

Time to First Optimal Glycemic Control and its Predictors Among Type 1 Diabetic Children <15 Years in Bahir Dar City Public Referral Hospitals, North West Ethiopia: A Retrospective Follow Up Study

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Abstract

Background: Recognizing the level of glycemic control of a client is an important predictor of the development of complication and risk of death from diabetes. However, the other most important predictor which is the time that the patient stayed in that poor glycemic level before reaching optimal glycemic control has not been studied so far.

Objective: The aim of this study was to estimate time to first optimal glycemic control and identify predictors among type 1 diabetic children <15 years in Bahir Dar city public referral hospitals, Northwest, Ethiopia, 2021

Methods: Retrospective cohort study was conducted at Bahir Dar city public referral hospitals among randomly selected sample of 385 patients with type 1 diabetes who were on follow up from January 1, 2016 to February 30, 2021. Data were collected by using data abstraction tool and then entered into Epi-data version 4.2 and exported into STATA 14.0 statistical software. Descriptive statistics, Kaplan Meier plots and median survival times, Log-rank test and Cox-proportional hazard regression were used for analysis. After performing Cox-proportional hazard regression, model goodness-of-fit and assumptions were checked. Finally, association between independent variables and time to first optimal glycemic control in months were assessed using multivariable Cox Proportional Hazard model and Variables with p-value < 0.05 were considered as statistically significant.

Result: Median survival time to first optimal glycemic control among type 1 diabetic client was 8 months (95%CI: 6.9-8.9). First optimal glycemic achievement rate was 8.2(95%CI: 7.2-9.2) per 100 person/month observation. Factors that affect time to first optimal glycemic control were age (AHR=0.32;95%CI=0.19-0.55), weight(AHR=0.96;95%CI=0.94-0.99), primary care giver(AHR=2.09;95%CI=1.39-3.13), insulin dose (AHR=1.05;95%CI=1.03-1.08), duration of diabetes (AHR=0.64;95%CI=0.44-0.94), adherence (AHR=9.72;95%CI=6.09-15.51), carbohydrate counting(AHR=2.43;95%CI=1.12-5.26), and comorbidity (AHR=0.72;95%CI=0.53-0.98).

Conclusion and Recommendation: The median survival time to first optimal glycemic control in this study was long. Age, weight, primary care giver, insulin dose, duration of diabetes, adherence, and carbohydrate counting including history of comorbidity were determinant factors. Therefore, clinicians should advice weight reduction, increase the dose of insulin during initial treatment, counsel their parents about adherence of insulin drug and auditing their children diet as prescription helps to reduce the length of glycemic control.

Introduction

Diabetes mellitus(DM) is a serious, chronic and progressive disease that occurs either when the pancreas does not produce enough insulin or the body can not properly use the insulin it produces(1). There are three classification of diabetes mellitus commonly accepted by different scholars(1, 2). These are: type one diabetes mellitus(T1DM) ,type two diabetes mellitus(T2DM) and gestational diabetes(3). According to American diabetic association(ADA) type one is the commonest type in pediatrics age categories(2).

Type 1 diabetes also known as insulin dependent, juvenile or child hood onset DM which is characterized by deficient insulin production in the body(1). It encompasses a group of metabolic disease causing in hyperglycemia(2). Juvenile diabetes is currently not preventable but we can control and prevent its complication. Otherwise, uncontrolled diabetes over time may lead to a serious damage to the heart, blood vessels, eyes, kidneys and nerves(1-5) .

A patient indicating any of the following can diagnosed as having diabetes based on ADA and international society of pediatrics and adolescent diabetes(ISPAD): fasting blood glucose(FBG) ≥ 126 mg/dL (11.1 mmol/L), poly symptoms of diabetes plus random blood sugar ≥ 200 mg/ (7 mmol/L) or 2 hour plasma glucose during glucose tolerance test. ≥ 200 mg/ (7 mmol/L) and glycosylated/glycated (Hb A1) ≥ 6.5 %.(2, 6).

Glycemic control is a level of glucose in diabetic clients(1);Glycemic control followed by the diagnosis was reflected by optimal and poor metabolic control as mean HbA1c <7.5% and >7.5% respectively and /or average FBG level between 80-150mg/dl and either < 80 or >150 mg/dl respectively(6-8, 80) and HbA1c can be calculated from the following formula, if HBA1c is not consistently available for some of the clients; estimated average glucose level in (mg/dl)= $28.7 \times \text{HbA1c} - 46.7$ (8).

Diabetes mellitus pandemic have become one of the largest global health emergencies among non-communicable disease in this century(3). In many countries, over 500 000 children < 15 years old are diagnosed with T1DM(4, 6-8)with an average incidence of 3-4% per year worldwide(6, 7). This increment is also noted more alarmingly in developing countries(9, 10-14).

Although there are a lot of advanced management of T1DM, more than 70% of them were unable to maintain their glycaemia (10, 11). More over noncompliance rate escalating 50% that highlights the need for focusing on timely optimal glycemic control (10). Many children had also suffered from T1DM which is associated with high morbidity, mortality rate and most of the time the poor has been highly affected by this disease (9, 15, 16). Both In developed and developing nations the prognosis of children with T1DM is poor (14). As a result, optimal glycemic control were oscillating from 2.6–39.1% (11, 15, 17). Many are not detected and those diagnosed have dramatically reduced their life expectancy by one year, (17–19). Poor glycemic control was much higher among type one patients (82.9%) as compared with type two diabetics (57.7%) (14, 20, 21).

A varieties of factors that predict glucose control in children with T1DM have documented (7, 18–22). High proportion of patients with uncontrolled glycemic level were due to sociodemographic factors, concomitant disease, personal and other clinical factors (16, 17, 23); health care system with limited resources, lack of trained health personnel and in ability of the patient or family to use and afford treatment expenditures (10, 24).

Uncontrolled glycemic situation results complication which can hurt many parts of the body including growth failure later in time (3, 22–24). As a result, both acute and chronic complications were reported in different studies (24). Adverse effects like lipodystrophy is one of the clinical complication which may occur related to insulin injection and leads to insulin absorption problems, which ultimately can hinder first optimal glycemic control (25, 26). The most common complication prior in three months were hypoglycemia (21–42%) followed by 31.5%–39% of diabetic keto acidosis (DKA), 10.5%–32.9% of nephropathy, 13.6% of neuropathy, 10.5% of convulsion, 10.3% of retinopathy (27–29). Sustained abnormal blood sugar fluctuation for periods of greater than two months can also contribute to high burden of the disease, hospitalization and negative consequences of disease outcomes (30, 32).

Similarly, study in Ethiopia highlights the difficulty of achieving glycemic control early in time. As a result, early occurrence of both retinopathy and maculopathy among diabetic children were reported (13). Another study In Ethiopia specifically in Gojjam, also indicates 58.5% DKA among 354 T1DM children with the incidence rate of 2.27/100 children/month of observation. (31).

However, strict glycemic control minimizes the incidence and progression of such possible complication (14–17). The Diabetes Control and Complication Trial (DCCT) and the follow-up study Epidemiology of Diabetes Interventions and Complications (EDIC) shows that, good glycemic control with in short duration delays the development of both acute and chronic complication in T1DM patients by 35–76% (9). Novel treatment are emerging to manage T1DM with the ultimate goal being to achieve glycemic control, limit weight gain, reduce comorbidities and improve quality of life (7). T1DM treatment is based on frequent monitoring of blood glucose and administration of insulin, in line with their meal and exercise (33–35). It was recommended that T1DM children should check their blood glucose at least four times a day (6). And which expected to bring 26.2% satisfactory glycemic control level (7, 35). People with diabetes can live longer and have a healthy life if their diabetes is become aware of early and well-managed by multidisciplinary approach with the allocation of accessible resources (10, 36, 37). Being updated about the recent diabetes care can also help in improving first glycemic control (15, 38).

In Ethiopia a little studies were conducted to recognize level of glycemic control among type one diabetic children (16). However, the other most important parameter, which is the time, in which, the patient stayed on that poor glycemic level before reaching optimal glycemic control has not studied so far. If efforts are not made to recognize the contributing factors for optimal glycemic control with possible time frame, the number of children affected will preserve growing and this in turn lead to an emotional and economical burden on both the clients and the families at large (6). And it will also disturb the sustainability of our health care system which is still over burdened with communicable diseases.

