG level from each meal, the SMBG level at dinner meal had highest correlation with A1C ($r = 0.705$, $p < 0 .01$) and SMBG level at lunch meal was the least ($r = 0.504$, $p < 0.01$). For breakfast meal SMBG level before meal was moderately correlated with A1C ($r = 0.652$, $p < 0.01$). There was low correlation between SMBG level and A1C during every time point except at mean 1-hour post lunch level where there was no correlation ($r = 0.189$, $p = 0.248$). For dinner there were moderate correlation of SMBG level before and 1-hour after meal ($r = 0.628$ and $0 .617$ at $p < 0.01$, respectively).

Twenty-five patients treated with insulin combined with oral antidiabetic agents. Pearson correlation between SMBG level and A1C were in Table 9. SMBG level from total 3 meals combined and lunch time SMBG level were moderately-high correlated with A1C ($r = 0.786$, and $0 .783$ at $p <0 .01$, respectively). For breakfast, pre-meal SMBG level shown the highest correlation ($r = 0.638$, $p < 0.01$)) while 4-hour after breakfast level was the lowest ($r = 0.462$, $p < 0.05$). For lunch correlation was highest at the 4-hour after meal SMBG level ($r = 0 .725$, $p < 0.01$) followed by 2-hour after meal level ($r = 0.705$, $p < 0.01$). For dinner correlations of SMBG level and A1C were low but

still statistical significant at every time point except before meal level where it was not statistically significant ($r = 0.314$, $p = 0.127$).

Under examinations there were some differences in the correlations between SMBG level and A1C in different group of patient. In the patients who used oral antidiabetic agents the correlations from whole lunch meal level and at every time point during that meal were lower than the other 2 groups. The correlation for lunch meal SMBG level was moderately-low ($r = 0.504$, $p < 0.01$). SMBG level showed low correlation at every time point during that meal and SMBG level at 1-hour after lunch was correlated with no statistically significant ($r = 0.189$, $p = 0.248$). However in the group that used insulin combined with oral agent, post meal SMBG level at every time point correlated well with A1C ($r = 0.674$, $r = 0.705$, $r = 0.725$ at $p < 0.01$, respectively). Their 3 meals and lunch meal SMBG levels were moderately-high correlated with A1C ($r = 0.786$ and $r = 0.783$ at $p < 0.01$)

Table 9 Correlations between SMBG level and A1C in different group of patients

SMBG	Pearson correlation All patients (n=64)	Pearson correlation Oral agent user (n=39)	Pearson correlation Insulin combined with oral agent user (n=25)
3 meals	.766**	.695**	.786**
Breakfast	.700**	.662**	.677**
Lunch	.713**	.504**	.783**
Dinner	.619**	.705**	.537**
Before breakfast	.689**	.652**	.638**
1 h post breakfast	.441**	.458**	.556**
2 h post breakfast	.601**	.564**	.593**
4 h post breakfast	.535**	.399*	.462*
Before lunch	.631**	.478**	.549**
1 h post lunch	.479**	.189	.674**
2 h post lunch	.583**	.410**	.705**
4 h post lunch	.671**	.529**	.725**
Before dinner	.504**	.628**	.314
1 h post dinner	.517**	.617**	.509**
2 h post dinner	.535**	.577**	.475*
4 h post dinner	.524**	.569**	.481*

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Looking at insulin combined with oral agent users, they could separated into 2 groups: the ones that used insulin injection twice daily (b.i.d.) (N =11) and the ones that used insulin injection three times daily(t.i.d.) as basal-bolus insulin (N = 10).
Their SMBG levels were not statistically different. Relationships between SMBG level and A1C were calculated using Pearson correlation coefficient and were shown in Table 10. In the group that treated with insulin injection twice daily there were only lunch and mean 1 hour post lunch SMBG levels that significantly correlated with A1C ($r = 0.702$, and 0.617, $P < 0.05$). On the other hand the group that treated with insulin three times daily had high correlation between SMBG levels and A1C. Total 3 means SMBG level correlated very strongly with A1C ($r = 0.949$, $p < 0.01$) as with lunch SMBG level ($r = 0.887$, $p < 0.01$). SMBG levels before breakfast, 1 hour after breakfast, 2- and 4- hour after lunch were also correlated high with A1C.

Table 10 Correlations between SMBG level and A1C in insulin combined user

SMBG	Pearson correlation All insulin combined (N=25)	Pearson correlation Insulin b.i.d (N=11)	Pearson correlation Insulin t.i.d. (N=10)
3 meals	.786**	.601	.949**
Breakfast	.677**	.432	.872**
Lunch	.783**	.702*	.887**
Dinner	.537**	.448	.482
Before breakfast	.638**	.441	.866**
1 h post breakfast	.556**	.205	.855**
2 h post breakfast	.593**	.383	.758*
4 h post breakfast	.462*	.226	.578
Before lunch	.549**	.431	.621
1 h post lunch	.674**	.617*	.798**
2 h post lunch	.705**	.599	.779**
4 h post lunch	.725**	.529**	.884**
Before dinner	.314	.124	.307
1 h post dinner	.509**	.397	.595
2 h post dinner	.475*	.434	.371
4 h post dinner	.481*	.485	.317

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

6. Relationship between the AUC of glucose and A1C in type 2 diabetic patients

Relationships between the AUC of glucose after 3 main meals and each main meal and A1C in 64 type 2 diabetic patients were examined using Pearson correlation. Results were in Table 11. AUC of glucose at each time point was correlated with A1C. There was a moderate-high relationship between AUC of total 3 meals glucose and A1C, $r = 0.746$ ($p < 0.01$). Considering each meal, moderate relationship between AUC of glucose for breakfast ($r = 0.670$), lunch ($r = 0.687$), and dinner ($r = 0.604$) at $p < 0.01$ were found. Comparing within the same meal, for breakfast AUC of glucose between 2-4 hour post meal had the strongest relationship ($r = 0.626$), while AUC of glucose between 2-4 hour post lunch had a moderate relationship ($r = 0.676$) and AUC of glucose between 0-1 hour post dinner had strongest relationship with A1C ($r = 0.584$) at $p < 0.01$. Out of 64 patients there were 39 patients who used only oral antidiabetic agents, and 25 who used insulin combined with oral antidiabetic agents. Relationships between the AUC of glucose after 3 main meals and each main meal and A1C in these patients were examined using Pearson correlation (Table 11). There were moderate relationships between AUC of glucose for each meal and for mean 3 meals combined (breakfast , $r = 0.632$; dinner, $r = 0.680$; and 3 meals , $r = 0.673$) with A1C at $p < 0.01$ with the exception of lunch meal which shown weaker relationship ($r = 0.478$, $p < 0.01$).

Results of correlation between AUC of glucose and A1C from twenty-five patients who used insulin combined with oral antidiabetic agents were shown in Table 11. The correlation between AUC of glucose from 3 meals and A1C was high ($r = 0.778$, $p < 0.01$). Comparing between each meal, AUC of glucose from lunch meal had the highest correlation closed to from 3 meals ($r = 0.759$, $p < 0.01$) while dinner meal was the lowest ($r = 0.582$). AUC of glucose between 0-1 hour post breakfast was highest among the other points from the same meal ($r = 0.630$, $p < 0.01$). For lunch meal the correlations from each time point were moderately with AUC of glucose between 2-4 hour post meal being highest ($r = 0.727$, $p < 0.01$).