Therefore, this study was aimed to estimate time to first optimal glycemic control among type 1 diabetic children in Bahir Dar city public referral hospitals, Northwest, Ethiopia.

Methods And Materials

Study area and period

The study was conducted in Bahir Dar city; located 565Km far from Addis Ababa, the capital city of Ethiopia, at Amhara national regional state, North West Ethiopia. In Bahir Dar city there are two public referral hospitals, one primary hospitals, ten health center and four private hospitals. And this study was conducted in the two public referral hospitals, namely: Felege Hiwot comprehensive specialized referral hospital (FHCSH) and Tibebe Ghion specialized teaching hospital (TGSTH). Each of this hospital can be expected to

serve for more than 10 million populations coming from Bahir Dar city, west Gojjam zone, east Gojjam zone, awi zone, north and south wollo zones, south & north Gondar zones, partial part of Benshangul Gumuz and Oromia region. FHCSH has currently a total of 1431 man power in each discipline with 500 formal beds, 11 wards, 39 clinical and non-clinical departments /service unit / providing Diagnostic, curative, Rehabilitation and preventive service at outpatient & inpatient based. Similarly TGSTH is a teaching hospital under Bahir Dar University College of medicine and health sciences that has 459 bed capacity and with around 14 outpatient departments.

Apart from other services both referral hospitals provide diabetic treatment services by nurse practitioners, pediatrics residents and pediatricians.

The study period address from 1st January, 2016 to February 30 /2021.

Study design

An institution based retrospective follow up study was employed.

Source population

The source population were all type 1 diabetes mellitus children <15 years old who had follow up at diabetes clinic of the two referral hospitals.

Study population

The study population were all type 1 diabetes mellitus children <15 years old who were on follow up during the study period.

Study unit

All type one diabetic children's chart that were selected randomly for investigation.

Inclusion criteria

Children age less than 15 years old and diagnosed with T1DM with regular follow up and had at least one HbA1c and/or a three month consecutive measurements of fasting blood sugar (FBS) with clear date of diagnosis between January 1/2016 to February 30/2021 were included.

Exclusion criteria

Children's medical record/chart with incomplete information (such as HbA1c/average FBG and other relevant predictors like age with date of diagnosis, sex, treatment modality, frequency of follow up visit and last visit health condition of the children), those having less than 3 month follow up during the study period and those cases transferred in with unclear date of diagnosis from other institution were excluded from the study.

Sample size determination

Sample size was determined by double proportion formula after taking of predictors associated to optimal glycemic control from previous study conducted by retrospective cohort design (50) with the help of epi info version 7 by considering the following statistical assumptions: 95% Confidence Interval (CI), power 80%, percent of outcome in unexposed group 8.93%, risk ratio 0.253, marginal error 5% (50). The calculated total sample size is 378, then by adding 10% for data incompleteness from the client chart, the final sample size became 416.

Sampling technique and procedure

The study participants were selected from the registration book. The medical records of children who were on follow up with type one diabetes mellitus from January 2016 to February 2021 were selected. A total of 721 children were recorded from the registration book of the two referral hospitals (sampling frame). Of which 416 cards were sampled using a simple random sampling technique by a computer generating method. Finally, cards that fulfilled the criteria were reviewed.

Dependent variables

Time to first optimal glycemic control

Independent variables

Socio demographic (age, gender, Residence); Institutional related variable (frequency of clinic visit); Diabetic related variables (duration of diabetes, diabetes related complication.); Comorbidities (preceding infections and other pathology) and treatment related variables (insulin therapy and adherence, noncompliance and other self-monitoring practice)

Age of the participants, frequency of glycemic control, body mass index and duration of diabetes were categorized in to groups in order to align with the other literatures(36,40,50)

Operational definitions

Optimal glycemic control: Optimal glycemic control is defined as the three consecutive month HbA1c <7.5% and/or average FBG of 80–150 mg/dl with more or less stringent glycemic goals for individual clients based on age/life expectancy, comorbid condition, advanced complication, hypoglycemia unawareness and individual patient considerations (6- 8,80).

Event: Achieving first optimal glycemic control during the study period

Survival time: The time starting from date of diagnosis to first optimal glycemic control was determined for each participant

Censoring: Patients died, lost to follow up, transfereed out, and complete the follow up period without achieving optimal glycemic control

Time to event: Time between diagnosis up to achieving first optimal glycemic control or censoring with measure of interest in month

Carbohydrate counting: Practicing healthy diet at home by non-refined carbohydrate utilization and eating consistent amount of food regularly with application of food pyramid as a meal planning tool to optimize blood sugar level (35).

Data collection procedure

The data were collected from patients chart that visit Felege Hiwot comprehensive specialized referral hospital and Tibebe Ghion specialized teaching hospital. Data that were relevant to measure the association between times to first optimal glycemic control among diabetic children were collected by two BSc nurses supervised by one senior nurse having second degree in public health.

Patient records were retrieved using their medical registration number identified in the total DM case load in the logbook of registration follow up form. Then medical registration number (MRN) of all diabetic pediatric patient were sorted. After that, the sample selection mechanism was simple random sampling technique, in which each of the patients had equal chance of being selected to be part of study.

A structured data extraction tool adapted by considering study variables such as socio demographic, personal and clinical predictors from patients' charts.

Data quality assurance

Training was given for data collectors and supervisors about the objective and process of data collection by the principal investigator. Pretest was done on 5 % of sample size. Then pretested data abstraction tool/check list that comprises of questions to measure the relevant variables were used to collect the necessary data from the patient medical chart by those trained data collectors. Data quality

was also assured by designing proper data abstraction tool and through continuous supervision. All collected data were checked for completeness and clarity.

Data processing and statistical analysis

The collected data was coded, enter, cleaned and stored into Epi-data version 3.1 and exported into STATA 14.0 statistical software for analysis. Descriptive statistics were presented with frequency tables, Kaplan Meier (KM) plots and median survival times. Months are used as a time scale to calculate time to first optimal glyceemic control. The outcome of each participant was dichotomized in to censored or event (first optimal glyceemic control)

Kaplan-Meier technique was used to measure survival experience of diverse groups of patients by using survival curves. Log-rank test was used to assess significant difference among survival distributions of groups for equality. After performing the Cox-proportional hazard regression, model goodness-of-fit was checked by Cox Snell residuals & assumptions was checked by using Shenfield residual test and graphically by using log minus log function survival curves.

Bivariable analysis was performed to calculate crud hazard ratio (CHR) and to screen out potentially significant independent variables at p value < 0.25 level of significance.

Association between the significant independent variables and the time to first optimal glyceemic control was assessed using multivariable Cox Proportional Hazard (PH) model.

Adjusted hazard ratio (AHR) and 95% CI for HR were used to test significance and interpretation of results.

Variables with p-value < 0.05 were considered as statistically associated with the time to first optimal glyceemic control in months.

Ethical considerations

Ethical clearance was obtained from the institutional review board (IRB) of Bahir Dar University (IRB number 01-008). Written supportive letter was taken from pediatrics department of the hospitals on behalf of the patients. This study had no any danger or negative consequences for the study participants. Medical record numbers were used for the data collection and personal identifiers of the client were not used in this research report. Access to collected information was limited to the principal investigator and confidentiality had preserved throughout the time.

Results

Socio demographic characteristics *with censoring and event status*

Four hundred sixteen (416) medical records were reviewed; off which, thirty one (7.5%) cases were excluded from the study due to pertinent data being missing. As a result, 385 clients were included in the study which is 92.5% in response rate.

Mean age of the study participant was 8.2 ± 4.7 years with 2.4 years mean duration of diabetes.

More than half of the patients were male (53%) and proportion of first optimal glyceemic achievement among male is (72%) which is almost proximal to female (71.3%).

Majority of the patients (64.7%) were from rural area. However, the Proportion of patients who achieved first optimal glyceemic control among rural is (68.7%) which is lower than clients from urban area residents (77.2%).

Those clients having >4 clinical visit for the last year of their follow up had higher proportional glyceemic control (82.3%) than clients having clinical visit ≤ 4 (66.3%). (Table 2).

Median survival time to first optimal glyceemic control

The estimated median survival time to achieve first glyceemic control was 8 months with inter quartile range of (6.9-8.9).

The median survival time to first optimal glycemic control among type one diabetic children were varied by various categories of predictors. For example, the median survival time to achieve first optimal glycemic control among under 5 children was 6.8 where as in above 5-10 and >10-14 years was 8, 8.5 respectively. (Table 5).

Incidence rate of optimal glycemic achievement rate

From 385 study participants, 276(71.7%) of the clients have achieved glycemic control with mean value of FBG&HA1c (112±3mg/dl, 5.6%) respectively; whereas 109(28.3%) were censored. The lowest and the highest length of follow up were 2.9 and 36.4 months respectively, and the total person-time risk was 3373 months.

The overall first optimal glycemic control rate was 8.2(95%CI: 7.2-9.7) per 100 person/month observation. Optimal glycemic achievement rate among male and female children with type 1 diabetes was 7.9(95%CI: 6.7-9.3) per 100 person/month and 8.4(95%CI: 7.1-10.0) per 100 person/month observation respectively which is nearly comparable in both sex.

Diabetes related variables *with censoring and event status*

Concerning complication, 83.4% of the patients had history of one or more diabetes related complication .Majority of the clients had diabetic keto acidosis (DKA) (81%) including the episodes at the time of diagnosis followed by hypoglycemia (19.7%), other complication (4.9%) and chronic complication (0.8%). The proportion of patients who achieved optimal glycemic control is relatively higher among those with no history of diabetes related complication (76.6%) as compared to those with history of complication (70.7%).Mixed insulin (lent & regular) drugs had given for the majority of the patients (62.9%) during the initiation of treatment as compared to other regimens like NPH with regular and NPH alone (20%, 17.1%) respectively. (Table 3).

Comorbidity related variables *with censoring and event status*

In regard to comorbidity, 69.6% of the patients had history of comorbid illness and only 30.4% of them didn't have recognized history of comorbid illness. Majority of the clients had malnutrition (38.7%) followed by pneumonia (16.1%), urinary tract infection (13.8%), acute gastro enteritis (10.1%), fungal infection (7%) and upper respiratory tract infection (6.5%).Nearly half (48%) of the patients had more than one comorbid illness. The proportion of clients who achieved first optimal glycemic control is higher among those with no history of comorbid illness (74.4%) than those with one or more comorbid illness (70.5%). (Table 4).

Survival estimates for time to first optimal glycemic control

The survival status of children with type 1 diabetes was estimated by the Kaplan-Meier survival curve.

The curve tends to decrease rapidly with in the first one year indicating that most children achieved first optimal glycemic control within this time (Figure 2).

The survival estimates of clients were varied in relation to different predictors. (Figure 3).

Comparison of survival experience

The long rank test was used to assess differences in equality of survival distribution among diverse groups. The median survival time to achieve first optimal glycemic control among clients in the age groups of <=5 years showed shorter median time to achieve first optimal glycemic control (6.8 months) as compared with patients whose age group between 6-10 years (8months) and 11-14 years (8.5 months).and the survival time was significantly different among the age groups($X^2(2) = 6.05$, P-value = 0.0486).whereas, the median survival time to achieve first optimal glycemic control among male participant showed relatively longer time (8.5 months) than females (7.2 months).But the long rank test was not statistically significant($X^2(1)=0.92$,p-value=0.3378). (Table 5).

Regarding adherence, those clients who adhere to the management had shorter duration of time (5.7 months) to achieve first optimal glycemic control than those who didn't adhere towards the management of the disease(14.9 months).The long rank test was

statistically significant($\chi^2(1) = 131.75$, P-value <0.0001). The Kaplan Meier survival function showed that, clients with adherence have satisfactory survival experience by achieving their glycemic targets early in time. The figure also showed that, clients direct chance of achieving first optimal glycemic control increases for both group as the duration of treatment increases. (Figure 4).

Those patients having comorbid illness appears to extend time to first optimal glycemic control. The median survival time to achieve optimal glycemic control was shorter among patients with no history comorbid illness (6.3 months) than patients who had comorbid illness (8.9 months) with statistical significant difference among the group ($\chi^2(1) = 10.85$, P-value = 0.0010). (Table 5).

However, no statistically significance difference were shown for sex, residence, family history of diabetes militias ,number of clinic visit ,DKA as presentation and being malnourished in determining time to first optimal glycemic control. (Table 5 & Table 6).

Results of multivariable cox proportional hazard model

Goodness of fit checked by cox Snell residuals by plotting cox Snell residual against the cumulative hazard function. As a residuals follow unit of exponential distribution or a linear line through the origin with a unit gradient, which indicates a well fitted model to the observed data point and expected value. (Figure 5).

Proportional assumption of cox proportional hazard model was tested by using Schoen field residual test and graphically by using log minus log function on Stata version 14.2 (Table 6& Fig 6).The survival curve looks like parallel throughout the study time; which shows equitable fitting to the proportional hazard assumption.(Figure 6).

The independent variables such as age client educational status, primary care giver, dose of insulin at initiating of treatment, duration of diabetes, first insulin regimen, current insulin regimen, frequency of glycemic control, carbohydrate count, exercise, noncompliance, adherence, diabetes related acute complication, having history of comorbidity were significantly associated with time to first optimal glycemic control at the point less than 0.25 level of significance from bivariable analysis. However, only age, duration of DM, dose of insulin at initiating of treatment, weight, primary care giver, adherence to DM care, carbohydrate counting and history of comorbidity were found to be significantly associated with time to first optimal glycemic control in the multivariable cox regression hazard model less than 5% level of significance.

The presence of interaction among independent variables were checked by multicollinearity test but there was no significant interaction as it was confirmed by the value of variance inflation factor (VIF) which is less than ten..

Consequently, after adjusting other predictor, the hazard of achieving optimal glycemic control among the age groups >10-14 years were lower by 67.6% as compared with the age groups of the client<=5 years(AHR=0.324,95%CI=0.192-0.546).

Likewise, the hazard of achieving optimal glycemic control among clients with history of comorbid illness was lower by 24.3% compared to clients with no history of comorbid illness (AHR= 0.722, 95%CI=0.530-0.981).this means, the time needed to reach optimal glycemic control among clients with history of comorbid illness was significantly longer compared with clients with no history of comorbid illness.

However, the rate of achieving first optimal glycemic control among clients who adhered to diabetic care had 9.7 times increment than clients who didn't adhered to diabetic management (AHR=9.723, 95%CI=6.094-15.513). (Table 6).

Discussion

The aim of this study was to identify predictors of time to optimal glycemic control in Ethiopia. The estimated median survival time to achieve first glycemic control was 8 months with inter quartile range of (6.9-8.9).The finding in this study is in line with another study conducted among type 1 diabetic children in united states (38) but a little bit shorter than previous study conducted in Ethiopia(9.5months) (3).This could be due to differences in age pattern, type of diabetes and comorbidity among study participants(28, 31, 47, 49, 50, 55, 57–60).

The overall first optimal glycemic control rate was 8.2(95%CI: 7.2-9.7) per 100 person/month observation.The finding related to overall incidence rate to achieve glycemic target in this study is less than other studies conducted in Kenya (28%),Jordan (20.9%), Saudi Arabia (39.1%), and California(33%)(39, 40, 50, 51) but greater than a study done in Tanzania(2.6%)(26).This discrepancy can be due to differences in population characteristics, sample size, study methodology and overall health care system including resource allocation(10, 16, 17, 23, 24, 52).