For dinner the correlations between AUC of glucose and A1C were not that strong. The highest was at .568 ($p < 0.01$) between 2-4 hour post meal.

Upon examinations of the correlations between AUC of glucose and A1C in different group of patients, there were differences in the patients who used oral antidiabetic agents. In this group the correlations from lunch meal (whole meal, and at each time point, $r = 0.478$, $r = 0.376$, $r = 0.317$, $r = 0.534$, respectively at $p < 0$ .05) were lower. While the correlation between AUC of dinner meal glucose were strongest for the whole meal and at every time point ($r = 0.680$, $r = 0.707$, $r = 0.634$, $r = 0.624$, respectively at $p < 0.01$) (Table 11)

Table 11 Correlations between AUC of glucose and A1C in different group of patients

AUC glucose	Pearson correlation All patients (n=64)	Pearson correlation Oral agent user (n=39)	Pearson correlation Insulin combined with oral agent user (n=25)
3 meals	.746**	.673**	.778**
Breakfast	.670**	.632**	.618**
Lunch	.687**	.478**	.759**
Dinner	.604**	.680**	.582**
0-1 h Breakfast	.616**	.588**	.630**
1-2 h Breakfast	.572**	.561**	.578**
2-4 h Breakfast	.626**	.560**	.540**
0-1 h Lunch	.629**	.376*	.663**
1-2 h Lunch	.570**	.317*	.709**
2-4 h Lunch	.676**	.534*	.727**
0-1 h Dinner	.584**	.707**	.498*
1-2 h Dinner	.557**	.634**	.536**
2-4 h Dinner	.573**	.624**	.568**

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

7. Relationship between the SMBG level and A1C in different weight group type 2 diabetic patients

Of 64 patients there were 12 who considered having normal weight (BMI <23 kg/m^2) and 52 were overweight (BMI ≥ 23 kg/m^2). Detailed of correlations between SMBG level and A1C of normal weight patient were in Table 12. In normal weight patients SMBG level from breakfast, lunch, dinner and total 3 meals correlated moderately with A1C ($r > 0.70$, $p < 0.05$). The highest was at 3 meals level ($r = 0.785$, $p < 0.01$) followed by lunch meal level ($r = 0.777$, $p < 0.01$). For breakfast highest correlation was observed at 2-hour post meal level ($r = 0.713$, $p < 0.01$). For lunch correlations were high at 4-hour post and before meal levels ($r = 0.799$ and $r = 0.791$, $p < 0.01$). For dinner the correlations was highest at before dinner level ($r = 0.778$, $p < 0.01$) followed by 2-hour post meal level ($r = 0.634$, $p < 0.05$) and 4-hour post meal level ($r = 0.618$, $p < 0.05$).

The correlation between mean SMBG level and A1C from overweight fifty-two patients (BMI ≥ 23 kg/m^2) had been studied. The results were in Table 12. SMBG level from 3 meals was highly correlated with A1C ($r = 0.759$, $p < 0.01$) while the levels from each meal were also moderately correlated at $p < 0.01$; breakfast level ($r = 0.684$), lunch level($r = 0696$), and dinner level ($r = 0.604$). For breakfast the pre meal level was highest correlated ($r = 0.706$, $p < 0.01$) while 1-hour post meal level was the lowest ($r = 0.417$, $p < 0.01$). For lunch meal 4-hour post meal level was highest ($r = 0.643$, $p < 0.01$) followed by pre meal level ($r = 0.605$, $p < 0.01$) and 1-hour post lunch level was the lowest. For dinner the correlations were low. The highest was at 2-hour post meal level ($r = 0.518$, $p < 0.01$) and the lowest was at pre-meal level ($r = 0.441$, $p < 0.01$).

The correlations between SMBG level and A1C obtained from these two groups of patients were differences at some time point. (Table 11) In normal weight patients, the correlations were high ($r >0.700$, $p < 0.05$) at each meal, 3 meals, 2-hour post breakfast, before lunch, 4-hour post lunch, and before dinner SMBG level . While in the overweight group, the correlation over 0.700 was found only at pre breakfast and 3

meals SMBG levels. The correlation between breakfast SMBG level and A1C in normal weight patients was highest at 2-hour post meal level while in the overweight group the highest point was SMBG level before breakfast. For lunch the correlations from these two groups showed the same pattern which was high at pre meal and at mean 4-hour post meal levels but the number from normal weight group was higher. For dinner the pre meal SMBG level from the normal weight group had high correlation ($r = 0.778$, $p < 0.01$).

Table 12 Correlations between SMBG level and A1C in normal and overweight patients

SMBG	Normal weight (N=12)		Overweight (N=52)	
	Pearson Correlation	Sig.(2-tailed)	Pearson Correlation	Sig.(2-tailed)
Breakfast	.740**	.006	.684**	.000
Lunch	.777**	.003	.696**	.000
Dinner	.707*	.010	.604**	.000
3 meals	.785**	.002	.759**	.000
Pre Breakfast	.599*	.040	.706**	.000
1h Breakfast	.517	.085	.417**	.002
2h Breakfast	.713**	.009	.565**	.000
4h Breakfast	.451	.141	.554**	.000
Pre Lunch	.791**	.002	.605**	.000
1h Lunch	.569	.054	.450**	.001
2h Lunch	.584*	.046	.580**	.000
4h Lunch	.799**	.002	.643**	.000
Pre Dinner	.778**	.003	.441**	.001
1h Dinner	.578*	.049	.499**	.000
2h Dinner	.634*	.027	.518**	.000
4h Dinner	.618*	.032	.503**	.000

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

8. Relationship between the AUC of glucose and A1C in different weight group type 2 diabetic patients

Correlations between AUC of glucose and A1C in normal weight type 2 diabetic patients (N =12) for each meal and interval between each time point were studied. The results were shown in Table 13. AUC of 3 meals glucose showed highest correlation with A1C ($r = 0.764$, $p < 0.01$) followed by AUC of glucose at lunch and at breakfast ($r = 0.742$, and $r = 0.722$, $p < 0.01$). For breakfast, the correlation was highest at AUC of glucose between 1-2 hour post meal ($r = 0.663$, $p < 0.05$). For lunch, the highest correlations were at AUC of glucose between 0-1 hour and AUC of glucose 2-4 hour post meal ($r = 0.741$ $p < 0.01$). For dinner, the strongest correlation was found at AUC of glucose between 0-1 hour post meal ($r = 0.732$, $p < 0.01$).

Considering meal time for overweight patients, correlation between AUC of glucose and A1C at 3 meals was highest at $r = 0.741$ ($p < 0.01$) followed by lunch time ($r = 0.671$, $p < 0.01$). For breakfast AUC of glucose between 2-4 hour post meal was highest ($r = 0.616$, $p < 0.01$) followed by mean AUC of glucose between 0-1 hour post mea l ($r = 0.604$,$p < 0.01$). For lunch meal the correlations obtained from AUC of glucose between 2-4 hour and between 0-1hour post meal were the first and second highest ($r = 0.659$ and $r = 0.602$ at $p < 0.01$) the same as observed from breakfast meal. For dinner the correlations were moderate with all three intervals and did not differ that much. The highest was at AUC of glucose between 2-4 hour post dinner ($r = 0.557$, $p < 0.01$). However it was lower than that obtained from the same interval at breakfast and lunch. All results were shown in Table 13.