In regard to predictors, the age of the participant was found to be significantly associated variables that determine time to first optimal glycemic control. The study showed that, the time needed to reach first optimal glycemic control is longer among clients of age group >10-14 years followed by the age group 6-10 years compared to clients in the age group ≤5 years (AHR=0.324, 95%CI=0.192-0.546), indicating that for children older than 10 years, the rate of achieving optimal glycemic control decreases as age increases which is in line with study done in Tanzania, Bulgaria, Iraq, Taiwan and Jordan (26, 46, 47, 49, 50). This can be due to the fact that As a child develops, he/she undergoes a variety of physical and life style changes (24). In addition to this, it can be also due to hormonal effect at pubertal age of the child and decline in parental supervision over different clinical aspects of diabetic care in the adolescents (46, 50).

Weight of the client also significantly associated with time to first optimal glycemic control. Rate of glycemic achievement decreases by 3.6% as weight increase by one unit which means the weight of the client is 0.964 times less likely associated with optimal glycemic achievement rate. This could be due to, weight gain may contribute to increased insulin resistance and cardio metabolic risk such as increased dyslipidemia and blood pressure (62). It is in line with another controlled study among T1DM patients which stated previously as "normal weight preschool children have better glycemic control than age matched overweight children (63, 64)." It can significantly imply that, body weight status may impede achievement of glycemic targets within the expected time in this group of patients. Therefore, having regular exercise which is non-strenuous can be encouraged. The recommendation is supported by the study conducted in United Kingdom and the authors of International society of pediatrics and adolescents diabetes (ISPAD) guide line revised since 2018 GC (6, 34).

Dose of insulin at initiation of treatment increases first optimal glycemic achievement rate by 1.053 times as dose of insulin increases by one unit. This finding is supported by the study done in many countries such as India, China, Germany, Austria, and Luxembourg (66-70).

This study also showed that, primary care giver during the follow up period was significantly associated with optimal glycemic control. Especially those clients whose care giver mother and father was two times more likely associated with first optimal glycemic control as compared with clients supported by their mothers alone. The finding was supported by the study conducted in Tanzania and middle east Jordan (32, 50).

In regard to adherence to diabetic care, those clients with adherence had 9.7 fold of instantaneous chance of increasing their glycemic achievement rate as compared with those clients with no adherence to wards their diabetic management. Which is in line with the study conducted in Ethiopia entitled with incidence of diabetic keto acidosis and its predictors among type one diabetic children (31). Correspondingly, those clients well adhered to Diet counseling specifically on food pyramid and non-refined carbohydrate utilization were found to have increasing their glycemic achievement rate by 2.4 folds as compared with those clients with no habit of practicing healthy diet at home and the finding is in line with the study conducted in Uganda (35, 54, 64).

Duration of diabetes was also significantly associated with time to first optimal glycemic control in this study. Those clients living with diabetes for more than or equal to four years were 35.8% times less likely to achieve optimal glycemic control as compared with clients who were living with diabetes less than two years. This could be due to age maturation with advancement of the disease following to diabetic duration as it was explained above (24, 46, 50). This finding is similar with the study done in Tanzania (31) but different with study done in Cameroon (75).

In addition to the above factors, having comorbid illness is another important predictors that can affect time to optimal glycemic control. The rate of achieving optimal glycemic control among clients with history of comorbid illness were 27.8% times less likely as compared with clients with no comorbid illness. This is because having comorbid illness has an influence on diabetes disease progress with impairment of glucose metabolism possibly lead to deterioration of glycemic control. Comorbid illness such as infection might also cause high level of counteracting hormones which triggering an episode of hyperglycemia and could also be due to the effect of taking many drugs which can lead to drug interaction and also can decrease drug adherence which interferes with drug effectiveness. This finding is in line with the studies conducted in Saudi Arabia, Brazil and university of California, San Francisco (18, 57-60).

Strength and Limitation of the Study

Strength of the study

Since the data were collected from two referral hospitals, the finding can have more power in regard to generalizability.

Limitation of the study

Since the data were collected from medical records, variables like parental socio economic factors cannot be addressed through card review which may affect the outcome of the study.

Fasting blood glucose level (FBG) measurements obtained from medical records might be subjected to measurement errors that lead to underestimated or overestimated of the result. However, effort was made to overcome this issues by taking the mean value of three month consecutive value of FBG measurements.

Conclusion And Recommendation

The median survival time to first optimal glycemic control in this study was long compared to other studies. Age, weight, primary care giver, insulin dose, duration of diabetes, adherence, and carbohydrate counting including history of comorbidity were determinant factors. Therefore, clinicians should advice weight reduction, increase the dose of insulin during initial treatment, counsel their parents about adherence of insulin drug and auditing their children diet as prescription helps to reduce the length of glycemic control.

Abbreviations

ADA: American Diabetic Association; BGM: Blood Glucose Monitoring; CGM: Continuous Glucose Monitoring; DCCT: Diabetes Control and Complication Trial; DM: Diabetes Mellitus; EDIC: Epidemiology of Diabetes Interventions and Complications; FBS: Fasting Blood Glucose; HbA1c: Glycated Hemoglobin A1C; IDF: International Diabetic Federation; ISPAD: International Society of Pediatrics and Adolescent Diabetes; NCDs: Non Communicable Diseases; SMBG: Self-Monitoring of Blood Glucose; SSA: Sub Saharan Africa; T1DM: Type 1 Diabetes Mellitus; URTI: Upper Respiratory Tract Infection; WHO: World Health Organization; EMOH: Ethiopian Ministry Of Health

Declarations

Ethical approval and consent to participate

Ethical clearance and approval were obtained from the institutional review board (IRB) of Bahir Dar University (IRB number 01-008).Written supportive letter was taken from pediatrics department of the hospitals on behalf of the patients. This study had no any danger or negative consequences for the study participants. Medical record numbers were used for the data collection and personal identifiers of the client were not used in this research report. Access to collected information was limited to the principal investigator and confidentiality had preserved throughout the time.

Consent for publication

Not applicable

Availability of data and materials

Data will be available upon consortium approval.

Competing interests

All authors declared that they have no competing interests.

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Authors' contribution

Fentahun Meseret had a substantial contribution from conception to the acquisition of the data. All the authors had a great contribution to the study design, analysis, and interpretation of the findings. Fentahun Meseret drafted the manuscript. All authors revised the drafted manuscript carefully for important intellectual contents. All authors read and approved the final manuscript.

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Tables

Table 1: sociodemographic and institution related variable with censoring and event status among type 1 diabetic clients, Bahir Dar, Ethiopia, 2021 (n=385)

Variables	Category	Event and censored status		Total
		No. of event	No.of censored	
Age group in years	<=5	83(68%)	39(32%)	122(31.7%)
	>5-10	79(85.9%)	13(14.1%)	92(23.9%)
	>10-14	114(66.7%)	57(33.3%)	171(44.4%)
Sex	Male	147(72%)	57(27.9%)	204(53%)
	Female	129(71.3%)	52(28.7%)	181(47%)
Resident	Urban	105((77.2%)	31(22.8%)	136(35.3%)
	Rural	171(68.7%)	78(31.3%)	249(64.7%)
Number of clinic visit during the last year of follow up	<=4	169(66.3%)	86(33.7%)	255(66.2%)
	>4	107(82.3%)	23(17.7%)	130(33.8%)

Table 2: Diabetes related variable with censoring and event status among type 1 diabetic clients, Bahir Dar, Ethiopia, 2021(n=385)

Variables	Category	Event and censored status		total
		No. of event	No.of censored	
History of diabetes related complication	NO	49(76.6%)	15(23.4%)	64(16.6%)
	Yes	227(70.7%)	94(29.3%)	321(83.4%)
DKA	NO	53(72.6%)	20(27.4%)	73(19%)
	Yes	223(71.5%)	89(28.5%)	312(81%)
Hypoglycemia	NO	211(68.3%)	98(31.7%)	309(80.3%)
	Yes	65(85.5%)	11(14.5%)	76(19.7%)
Chronic complication	NO	274(71.7%)	108(28.3%)	382(99.2%)
	Yes	2(66.7%)	1(33.3%)	3(0.8%)
Other complication*	NO	259(71.9%)	101(28%)	360(93.5%)
	Yes	12(63.2%)	7(36.8%)	19(4.9%)
More than one complication	NO	245(72%)	95(27.9%)	340(88.3%)
	Yes	31(68.9%)	14(31.1%)	45(11.7%)
Diabetes related hospitalization	NO	52(74.3%)	18(25.7%)	70(18.2%)
	Yes	224(71.1%)	91(28.9%)	315(81.8%)
Insulin Regimen	Mix(regular &lent)	154(63.6%)	88(36.4%)	242(62.9%)
	NPH ®ular	70(90.9%)	7(9%)	77(20%)
	NPH only	52(78.8%)	14(21.2%)	66(17.1%)
Non Compliance (dose omission, drug skipping, inappropriate insulin storage)	NO	219(85.5%)	37(14.5%)	256(66.5%)
	Yes	56(43.8%)	72(56.3%)	128(33.2%)
Duration of diabetes	<2	75(0.5%)	75(0.5%)	150(39%)
	[2-4)	80(80.8%)	19(19.2%)	99(25.7%)
	>=4	121(89%)	15(11%)	136(35.3%)
Adherence to diabetic care	NO	91(46.7%)	104(53.3%)	195(50.6%)
	Yes	185(97.4%)	5(2.6%)	190(49.4%)
Family history of diabetes mellitus	NO	238(71.7%)	94(28.3%)	332(86.2%)
	Yes	38(71.7%)	15(28.3%)	53(13.8%)

*other complication includes insulin injection site swelling together with lipohypertrophy and dystrophy

Table 3: comorbid illness related variable with censoring and event status among type 1 diabetic clients, Bahir Dar city public referral hospitals, Northwest, Ethiopia, 2021 (n=385)

Variables	Category	Event and censured status		total
		No. of event	No.of censured	
History of comorbid illness	NO	87(74.4%)	30(25.6%)	117(30.4%)
	Yes	189(70.5%)	79(29.5%)	268(69.6%)
Cardio vascular disease(CVD)	NO	273(72%)	106(28%)	379(98.4%)
	Yes	3(50%)	3(50%)	6(1.6%)
Hypertension(HTN)	NO	272(71.8%)	107(28.2%)	379(98.4%)
	Yes	4(66.7%)	2(33.3%)	6(1.6%)
Urinary tract infection(UTI)	NO	244(73.5%)	88(26.5%)	332(86.2%)
	Yes	32(60.4%)	21(39.6%)	53(13.8%)
Pneumonia(CAP)	NO	234(72.4%)	89(27.6%)	323(83.9%)
	Yes	42(67.7%)	20(32.3%)	62(16.1%)
Upper respiratory tract infection(URTI)	NO	264(72.5%)	100(27.5%)	364(94.5%)
	Yes	15(60%)	10(40%)	25(6.5%)
Acute gastro enteritis(AGE)	NO	248(71.7%)	98(28.3%)	346(89.9%)
	Yes	28(71.8%)	11(28.2%)	39(10.1%)
Malnutrition	NO	191(71.5%)	76(28.5%)	267(69.4%)
	Yes	107(71.8%)	42(28.2%)	149(38.7%)
Autoimmune disease	NO	270(72.2%)	104(27.8%)	374(97.1%)
	Yes	6(54.5%)	5(45.5%)	11(2.9%)
Tuberculosis(TB)	NO	273(72%)	106((28%)	379(98.4%)
	Yes	3(50%)	3(50%)	6(1.6%)
Meningitis	NO	274(73%)	101(26.9%)	375(97.4%)
	Yes	2(20%)	8(80%)	10(2.6%)
Malaria	NO	268(72%)	104(28%)	372(96.6%)
	Yes	8(61.5%)	5(38.5%)	13(3.4%)
Fungal infection	NO	262(73.2%)	96(26.8%)	358(93%)
	Yes	14(51.9%)	13(48.1%)	27(7%)
More than one comorbid illness	NO	146(73%)	54(27%)	200(51.9%)
	Yes	130(70.3%)	55(29.7%)	185(48%)

Table 4: comparisons of optimal glycemic control among type 1 DM clients, Bahir Dar city public referral hospitals, Northwest, Ethiopia, 2021(n=385)

X²:chi-square, DF: Degree of freedom, KG: kindergarten

Table 5:Test of proportional-hazards assumption by Schoen field residual test (Global test) among type 1 DM clients, Bahir Dar city

Variables	Category	Test of equality over groups				
		Median survival time(months)	Mean survival time(months)	Log rank		
				χ^2	DF	P-value
Age group in years	<=5	6.8	8.5	6.05	2	0.0486
	>5-10	8	9.8			
	>10-14	8.5	10.2			
Sex	Male	8.5	9.9	0.92	1	0.3378
	Female	7.2	9.2			
Resident	Urban	7.6	9.6	0.02	1	0.8911
	Rural	8	9.6			
Education status of children	KG/not started	7.1	8.9	11.23	2	0.0036
	Primary school	9	10.6			
	High school	14.8	13			
Family history of diabetes	NO	7.8	8.7	0.28	1	0.5987
	Yes	8	9.4			
Number of clinic visit	<=4	7.7	8.5	1.31	1	0.2521
	>4	8	9.4			
Adherence to diabetic care	NO	14.9	10.9	131.75	1	<0.0001
	Yes	5.7	6.7			
Insulin regimen	Mixed(lent &Regular)	7.1	8.4	15.87	2	0.0004
	NPH& Regular	9.2	10.1			
	NPH only	9.8	12.3			
Duration of Diabetes in year	< 2	5.5	6.2	54.93	2	<0.0001
	[2-4)	8.6	10			
	>=4	11.1	11.4			
Carbohydrate count	NO	10.2	11.1	40.26	1	<0.0001
	Yes	5.5	6.9			
Noncompliance	NO	6.4	8.2	42.30	1	<0.0001
	Yes	14.8	14.9			
Diabetes related acute complication	NO	7.7	9.5	2.94	1	0.0862
	Yes	8	9.6			
Diabetic ketoacidosis	NO	6.2	9.5	0.12	1	0.7289
	Yes	8	9.6			
Chronic complication	NO	7.8	8.7	0.59	1	0.4434
	Yes	12.1	18.5			
Other complication	NO	7.8	9.5	1.02	1	0.3131

	Yes	10.2	11.3			
More than one complication	NO	7.8	9.3	0.21	1	0.6448
	Yes	8.9	10			
History of comorbidity	NO	6.3	8.3	10.85	1	0.0010
	Yes	8.9	10.1			
Wasting	NO	8.2	8.9	1.07	1	0.3003
	Yes	6.8	8.6			
Stunting	NO	7.8	8.8	0.15	1	0.7019
	Yes	9.8	8.4			
Cardio vascular disease	NO	7.8	8.8	0.01	1	0.9229
	Yes	12.1	10.2			
Pneumonia	NO	7.7	8.9	0.89		0.3460
	Yes	9	8.1			
Acute gastro enteritis	NO	7.7	9.4	2.05	1	0.1524
	Yes	10.2	11.5			
More than one comorbid illness	NO	7.7	9.5	0.21	1	0.6448
	Yes	8.7	9.7			

public referral hospitals, Northwest, Ethiopia, 2021(n=385)

Variables	Rho	χ^2	DF	P-value	
Age	0.03898	0.39	1	0.5310	
Educational status of children	0.06785	1.01	1	0.3138	
Primary care giver	0.13921	3.91	1	0.050	
Weight the client		0.06590	0.97	1	0.3253
Duration of diabetes	0.01613	0.08	1	0.7784	
Insulin regimen	0.12133	2.82	1	0.0934	
Dose of insulin	0.07640	1.21	1	0.2715	
Frequency of glycemic control	-0.00730	0.01	1	0.9230	
Carbohydrate counting	0.13800	3.28	1	0.0700	
Exercise	0.02123	0.09	1	0.7580	
Noncompliance	0.08636	1.37	1	0.2410	
Adherence	-0.03696	0.25	1	0.6154	
Diabetes related complication	0.01547	0.06	1	0.8037	
Comorbidity	-0.08886	1.89	1	0.1689	
global test	42.48		19	0.5368	

Rho: spearman rank correlation coefficients, X2: chi Square, DF: Degree of freedom

Table 6: Results for the final cox regression hazard model among type 1DM clients Bahir Dar city public referral hospitals, Northwest, Ethiopia, 2021 (n=385)