Looking at the correlations between AUC of glucose and A1C obtained from normal- and overweight patients there were some discrepancy. The correlations from 3 meals in both were highest when compared among meal. For breakfast the correlations in normal weight group were not that differences among different time point but in the overweight group the correlation between 1-2 hour post meal was lowest ($r = 0.542$, $p < 0.01$). Considering the correlation pattern for each meal, AUC of glucose between 1-2 hour post lunch and between 1-2 hour post dinner were the lowest in both groups. (Table 13)

Table 13 Correlations between AUC of glucose and A1C in normal and overweight patients

AUC glucose	Normal weight (n=12)		Overweight (n=52)	
	Pearson Correlation	Sig.(2-tailed)	Pearson Correlation	Sig.(2-tailed)
3 meals	**.764****	.004	**.741****	.000
Breakfast	.722**	.008	.651**	.000
Lunch	**.742****	.006	**.671****	.000
Dinner	.681*	.015	.593**	.000
0-1 h Post Breakfast	.635*	.027	.604**	.000
1-2 h Post Breakfast	.663*	.019	.542**	.001
2-4 h Post Breakfast	.640*	.025	**.616****	.000
0-1 h Post Lunch	**.741****	.006	.602**	.000
1-2 h Post Lunch	.615*	.033	.554**	.000
2-4 h Post Lunch	**.741****	.006	**.659****	.000
0-1 h Post Dinner	.732**	.007	.548**	.000
1-2 h Post Dinner	.628*	.029	.543**	.000
2-4 h Post Dinner	.661*	.019	.557**	.000

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

9. Model for prediction of A1C value

9.1 Model for prediction of SMBG level and A1C

Multiple regression analysis was performed to create the model for prediction of A1C from SMBG level at different time points for all 64 patients, 39 patients who used oral antidiabetic agents and 25 who used combination of insulin and oral agents. The best fitted equation for prediction of A1C was considered by the fact that it gave high R^2 without too many factors to be put into. For 64 patients the best model obtained from backward elimination method had R^2 = 0.65 (65%, p =0.00) and incorporated only 4 factors related to SMBG level. (Table 14)

Table 14 Model Summary of linear regression for prediction of A1C in 64 patients

Model	R	R^2	Adjusted R^2	Std.Error of the Estimate
1	0.81(a)	0.65	0.63	0.74

a Predictors: (Constant), ac B, 4-h L, ac L, 2-h B

Coefficients [a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig
		B	Std. Error	Beta		
1	(Constant)	3.34	0.40		8.29	0.00
	ac B	0.19	0.06	0.31	2.99	0.00
	2-h B	0.09	0.05	0.20	1.96	0.06
	ac L	0.09	0.05	0.19	1.82	0.07
	4-h L	0.14	0.04	0.31	3.15	0.00

a Dependent Variable: A1C

The equation for prediction of A1C from SMBG level from 64 patients was shown below:

A1C = 3.34 + 0.19 (ac B) + 0.09 (2-h B) + 0.09 (ac L) + 0.14 (4-h L)

For 39 oral agent users, the linear regression (backward elimination method) also gave the equation that had R^2 = 0.71 (71%, p =0.00) with 4 factors to be used. The model was shown in Table 15

Table 15 Model Summary of linear regression for prediction of A1C in 39 patients

A Model	R	R^2	Adjusted R^2	Std.Error of the Estimate
1	0.84(a)	0.71	0.67	0.54

a Predictors: (Constant), ac B, 1-h L, ac D, 1-h D

Coefficients [a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig
		B	Std. Error	Beta		
1	(Constant)	3.41	0.52		6.62	0.00
	ac B	0.27	0.06	0.43	4.28	0.00
	1-h L	-0.12	0.05	-0.27	-2.30	0.03
	ac D	0.15	0.05	0.33	2.89	0.01
	1-h D	0.16	0.50	0.44	3.27	0.00

a Dependent Variable: A1C

The equation for prediction of A1C from SMBG level from 39 patients was shown below:

A1C = 3.41 + 0.27 (ac B) – 0.12 (1-h L) + 0.15 (ac D) + 0.16 (1-h D)

For 25 patients who were treated with insulin combined with oral antidiabetic agents, the linear regression (backward elimination method) calculated the equation model that had R^2 = 0.62 (62%, p =0.00). (Table 16)

Table 16 Model Summary of linear regression for prediction of A1C in 25 patients

Model	R	R^2	Adjusted R^2	Std.Error of the Estimate
1	0.79(a)	0.62	0.60	0.80

a Predictors: (Constant), mean 3 meals

Coefficients [a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig
		B	Std. Error	Beta		
1	(Constant)	3.32	0.80		4.14	0.00
	Mean 3 meals	0.53	0.09	0.79	6.11	0.00

a Dependent Variable: A1C

The equation for prediction of A1C from SMBG level from 25 patients was shown below:

A1C = 3.32 + 0.53 (mean 3 meals)

9.2 Model for prediction of AUC of glucose and A1C

Multiple regression analysis was performed to create the model for prediction of A1C from AUC of glucose at different time interval for all 64 patients, 39 patients who used oral antidiabetic agents and 25 who used combination of insulin and oral agents. For 64 patients there best model obtained from backward elimination method had R^2 = 0.61 (61%, p =0.00) and incorporated only 4 factors related to AUC of glucose. (Table 17)

Table 17 Model Summary of linear regression for prediction of A1C from AUC of glucose in 64 patients

Model	R	R^2	Adjusted R^2	Std.Error of the Estimate
1	0.78(a)	0.61	0.58	0.79

a Predictors: (Constant), AUC 0-1 h B, AUC 1-2 h L, AUC 0-1 h L, AUC 2-4 h L

Coefficients [a]

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig
	B	Std. Error	Beta		
1 (Constant)	3.54	0.48		7.37	0.00
AUC 0-1 h B	0.15	0.06	0.26	2.42	0.02
AUC 0-1-h L	0.31	0.09	0.52	3.56	0.00
AUC 1-2 h L	-0.34	0.12	-0.62	-2.87	0.01
AUC 2-4-h L	0.18	0.04	0.70	4.02	0.00

a Dependent Variable: A1C

The equation to predict A1C from AUC of glucose in 64 patients was shown below:

A1C = 3.54 + 0.15 (AUC 0-1 h B) + 0.31 (AUC 0-1 h L) – 0.34 (AUC 1-2 h L) + 0.18 (AUC 2-4 h L)

For 39 oral agent users, the linear regression (stepwise regression, forward selection, and backward elimination method) gave the same equation that had R^2 = 0.62 (62 %, p =0.00) with 3 factors to be used. The model was shown in Table 18

Table 18 Model Summary of linear regression for prediction of A1C from AUC of glucose in 39 patients

Model	R	R^2	Adjusted R^2	Std.Error of the Estimate
1	0.79(a)	0.62	0.59	0.61

a Predictors: (Constant), AUC 0-1 h B, AUC 1-2 h L, AUC 0-1 h D,

Coefficients [a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig
		B	Std. Error	Beta		
1	(Constant)	3.83	0.54		7.15	0.00
	AUC 0-1-h B	0.17	0.06	0.35	2.86	0.01
	AUC 1-2 h L	-0.15	0.07	-0.29	-2.12	0.04
	AUC 0-1 h D	0.34	0.07	0.72	4.99	0.00

a Dependent Variable: A1C

The equation to predict A1C from AUC of glucose in 39 patients was shown below:

A1C = 3.83 + 0.17(AUC 0-1 h B) – 0.15 (AUC 1-2 h L) + 0.34 (AUC 0-1 h D)