Variable	CHR(95%CI)	AHR(95% CI)	P-value
Insulin dose at initiation of Rx	0.982(0.969-0.993)*	1.053(1.029-1.078)	< 0.001**
Weight of the client	0.978(0.965-0.992)*	0.964(0.939-0.989)	0.005**
Age group in years at diagnosis			
<=5®			
>5-10	0.802(0.587-1.097)	0.926(0.619-1.384)	0.707
>10-14	0.599(0.448-0.801)*	0.324(0.192-0.546)	<0.001**
Sex of the participant			
Male®			
Female	1.116(0.879-1.416)		
Resident			
Urban®			
Rural	1.010(0.790-1.292)		
Primary care giver			
Mother alone®			
Mother and Father	0.848 (0.617-1.165)	2.092(1.397-3.132)	<0.001**
Father alone	0.824 (0.493-1.378)	1.171(0.631-2.171)	0.617
Other	0.685 (0.475-0.988)*	0.801(0.491-1.305)	0.372
Educational status of children			
K/not started®			
Primary school	0.746 (0.527-1.057)	0.868(0.574-1.314)	0.505
High school	0.684 (0.471-0.992)*	1.333(0.745-2.386)	0.333

Table 7: Results for the final cox regression hazard model among type 1DM clients Bahir Dar city public referral hospitals, Northwest, Ethiopia, 2021 (n=385) cont...

Insulin regimen			
Lent& regular®			
NPH& regular	0.840(0.631-1.118)*	0.757(.538-1.066)	0.111
NPH alone	0.704(0.511-0.970)*	1.305(0.856-1.990)	0.216
Carbohydrate counting			
NO®			
Yes	4.173(2.332-7.468)*	2.433(1.124-5.263)	0.024**
Frequency of glycemic control per day			
<3®			
>=3	1.904(1.409-2.574)*	1.259(0.887-1.788)	0.198
Physical exercise			
NO®			
Yes	2.574 (1.991-3.326)*	1.178(0.841-1.649)	0.341
Noncompliance behavior assessed by clinician at health care visit			
NO®			
Yes	0.334 (0.248-0.451)*	1.222(.805-1.853)	0.346
Adherence to diabetic care			
NO®			
Yes	6.522(4.901-8.679)*	9.723(6.094-15.513)	<0.001**
Duration of DM in years			
<2®			
[2-4)	0.559(0.401-0.781)	0.736(0.509-1.063)	0.102
>=4	0.486(0.356-0.664)*	0.642(0.436-0.944)	0.024**
Diabetes related acute complication			
NO®			
Yes	1.591(1.031-2.457)*	1.084(.653-1.799)	0.755
Other complication			
NO®			
Yes	0.746(0.456-1.221)		
History of comorbidity			
NO®			
Yes	0.627 (0.484-0.811)*	0.722(0.530-0.981)	0.038**

CHR=Crud hazard ratio, AHR=Adjusted hazard ratio, Rx=Treatment, ®=Reference group and * & ** indicates statistically significant variable with bivariable & multivariable cox regression hazard model respectively.

Figures

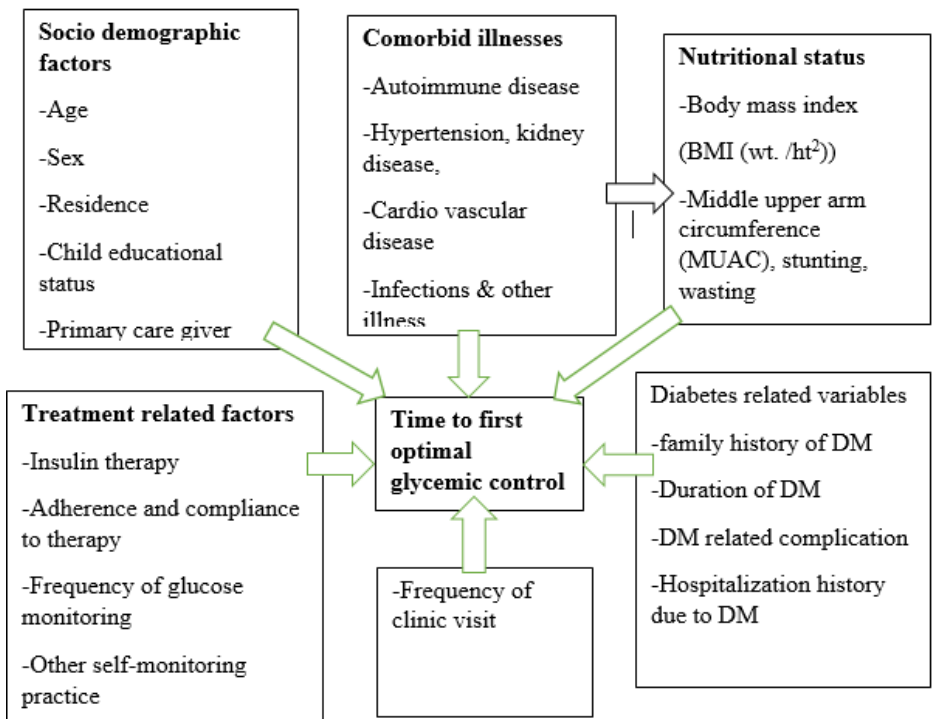


Figure 1

Time to glycemic control concept map among type 1 diabetic children in Bahir Dar city public referral hospitals, Northwest, Ethiopia, 2021; adapted from (36,40,50,79)

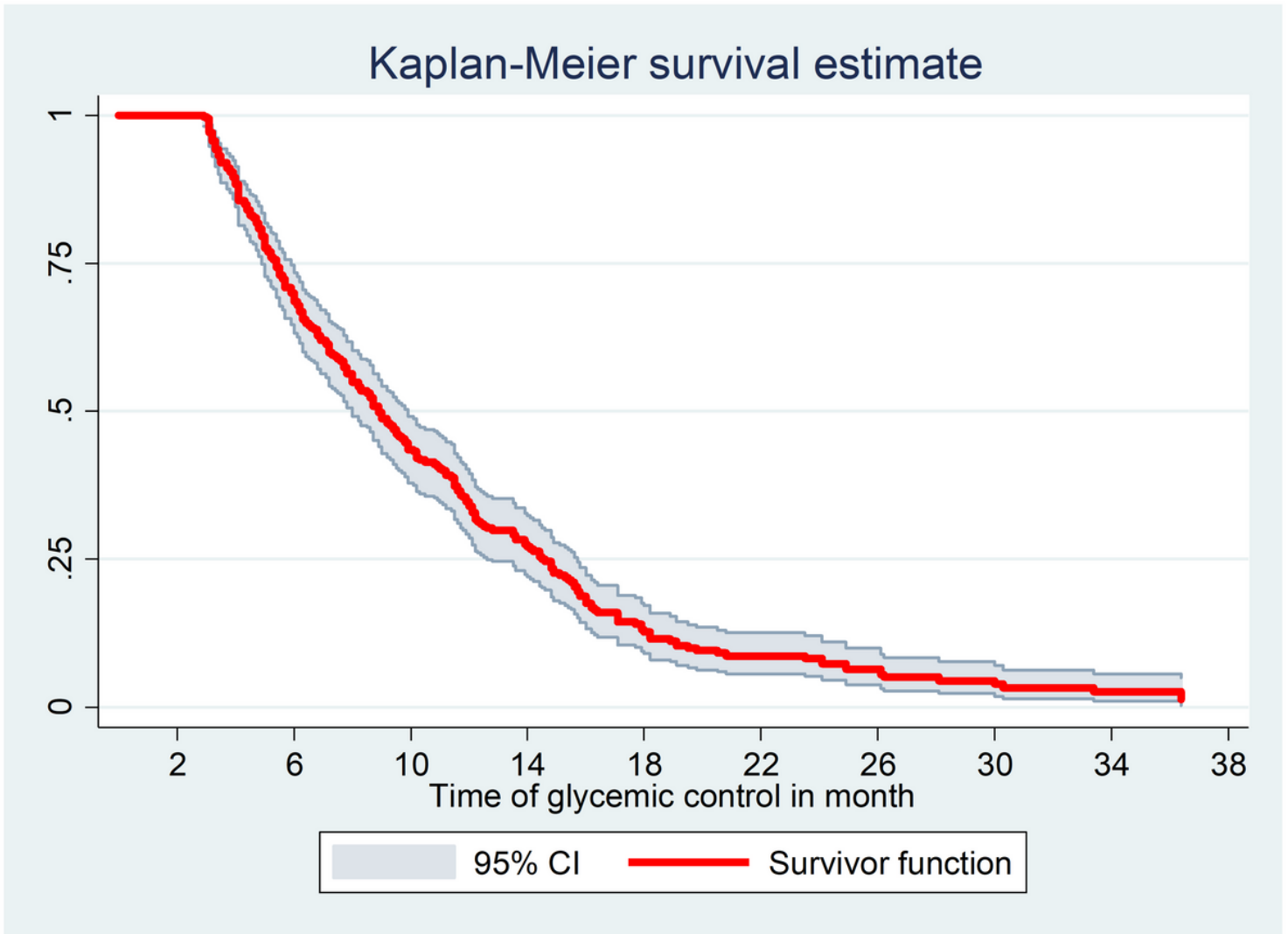


Figure 2

Kaplan-Meier survival estimate of time to first optimal glycemic control among type 1 diabetic children having follow up at Bahir Dar city public referral hospitals, 2021

Kaplan-Meier survival estimates

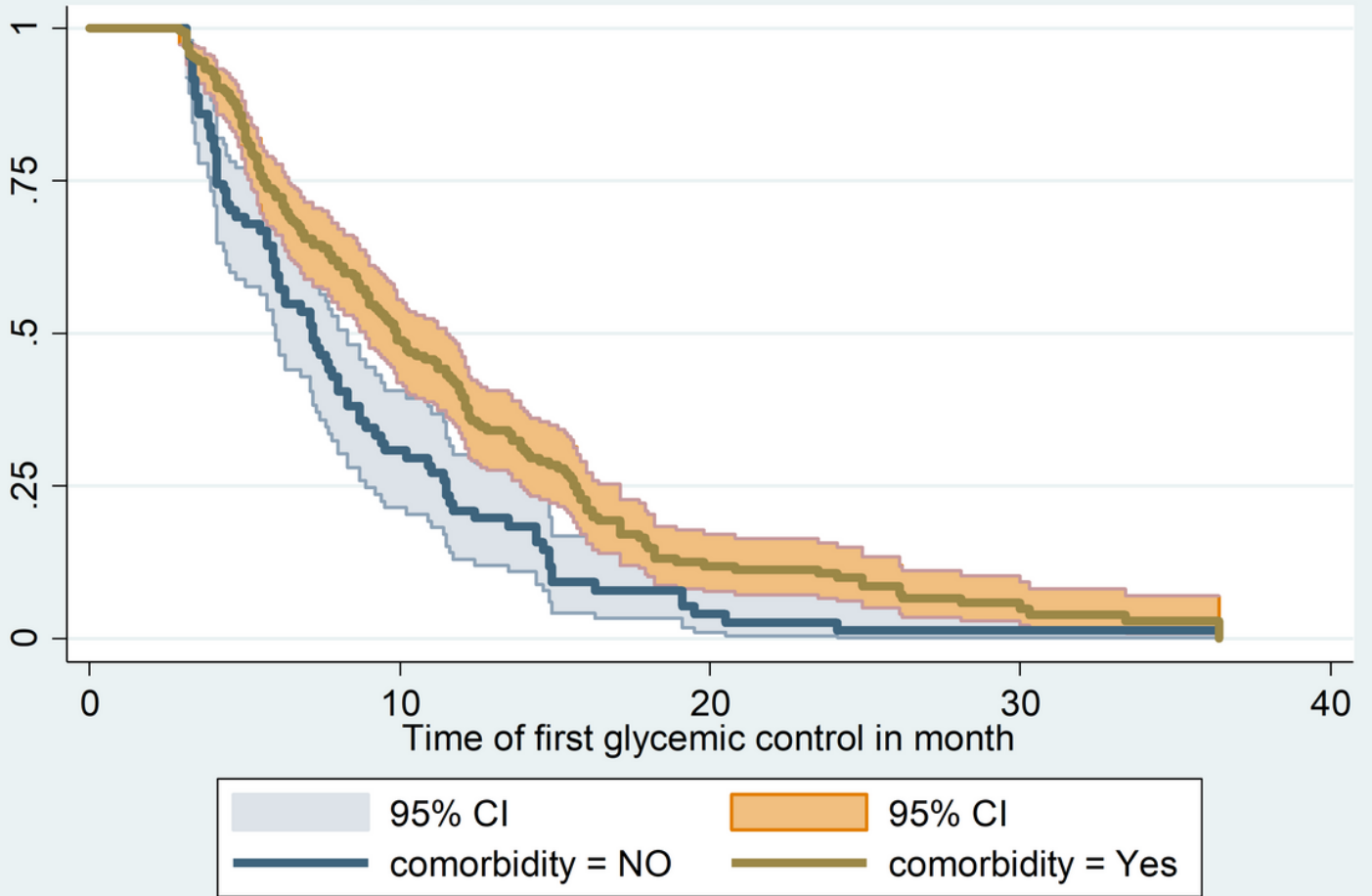


Figure 3

Kaplan Meier survival estimate for time to optimal glycemic control among type 1 diabetic children with history of comorbidity in Bahir Dar city public referral hospitals, Northwest, Ethiopia, 2021

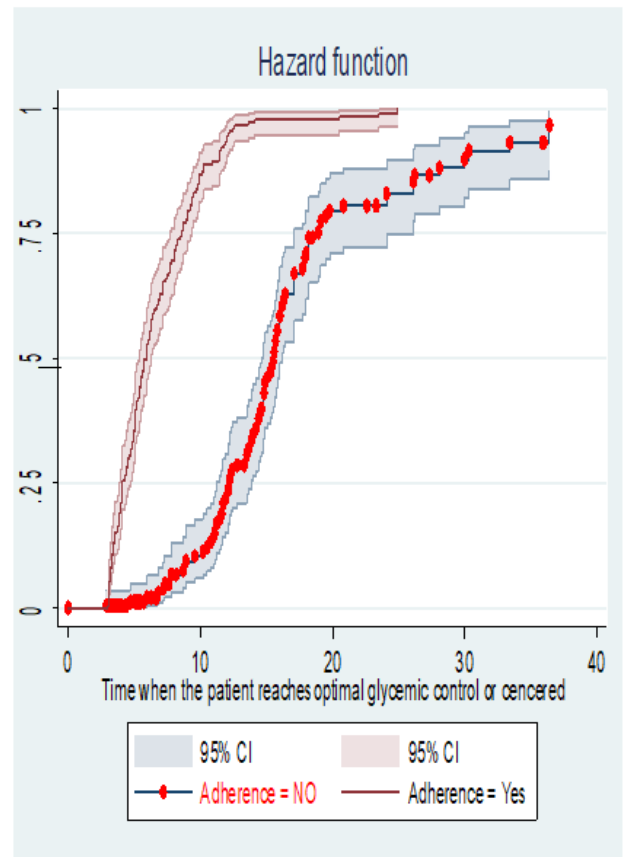
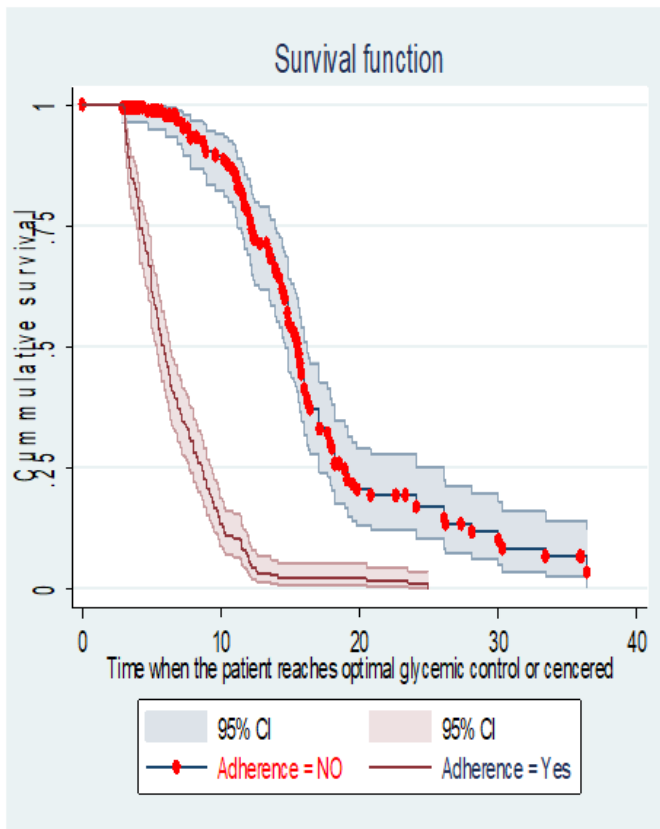