For 25 patients who were treated with insulin combined with oral antidiabetic agents, the linear regression (backward elimination) calculated the model that had R^2 = 0.63 (63%, p =0.00). (Table 19)

Table 19 Model Summary of linear regression for prediction of A1C from AUC of glucose in 25 patients

Model	R	R^2	Adjusted R^2	Std.Error of the Estimate
1	0.79(a)	0.63	0.59	0.76

a Predictors: (Constant), AUC 2-4 h L, AUC 2-4 h D

Coefficients [a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig
		B	Std. Error	Beta		
1	(Constant)	4.38	0.68		6.45	0.00
	AUC 2-4 h L	0.11	0.03	0.60	4.21	0.00
	AUC 2-4-h D	0.09	0.04	0.34	2.38	0.03

a Dependent Variable: A1C

The equation to predict A1C from AUC of glucose in 39 patients was shown below:

A1C = 4.38 + 0.11 (AUC 2-4 h L) + 0.09 (AUC 2-4-h D)

9.3 Model for prediction of SMBG level and A1C in different weight group of patients

There were 2 groups of patients based on the weight factor, one with BMI< 23 kg/m^2 (12 patients) was labeled as normal weight group, and the other with BMI ≥ 23 kg/m^2 (52 patients) was labeled as overweight group. Multiple regression analysis was performed to create the model for prediction of A1C from SMBG level for these 2 groups For normal weight patients the best model obtained from stepwise selection method had R^2 = 0.80 (80% , p =0.00) and incorporated only 1 factor related to SMBG level. (Table 20)

Table 20 Model Summary of linear regression for prediction of A1C from SMBG level in 12 patients

Model	R	R^2	Adjusted R^2	Std.Error of the Estimate
1	0.80(a)	0.64	0.60	0.77

a Predictors: (Constant), 4-h L

Coefficients [a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig
		B	Std. Error	Beta		
1	(Constant)	4.03	0.75		5.36	0.00
	4-h L	0.42	0.10	0.80	4.20	0.00

a Dependent Variable: A1C

The equation to predict A1C from AUC of glucose in 12 patients was shown below:

A1C = 4.03 + 0.42 (4-h L)

For the overweight group (N = 52) the best model calculated from using backward elimination linear regression. It gave had R^2 = 0.79 (79%, p =0.00). (Table 21)

Table 21 Model Summary of linear regression for prediction of A1C from SMBG level in 52 patients

Model	R	R^2	Adjusted R^2	Std.Error of the Estimate
1	0.79(a)	0.63	0.60	0.77

a Predictors: (Constant), ac B, 4-h L, ac L

Coefficients [a]

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig
	B	Std. Error	Beta		
1 (Constant)	3.52	0.46		7.71	0.00
ac B	0.26	0.07	0.41	3.56	0.00
ac L	0.11	0.05	0.23	2.15	0.04
4-h L	0.14	0.05	0.31	2.83	0.00

a Dependent Variable: A1C

The equation to predict A1C from AUC of glucose in 52 patients was shown below:

A1C = 3.52 + 0.26 (ac B) + 0.11 (ac L) + 0.14(4-h L)

9.4 Model for prediction of AUC of glucose and A1C in different weight group

In different weight groups besides finding the equations for prediction of A1C from SMBG level, the equation for prediction of A1C from AUC of glucose was also calculated. For normal weight patients the best model obtained from backward elimination method had R^2 = 0.85 (85%, p = 0.01) and incorporated only factors related to AUC of glucose. (Table 22)

Table 22 Model Summary of linear regression for prediction of A1C from AUC of glucose in 12 patients

Model	R	R^2	Adjusted R^2	Std.Error of the Estimate
1	0.92(a)	0.85	0.77	0.59

a Predictors: (Constant), AUC 0-1 h B, AUC 0-1 h L, AUC 1-2 h L, AUC 1-2 h B

Coefficients [a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig
		B	Std. Error	Beta		
1	(Constant)	2.98	0.79		3.77	0.01
	AUC 0-1 h B	-0.38	0.20	-0.70	-1.93	0.09
	AUC 1-2 h B	0.58	0.16	1.27	3.54	0.00
	AUC 0-1 h L	1.29	0.31	1.89	4.23	0.00
	AUC 1-2 h L	-0.94	0.29	-1.54	-3.19	0.02

a Dependent Variable: A1C

The equation to predict A1C from AUC of glucose in 12 patients was shown below:

A1C = 2.98 - 0.38 (AUC 0-1 h B) + 0.58 (AUC 1-2 h B) + 1.29 (AUC 0-1 h L)

0.94 (AUC 1-2 h L)

For 52 patients who were overweight the best model calculated from using backward elimination linear regression. It gave R^2 = 0.64(64%, p =0.00). (Table 23)

Table 23 Model Summary of linear regression for prediction of A1C from AUC of glucose in 52 patients

Model	R	R^2	Adjusted R^2	Std.Error of the Estimate
1	0.80(a)	0.64	0.60	0.78

a Predictors: (Constant), AUC 2-4 h D, AUC 0-1 h B , AUC 2-4 h B, AUC 2-4 h L, AUC 1-2 h B

Coefficients [a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig
		B	Std. Error	Beta		
1	(Constant)	2.91	0.57		5.11	0.00
	AUC 0-1 h B	0.39	0.13	0.67	3.07	0.00
	AUC 1-2 h B	-0.34	0.13	-0.66	-2.50	0.02
	AUC 2-4 h B	0.12	0.05	0.46	2.76	0.01
	AUC 2-4 h L	0.07	0.03	0.29	2.37	0.02
	AUC 2-4 h D	0.07	0.03	0.22	2.00	0.05

a Dependent Variable: A1C

The equation to predict A1C from AUC of glucose in 52 patients was shown below:

A1C = 2.91 + 0.39 (AUC 0-1 h B) - 0.34 (AUC 1-2 h B) + 0.12 (AUC 2-4 h B) + 0.07 (AUC 2-4 h L) + 0.07 (AUC 2-4 h D)

CHAPTER V
DISCUSSION AND CONCLUSION

1. Patient characteristic

This study evaluated the relationship between AUC of glucose, SMBG level and A1C in type 2 diabetic patients. Total of sixty-four patients were studied. Characteristics of typical type 2 diabetic patients are obese or overweight, having hypertension and abnormalities of lipoprotein metabolism.[3,28] Most of the patients were older than 50 year old (53 patients) , overweight (52 patients), had been diagnosed as having diabetes for more than 5 years (50 patients), had common conditions coexisting with type 2 diabetes such as hypertension and dyslipidemia or dyslipidemia or hypertension alone (59 patients). Sixty-one percent of patients (39) used oral antidiabetic agents which followed the present recommendation that suggest the use of one agent first then if needed proceed to combination of two oral agents or added basal insulin.[2,25] Their mean SMBG levels for preprandial (7.41 ± 1.99 mmol/L for breakfast, 7.52 ± 2.44 mmol/L for lunch, and 7.79 ± 2.14 mmol/L for dinner) were a little higher than the recommended which is 3.9-7.2 mmol/L(70-130 mg/dL).[2] Peak postprandial blood glucose seemed to occur at 1hour after meal in all 3 meals (10.63 ± 2.86 mmol/L for breakfast, 8.91 ± 2.30 mmol/L for lunch, and 9.54 ± 2.42 mmol/L) and is not differ from the recommendation (<10 mmol/L) measured at 1-2 hour after the beginning of eating.[2]