Figure 4

survival and hazard function of adherence by time (in month), Bahir Dar city public referral hospitals, Northwest, Ethiopia, 2021

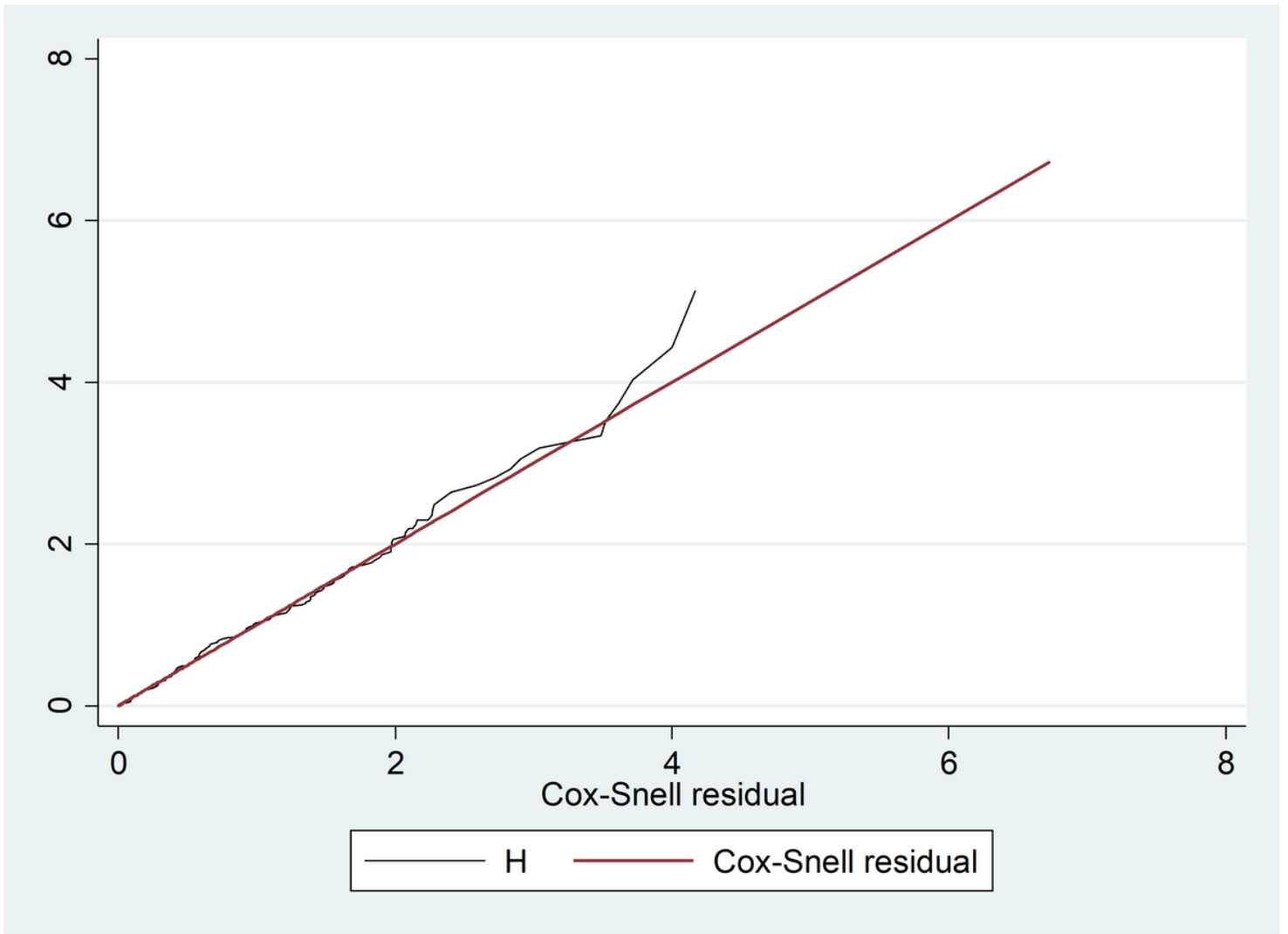


Figure 5

Model goodness of fit by cox Snell residual among type 1 DM clients, Bahir Dar city public referral hospitals, Northwest, Ethiopia, 2021(n=385)

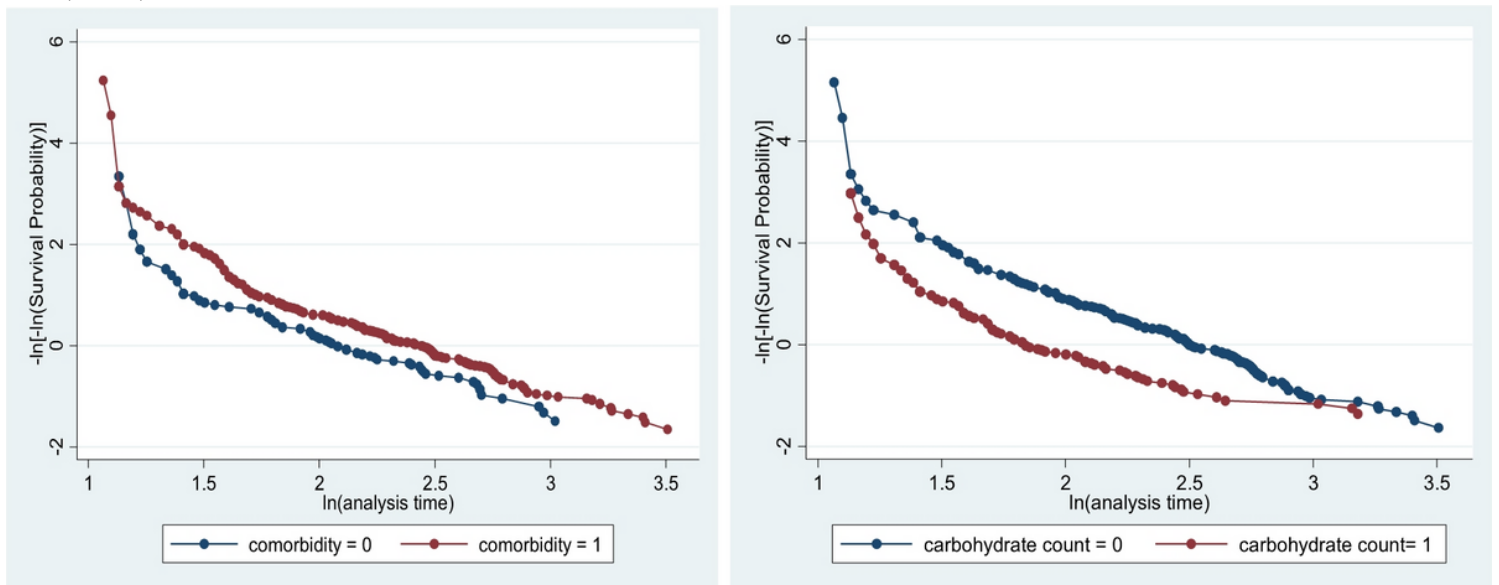


Figure 6

log of minus the Log of survival function by comorbidity and carbohydrate count for time to first optimal glycemic control among type 1 diabetic children, Bahir Dar, 2021