2. Relationship between SMBG, AUC of glucose and A1C

There were correlations between all points of SMBG level and A1C in all 64 type 2 diabetes and all were statistically significant ranging from r = 0.441-0.766. Mean 3 meal was highest and 1-hour post breakfast was the lowest. Blood glucose level from all 3 meals shows a strong correlation with A1C in all and in subgroup patients. Makris et al.[43] showed a higher number than this study (r =0.93). Mean blood glucose was derived from SMBG levels six daily measurements (pre-meal, and 2 hour after for each meal) three times a week for 1 month, while in our study mean blood glucose derived

from four measurements per meal per day (pre-meal, 1-,2- and 4-hour post meal) alternating day twice. Pupillo et al. [42] showed a little lower number (r= 0.70) and only use SMBG levels pre breakfast meal and 2 hour post meal and not from repeated measurements over time. This shows that the frequency of SMBG measurements and measurement over time might influence the mean blood glucose value. Monnier et al. [20] concluded that postprandial glucose levels are the dominant contributor to A1C levels in patients with A1C <8.5%, while fasting glucose levels were more important in patients with A1C >8.5%. They concluded the results from looking at increment in AUC of glucose above fasting concentration and above 6.1 mmol/L(110 mg/dL) while the results in our study concluded from SMBG level and total area under the curve of glucose during the specific interval.

From thirty-nine patients who used only oral antidiabetic agents whether as mono- or combination therapy in this study, the correlations were found to be statistically significant at every point (range from 0.705-0.399) except at 1-hour post lunch where r = 0.189 ($p > 0.05$). The two points in time that highly correlated were blood glucose level before breakfast and before dinner. For twenty-five patients treated with insulin combined with oral antidiabetic agents correlations between all points of SMBG level and A1C were also statistically significant ($r = 0.462$-0.786, $p < 0.05$) except before dinner ($r= 0.314$, $p > 0.05$).

From the patients in this group, there were 11 patients who used insulin twice daily combined with oral agents and 10 patients who used insulin three times daily combined with oral agents. The correlations between SMBG level and A1C in these two groups were differed at different time point. In twice daily insulin users, the high correlation was found at blood glucose level for lunch time and at 1 hour post lunch. In the group that used insulin three times daily high correlations were found at mean 3 meals level , breakfast and lunch glucose level , before and 1 hour post breakfast and 2- and 4 hour post lunch SMBG levels. Blood glucose level during dinner meal showed no statistical significant at all in these two groups of insulin combined with oral agent users. The reason may be that during dinner our patients did not consume that much food

intake as they were trying to lose weight. Many studies showed the same results of high correlation for pre meal and post meal values with A1C. [15-18,20,33,35,38,40,43,45,49] Bonora et al. [14] also showed that in oral antidiabetic users who did 6- point SMBG (pre meal , 2 hour post meal for all 3 meals on 5 nonconsecutive days in 1 month had the strongest correlation of A1C and mean blood glucose level ($r = 0.685$, $p < 0.001$) and while pre-meal (breakfast and dinner) levels had high correlations. This is in accordance with our study that also found high correlations. This is may be due to the fact that the patients in our study also did frequent SMBG over a period. There is a good evidence that several glucose measurements of several weeks are better correlated to A1C than a single or fewer glucose measurements on a single day. [36, 52] Many studies done in diabetic patients who used insulin either type 1 or 2 showed that the pre-breakfast, pre-lunch, and pre-dinner glucose levels correlated with A1C. [12,15,35, 38, 45,48,54] Shimizu et al.[35] showed that in patients who treated with insulin either as b.i.d. or basal-bolus regimen among three pre-meals level, correlation was high at pre-lunch and was low at pre-dinner which were in accordance with our study. Patients in our study were also treated with the same insulin regimen. However the correlations between blood glucose at 1- , 2- and 4-hour post lunch and A1C in our study were high especially in the group treated with insulin three times daily combined with oral agents. This suggests that blood glucose post lunch especially at 2 and 4 hour after is important in this group of patients. While Yamamoto-Honda et al. [54] show low values at 1 and 2 hour post lunch. This may be due the fact that only 10.5% of patients used insulin combined with oral agents where 39.1% of patients (N = 25) in our study used the combinations of insulin and oral agents.

When we subgroup the patients into normal and overweight, we found that all points of SMBG levels correlated significantly with A1C in overweight patients as well as in all studied patients. The reason may be because 81.3% of patients (N = 52) was overweight so either we calculated the number of patients in total or subgroup, the trend is still the same. In normal weight patient (N=12) all points of SMBG levels were also correlated significantly with A1C except 1 hour post lunch which was also seen in

patients who treated with oral agents. Out of 12, there were only 3 patients who used insulin so majority of them use oral agents. So it seemed that BMI had no influence on the correlation as Koga et al. [55] found that while fasting plasma glucose significantly correlated with A1C, BMI had no correlation with A1C.

For all patients (N=64) all intervals of the AUC of glucose correlated significantly with A1C. The same finding was also seen in the subgroup analysis (N= 25 for insulin combined with oral agents, N= 39 for oral agent, N= 12 for normal weight and N= 52 for overweight). This is in accordance with the correlation between SMBG level and A1C since the AUC of glucose was calculated from SMBG level as seen in study in type 1 diabetic patients that showed glucose pre and post meal levels correlated with glucose area value. [58] Monnier et al. [20] also found that in type 2 diabetic patients there was a significant correlation (R^2 = 0.48, p <0.0001) between A1C and AUC of glucose calculated above 6.1 mmol/L(110 mg/dL) which reflected the increases in both fasting and postprandial blood glucose. Peter et al. [37] also found that in treatment naïve type 2 diabetes total area under the plasma glucose curve over 4-hour test period correlated with A1C (r = 0.851, p <0.001). Correlation between AUC of glucose 2 hour post meal from continuous interstitial glucose monitoring and A1C from Borg et al. [44] was higher than our study. This is may be because the AUC of glucose from their study was bigger than ours.

The equations to predict A1C from SMBG level and AUC of glucose were not the same for all patients, for different type of medication usage, and for different weight group. However the R^2 values were not that differ among the different groups of patients (N = 64 ,R^2 = 0.65; N = 39, R^2 = 0.71; N = 25, R^2 = 0.62) . Subgroup analysis by weight showed that the R^2 obtained from prediction model of A1C from SMBG level did not differ in normal and overweight patients (R^2 = 0.64, and 0.63, respectively) and did not differ from all 64 patients. However the R^2 obtained from prediction model of A1C from AUC of glucose in normal weight patients was higher than that obtained from overweight patients((R^2 = 0.85 , and 0.64, respectively).

Not that many studies examined the AUC of glucose.[19,37,44,50] They only studied it in term of increment from fasting blood glucose and in term of AUC under receiver operating curve to aid in diagnosis of disease. Our study examined AUC of glucose at intervals between meal for 3 meals and to associate them with A1C. The R^2 from equations to predict A1C from AUC of glucose in all and in subgroup of patients were not that differ ranging from 0.61-0.64. However in normal weight patients R^2 equaled to 0.85. This suggests that in this group of patient AUC of glucose may be an accurate indicator for A1C prediction.

From our study, the following conclusions are drawn:

1. AUC of glucose from 3 meals correlates best with A1C.

2. AUC of glucose lunch meal is best correlated with A1C when compared among meals.

3. AUC of glucose obtained during 2-4 hour after lunch correlates well with A1C and can be a representative of A1C level for type 2 diabetic patients.

4. AUC of glucose in normal weight patients correlates very strongly with A1C.

5. SMBG levels obtained from mean 3 meals (average 12 points) correlates best with A1C.

6. SMBG levels obtained from average 12 points (3 meals) is best correlated with A1C.

7. SMBG levels before breakfast and at 4 hour post lunch correlates well with A1C and can be a representative of A1C level for all type 2 diabetic patients , and for patients who used insulin combined with oral antidiabetic agents

8. SMBG level at 1 hour post lunch correlates well with A1C and can be a representative of A1C level for type 2 diabetic patients who use insulin injection (mainly mixture of regular and NPH insulin) twice daily combined with oral agents.

9. SMBG level before breakfast and before dinner correlates well with A1C and can be the representative of A1C level for type 2 diabetic patients who use oral antidiabetic agents.

The correlations between AUC of glucose and A1C followed the same pattern as the correlation between SMBG level and A1C. AUC of glucose is an accurate indicator for prediction of A1C, however it is not better indicator than SMBG level since it needs more blood glucose points to use in calculation while SMBG level uses only 1 or 2 points. As mentioned before, the best correlation would be from the mean blood glucose level from 3 meals however it is difficult to do in real-life situation. Therefore, apart from pre-breakfast blood glucose level that is routinely measured, 4 hour post lunch glucose level is a best option to do the measurement.

Limitation

1. Patients performed 12-point SMBG level (pre meal, 1-, 2-,and 4 hour after meal) twice in 2 weeks. This can be a confounding factor since it was not done on the same day. The correlations obtained in this study were not that high, the reason may be that the patients did not perform 3 A.M. level. This might not represents all information and it can lead to under or overestimation of blood glucose values.

2. Number of samples in this study may not be enough for some subgroup analysis.

3. This study wanted to study under real-life situation, therefore the food intake, patients' behaviors such as medication non-adherence and performing SMBG may have the effects on the blood glucose level.

4. This study only included patients that were stables type 2 diabetic patient , without any liver/kidney diseases or any diabetic related complications other than hypertension, ischemic heart disease or dyslipidemia. Therefore, the results may not be extrapolated to all diabetic patients.

Further Study

The study should be extended, and larger sample sizes are needed.

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APPENDICES

APPENDIX A
INFORMATION FOR PATIENTS
ข้อมูลสำหรับผู้เข้าร่วมวิจัย

การศึกษาทางคลินิก : พื้นที่ใต้โค้งของกลูโคส : ตัวชี้วัดที่แม่นยำกว่าในการควบคุมกลูโคสในผู้ป่วยเบาหวานชนิดที่ 2

เรียน ผู้ป่วยทุกท่าน

ท่านได้รับเชิญให้เข้าร่วมการศึกษาทางคลินิกโดยการใช้ค่าพื้นที่ใต้โค้งของกลูโคสเพื่อเป็นตัวชี้วัดที่แม่นยำกว่าในการควบคุมน้ำตาลในเลือด ก่อนที่ท่านตกลงเข้าร่วมการศึกษาดังกล่าว ขอเรียนให้ท่านทราบถึงเหตุผลและรายละเอียดของการศึกษาวิจัยนี้

โรคเบาหวานเป็นโรคเรื้อรังต้องอาศัยการดูแลอย่างต่อเนื่อง เพื่อป้องกันภาวะแทรกซ้อนทางระบบต่างๆของร่างกายต่างๆ เช่น โรคหลอดเลือดหัวใจ โรคไต อาการชาตามปลายมือเท้า และโรคตา ผู้ป่วยเบาหวานชนิดที่ 2 จะมีความผิดปกติเกี่ยวกับหลั่งอินซูลินร่วมกับภาวะดื้อต่ออินซูลิน ทำให้เกิดภาวะน้ำตาลกลูโคสในเลือดสูงได้ในภาวะหลังอดอาหารมาทั้งคืน และ/หรือหลังรับประทานอาหารแล้ว การควบคุมระดับน้ำตาลกลูโคสในเลือดโดยการตรวจวัดค่าฮีโมโกลบินเอวันซีหรือเอวันซี เป็นวิธีการที่เหมาะสมในการติดตามการใช้ยาของผู้ป่วยเบาหวาน ค่าเอวันซีนี้เป็นการวัดค่าเฉลี่ยของระดับกลูโคสในเลือดในระยะ 2-3 เดือนที่ผ่านมา และเป็นการวัดค่ากลูโคสทั้งหลังอดอาหารมาทั้งคืนและกลูโคสหลังรับประทานอาการแล้ว และพบว่าค่าเอวันซีมีความสัมพันธ์กับระดับกลูโคสในเลือดทั้งในภาวะอดอาหารทั้งคืน และ/หรือหลังมื้ออาการ

การวัดระดับกลูโคสในเลือดที่บ้านทั้งก่อนและหลังมื้ออาหารแล้วนำมาคำนวณหาพื้นที่ใต้โค้งของกลูโคส จะช่วยบอกถึงความสัมพันธ์กับค่าเอวันซีได้ การเจาะวัดกลูโคสเองที่บ้านโดยผู้ป่วยเป็นสิ่งที่ทำได้ไม่ยาก และเป็นการกระตุ้นให้ผู้ป่วยมีส่วนร่วมในการดูแลสุขภาพเองด้วย

วัตถุประสงค์ของการวิจัย

1. เพื่อศึกษาความสัมพันธ์ระหว่างค่าเฉลี่ยของพื้นที่ใต้โค้งของกลูโคสทั้งวัน (มื้ออาหารรวม 3 มื้อ) กับค่าเอวันซีในผู้ป่วยเบาหวานชนิดที่ 2
2. เพื่อศึกษาความสัมพันธ์ระหว่างพื้นที่ใต้โค้งของกลูโคสของอาหารแต่ละมื้อกับค่าเอวันซีในผู้ป่วยเบาหวานชนิดที่ 2
3. เพื่อศึกษาความสัมพันธ์ระหว่างความเข้มข้นของกลูโคส ณ จุดใดจุดหนึ่ง (ก่อน/หลังมื้ออาหาร) ของแต่ละมื้ออาหารกับค่าเอวันซีในผู้ป่วยเบาหวานชนิดที่ 2

4. เพื่อเปรียบเทียบความสัมพันธ์ของพื้นที่ใต้โค้งของกลูโคสกับค่าเอวันซีตามวัตถุประสงค์ข้อ 1 – 3 ในผู้ป่วยเบาหวานชนิดที่ 2 ที่ปกติและน้ำหนักเกิน
5. เพื่อเปรียบเทียบความสัมพันธ์ของพื้นที่ใต้โค้งของกลูโคสกับค่าเอวันซีตามวัตถุประสงค์ข้อ 1 – 3 ระหว่างผู้ป่วยเบาหวานชนิดที่ 2 ที่ใช้ยาเม็ดลดน้ำตาลในเลือด หรือผู้ที่ใช้ยายาฉีดร่วมกับยาเม็ด

สถานที่ทำการวิจัย

โรงพยาบาลตำรวจ

จะเกิดอะไรขึ้นกับท่านบ้าง

ถ้าท่านตกลงที่จะเข้าร่วมการศึกษานี้ ท่านจะได้รับการตรวจร่างกายกับแพทย์ตามปกติเหมือนที่ท่านเคยได้รับ ผู้วิจัยจะทำการอบรมวิธีใช้เครื่องตรวจวัดระดับน้ำตาลกลูโคสในเลือด (Accu-Check® Advantage II) แก่ท่านหรือญาติของท่าน และขอให้ท่านช่วยเจาะตรวจระดับน้ำตาลในเลือดที่บ้านด้วยตนเอง ถ้าท่านทำเองไม่ได้โปรดให้ญาติของท่านทำให้ และบันทึกลงในแบบบันทึกที่ผู้วิจัยเตรียมให้ท่าน ท่าน(หรือญาติของท่าน) จะต้องวัดระดับน้ำตาลกลูโคสในเลือดรวมทั้งสิ้น 6 วัน ภายในเวลา 2 สัปดาห์ โดยในแต่ละวันจะวัดระดับน้ำตาลของแต่ละมื้ออาหารและทำการเจาะตรวจเลือด 4 จุด รายละเอียดดังนี้

ทำการตรวจวัดระดับน้ำตาลในเลือดของแต่ละมื้ออาหาร มื้อละ 2 ครั้ง ดังนี้

วัน 1 , 7 ตรวจวัดน้ำตาลของมื้อ**เช้า**

วัน 3 , 9 ตรวจวัดน้ำตาลของมื้อ**กลางวัน**

วัน 5 , 11 ตรวจวัดน้ำตาลของมื้อ**เย็น**

โดยในแต่ละมื้อ ตรวจวัดระดับน้ำตาลในเลือด 4 จุด

1. ตรวจวัดระดับน้ำตาล**ทันทีก่อนรับประทานอาหาร**
2. วัดระดับน้ำตาล**หลัง**รับประทานอาหารแล้ว **1 ช.ม.**
3. วัดระดับน้ำตาล**หลัง**รับประทานอาหารแล้ว **2 ช.ม.**
4. วัดระดับน้ำตาล**หลัง**รับประทานอาหารแล้ว **4 ช.ม.**

โดยนับวันแรกที่เริ่มทำการตรวจวัดเป็นวัน 1 แล้วทำ**สลับมื้อ <u>วันเว้นวัน</u>** ถ้าวันใด**ลืม**ทำการตรวจวัด **หรือ**วัดได้**ไม่ครบ 4 จุด** ให้**ทำการตรวจมื้อนั้นใหม่ทั้งมื้อ**โดยทำในวันถัดไป จากนั้นเจาะตามตารางเดิมวันเว้นวัน

เมื่อครบ 2 สัปดาห์ กรุณานำบันทึกผลการตรวจวัดระดับน้ำตาลกลูโคสในเลือดของตัวท่านเองและเครื่องตรวจวัดระดับกลูโคสในเลือดมาให้ผู้วิจัยที่โรงพยาบาล หลังจากนั้น 2 เดือน ท่านจะได้รับการตรวจวัดค่าเอวันซี

ท่านจะต้องปฏิบัติตัวอย่างไรในระหว่างการเข้าร่วมศึกษา

หากท่านตกลงที่จะเข้าร่วมการศึกษาวิจัยนี้ จะมีข้อปฏิบัติดังต่อไปนี้

- ท่านจะต้องไม่เปลี่ยนแปลงพฤติกรรมใดๆ ไม่ว่าจะเป็นในแง่ของอาหารที่รับประทาน (หมายความถึงประเภทและจำนวน) และการออกกำลังกาย
- ท่านจะต้องไม่ใช้ยาอื่นนอกเหนือจากยารักษาเบาหวานหรือโรคอื่นที่เป็นอยู่ที่แพทย์เป็นผู้สั่งจ่าย

ประการสำคัญที่ท่านควรทราบ คือ

- การเข้าร่วมการศึกษานี้เป็นไปโดยสมัครใจ ท่านอาจปฏิบัติเสธที่จะเข้าร่วมหรือถอนตัวจากการศึกษานี้ได้ทุกเมื่อโดยไม่กระทบต่อการดูแลรักษาที่ท่านจะได้รับจากแพทย์
- หากท่านตกลงเข้าร่วมการศึกษานี้ ผู้วิจัยจะจ่ายค่าชดเชยการเดินทางให้ท่านเป็นเงินจำนวน 200 บาท/วัน ในวันที่นำผลการตรวจมาให้ (2 สัปดาห์หลังการตรวจเจาะ) และผู้วิจัยจะจ่ายค่าตรวจ AIC 2 เดือนต่อมาให้ในกรณีที่ต้องตรวจเพิ่มเติม
- ผู้วิจัยจะมีเครื่องตรวจและแผ่นตรวจวัดระดับน้ำตาลในเลือดให้ท่านนำไปใช้ที่บ้านเป็นเวลา 2 สัปดาห์ โดยท่านไม่ต้องเสียค่าใช้จ่ายใด และกรุณานำมาคืนผู้วิจัยเมื่อตรวจเสร็จเพื่อจะได้ใช้กับผู้ป่วยรายต่อไป
- ในระหว่างการวิจัย ผู้วิจัยอาจจำเป็นต้องให้ท่านออกจากการศึกษาหากแพทย์ได้พิจารณาแล้วว่าท่านมีสุขภาพไม่พร้อมที่จะอยู่ร่วมในการศึกษาต่อไป หรือท่านไม่สามารถปฏิบัติตัวตามข้อปฏิบัติดังกล่าวข้างต้น
- ผลของการศึกษานี้จะให้สำหรับวัตถุประสงค์ทางวิชาการเท่านั้น โดยข้อมูลต่างๆจะถูกเผยแพร่ในภาพรวมของการวิจัยเท่านั้นจะไม่มีการเผยแพร่ข้อมูลเป็นรายบุคคล

หากท่านมีปัญหาหรือข้อสงสัยประการใด กรุณาติดต่อ

ผศ. สุธาทิพย์ พิชญไพบูลย์ ภาควิชาเภสัชกรรม(คลินิก)

คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

โทร. 081-6143557, 02-2188407, 02-2188403

ขอขอบคุณในความร่วมมือของท่าน

APPENDIX B

ใบยินยอมเข้าร่วมการวิจัย (Consent form)

วันที่.....เดือน.....พ.ศ.....

ชื่อ-สกุล.....เลขที่ผู้ป่วย.....

อาศัยอยู่บ้านเลขที่.....ถนน.....แขวง/ตำบล.....

เขต/อำเภอ.....จังหวัด..... โทร.....

การวิจัยเรื่อง พื้นที่ใต้โค้งของกลูโคส : ตัวชี้วัดที่แม่นยำกว่าในการควบคุมกลูโคสในผู้ป่วยเบาหวานชนิดที่ 2

ข้าพเจ้าได้รับการอธิบายจากผู้วิจัยถึงรายละเอียดของการศึกษาวิจัยนี้ โดยได้รับทราบเกี่ยวกับวัตถุประสงค์ของการวิจัย วิธีการวิจัย รวมทั้งประโยชน์ที่จะเกิดขึ้นจากการศึกษาวิจัยอย่างละเอียดและมีความเข้าใจดีแล้ว ข้าพเจ้าได้ซักถามข้อสงสัย ซึ่งได้รับคำตอบจากผู้วิจัย จนข้าพเจ้าพอใจเป็นที่เรียบร้อยแล้ว

ข้าพเจ้ามีสิทธิ์จะขอถอนตัวจากการศึกษานี้ได้ทุกเมื่อ โดยสามารถแจ้งให้ผู้วิจัยทราบในทันที โดยไม่กระทบต่อการดูแลรักษาที่ข้าพเจ้าจะได้รับจากแพทย์

ข้าพเจ้าได้รับทราบว่า ในระหว่างการศึกษาวิจัยผู้วิจัยอาจจำเป็นให้ข้าพเจ้าออกจากการศึกษา หากแพทย์ได้พิจารณาแล้วว่าข้าพเจ้ามีสุขภาพไม่พร้อมที่จะอยู่ร่วมในการศึกษาต่อไปหรือข้าพเจ้าไม่สามารถปฏิบัติตัวตามข้อปฏิบัติร่วมดังกล่าวข้างต้น

ข้าพเจ้าได้รับทราบว่า ผลของการศึกษานี้จะใช้สำหรับวัตถุประสงค์ทางวิชาการเท่านั้น โดยข้อมูลต่างๆ จะถูกเผยแพร่ในภาพรวมของการวิจัยเท่านั้น จะไม่มีการเผยแพร่ข้อมูลเป็นรายบุคคล

หากข้าพเจ้ามีปัญหาหรือข้อสงสัยประการใด ข้าพเจ้าจะติดต่อกับ ผศ. สุธาทิพย์ พิชญไพบูลย์ ภาควิชาเภสัชกรรม (คลินิก) คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย โทร. 0-1614-3557, 02-2188407, 02-2188403

ข้าพเจ้ายินดีให้ข้อมูลของข้าพเจ้าแก่คณะผู้วิจัย เพื่อเป็นประโยชน์ในการศึกษาวิจัยครั้งนี้ และยินดีเข้าร่วมการศึกษานี้โดยสมัครใจ โดยได้ลงนามในใบยินยอมนี้ไว้เป็นหลักฐานต่อหน้าพยาน

ลงนาม ..... (ผู้ป่วย/อาสาสมัคร)

(.....)

ลงนาม ..... (ผู้วิจัย)

(.....)

ลงนาม ..... (พยาน)

(.....)

APPENDIX C

PATIENT INFORMATION DATA SHEET

Patient Name……..…… H.N……..……

Gender ☐ M ☐ F Status ☐ Single ☐ Married ☐ Divorce

Date of Birth ……Wt. …… Height ……..

Payment ☐ Own ☐ Social security ☐ 30 Baht ☐ Government ☐ Other

Occupation ☐ Own business ☐ Government ☐ Semi-government ☐ Office

Drug allergy ……

Social Hx : Smoking

Drinking

Date of Diagnosis ……..… Duration of illness ……..……..

Co-morbid disease / Complications

☐ Diabetic retinopathy

☐ Diabetic neuropathy

☐ Diabetic nephropathy

☐ Chronic liver disease

☐ Ischemic heart disease

☐ Hypertension

☐ Cerebrovascular disease

☐ Peripheral vascular disease

☐ Dyslipidemia

☐ Others

Medications

Date	Regimen		Comment

Laboratory / Physical Examination Result

Date											
BW (kg)											
BP (mmHg)											
PPG (mg/dL)											
FBG (mg/dL)											
AIC											
SCr (mg/dL)											
TC (mg/dL)											
TG (mg/dL)											
HDL (mg/dL)											
LDL-C (mg/dL)											
AST											
ALT											
Other											

ADR

Drug	S & Sx	Result

แบบบันทึกผลการตรวจ SMBG

คำชี้แจง

- กรุณาบันทึกผลการตรวจน้ำตาลในเลือดด้วยตนเองที่บ้านตามมื้ออาหารลงในแบบฟอร์มนี้ โดยใส่ วัน เดือน ปี เวลาที่เจาะตรวจและค่าน้ำตาลในเลือดที่ตรวจได้ และอาหารที่รับประทาน
- ให้นับวันแรกที่เริ่มทำการตรวจเป็นวัน 1 จากนั้นทำการตรวจ **<u>วันเว้นวัน</u>**
- ถ้าลืมตรวจ [ไม่ว่าจะลืมทั้งมื้อ (ตรวจเลือด 4 ครั้ง) หรือลืมบางเวลาก็ตามระหว่างมื้อนั้น] ให้ทำการตรวจวัดใหม่ทั้งมื้อ (4 จุด) ในวันถัดไป
  ตัวอย่างเช่น วัน 3 ควรตรวจน้ำตาลมื้อกลางวัน แต่ลืมทำ ให้ทำใหม่ในวันรุ่งขึ้นในวัน 4 และทำการตรวจตามตารางที่เหลือ โดยทำวันเว้นวันเช่นเดิม **หรือ** วัน 3 ตรวจน้ำตาลก่อนอาหารกลางวันและหลังอาหาร 1 ชั่วโมงแล้ว แต่ลืมตรวจหลังอาหาร 2 ชั่วโมงและ 4 ชั่วโมง ให้ทำการตรวจน้ำตาลมื้อกลางวันใหม่ทั้ง 4 จุด ในวันรุ่งขึ้น
- การตรวจน้ำตาลในเลือด ให้เจาะตรวจทันทีก่อนรับประทานอาหารมื้อนั้น (“0” ช.ม.) และที่ 1 ช.ม. หลังอาหาร, 2 ช.ม. หลังอาหาร, 4 ช.ม. หลังอาหาร
- กรุณาทำซ้ำมื้อละ 2 ครั้ง
- ถ้าท่านมีปัญหาหรือข้อสงสัย กรุณาติดต่อผู้วิจัย (ผ.ศ. สุธาทิพย์) ที่เบอร์ 0-1614-3557 , 0-2218-8407, 0-2318-6604

แบบบันทึกผลการตรวจ SMBG

ชื่อผู้ป่วย เพศ ☐ ชาย ☐ หญิง

H.N.

อาหารเช้า										
วัน	วันเดือนปี	ทันทีก่อนรับประทาน		1 ชม. หลังรับประทาน		2 ชม. หลังรับประทาน		4 ชม. หลังรับประทาน		อาหารที่รับประทาน
		เวลาที่เจาะ	ผล	เวลาที่เจาะ	ผล	เวลาที่เจาะ	ผล	เวลาที่เจาะ	ผล	
1										
7										

อาหารกลางวัน										
วัน	วันเดือนปี	ทันทีก่อนรับประทาน		1 ชม. หลังรับประทาน		2 ชม. หลังรับประทาน		4 ชม. หลังรับประทาน		อาหารที่รับประทาน
		เวลาที่เจาะ	ผล	เวลาที่เจาะ	ผล	เวลาที่เจาะ	ผล	เวลาที่เจาะ	ผล	
3										
9										

อาหารเย็น										
วัน	วันเดือนปี	ทันทีก่อนรับประทาน		1 ชม. หลังรับประทาน		2 ชม. หลังรับประทาน		4 ชม. หลังรับประทาน		อาหารที่รับประทาน
		เวลาที่เจาะ	ผล	เวลาที่เจาะ	ผล	เวลาที่เจาะ	ผล	เวลาที่เจาะ	ผล	
5										
11										

VITA

Mrs.Sutathip Pichayapaiboon was born on January 20th 1961 in Bangkok. She graduated Bachelor of Science in Pharmacy from Saint John's University, New York in 1984. She graduated Master of Science: major Pharmaceutical Science, area of concentration Clinical Pharmacy, from Saint John's University, New York in 1986.

She worked as a pharmacist at Phya Thai 1 Hospital in Bangkok from December 1986-November 1987. Since then she has been working at Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Chulalongkorn University. Her current position is Assistant Professor. She had been enrolled in Doctor of Philosophy Program major in Pharmaceutical Care at Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Chulalongkorn University since June 2007.