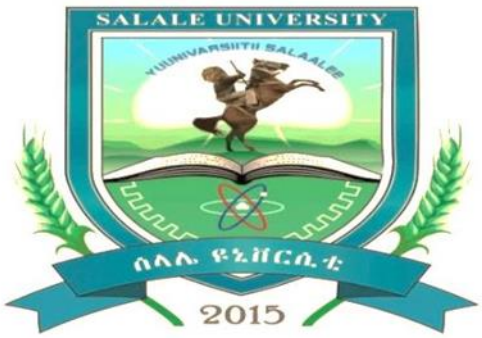

SALALE UNIVERSITY

COLLEGE OF HEALTH SCIENCE

DEPARTMENT OF NURSING

TIME TO FIRST OPTIMAL GLYCEMIC CONTROL AND ITS PREDICTORS AMONG TYPE 1 DIABETES CHILDREN AND ADOLESCENTS FOLLOW-UP AT PUBLIC HOSPITALS IN BORENA ZONE, OROMIA, SOUTHERN ETHIOPIA, 2024.

BY: KUBSA GUYO (BSc)

A RESEARCH THESIS SUBMITTED TO SALALE UNIVERSITY, COLLEGE OF HEALTH SCIENCE, DEPARTMENT OF NURSING IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER IN PEDIATRIC AND CHILD HEALTH NURSING

DECEMBER, 2024

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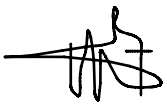
Name: Kubsa Guyo Boru Signature: 

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ABSTRACT

Background: Glycemic control refers to the level of blood sugar in diabetes patients. Recognizing a patient's level of glycemic control is an important measure to avoid complications and the risk of death from diabetes. However, the other most important variable, which is the time that the patient stayed at that suboptimal glycemic level before reaching optimal glycemic control, has not been studied so far, including both children and adolescents globally, as the author searches.

Objective: To determine the time to first optimal glycemic control and its predictors among type 1 diabetes children and adolescents follow-up at public hospitals in Borena zone, Ethiopia, 2024.

Methods: A hospital-based retrospective cohort study was conducted from June 25 to July 25, 2024, among 383 type 1 diabetes children and adolescents attending at public hospitals in the Borena zone, Ethiopia. A simple random sampling technique was used to select two hospitals. Medical record numbers were obtained from patient register logbooks. Then data was collected from patients' cards from January 1st, 2019, to January 31st, 2024, by using a simple random sampling method with a pretested checklist in each selected hospital. Data was collected using a data abstraction tool, then entered into Epi-data 4.6 and analyzed using Stata version 15. The Kaplan-Meier survival curve, along with log-rank tests, was used to estimate and compare survival times. A bivariate Cox regression model was used to select variables for the final model at a p-value ≤ 0.25. Multivariable Cox regression was used to identify predictors of time to first optimal glycemic control. The adjusted hazards ratio with a 95% confidence interval and a p-value <0.05 was used to determine statistical significance.

Results: The final analysis included 373 study participants, with a response rate of 97.3%. Median survival time to first optimal glycemic control among type 1 diabetic patients was 14.3 months (95%CI: 13-17). The first optimal glycemic achievement rate was 4.42 (95%CI: 3.8-5.1) per 100-person-month observation. Factors that affect time to first optimal glycemic control were the absence of health insurance (AHR: 0.566, 95%CI: 0.356-0.90), comorbidity (AHR: 0.654, 95%CI: 0.45-0.94), type of current insulin regimen (AHR: 3.76, 95%CI: 1.48-9.56), ≤4 follow-ups (AHR: 0.63, 95%CI: 0.42-0.95), and diabetic ketoacidosis (AHR: 0.53, 95%CI: 0.37-0.78).

Conclusion and Recommendation: Median survival time to first optimal glycemic control among type 1 diabetic patients was much longer. Which indicates that patients are being unprotected for complications. Absence of health insurance, diabetic ketoacidosis, type of current insulin regimen, ≤4 follow-up frequency, and comorbidity were independent predictors of time to optimal glycemic control. Therefore, diabetic care should be strengthened to shorten time to first optimal glycemic control. Hence, it should be better to give special attention to patients with identified predictors.

Keywords: Type 1 diabetes, Time to first optimal glycemic control, Optimal glycemic control, Children, Adolescents, Ethiopia.

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ABBREVIATIONS AND ACRONYMS

ADA: American Diabetes Association

AHR: Adjusted Hazards Ratio

BMI: Body Mass Index

CI: Confidence Interval

CSII: Continuous Subcutaneous Insulin Infusion

DCCT: Diabetes Control and Complications Trial

DKA: Diabetic ketoacidosis

DM: Diabetes Mellitus

EDIC: Epidemiology of Diabetes Interventions and Complication

FBS: Fasting Blood Sugar

GC: Glycemic Control

IQR Interquartile Range

IU: International Unit

ISPAD: International Society of Pediatrics and Adolescent Diabetes

HbA1c: Glycated Hemoglobin A1c

KM: Kaplan Meier

Km: Kilometers

MoH: Ministry of Health

MRN: Medical Registration Number

NPH: Neutral Protamine Hagedorn insulin

PH: Proportional Hazard

OGC: Optimal Glycemic Control

SGC: Suboptimal Glycemic Control

T1DM : Type 1 Diabetes Mellitus

WHO: World Health Organization

1. INTRODUCTION

1.1. Background of the study

Glycemic control (GC) is the regulation of blood sugar levels in diabetic patients, and the primary goal of treating diabetes mellitus (DM) is to prevent target organ damage and complications (1). The American Diabetes Association (ADA) defined diabetes as a "group of metabolic disorders characterized by serious, progressive, and chronic elevated levels of blood glucose (hyperglycemia) resulting when the pancreas does not produce enough insulin, the body cannot use proper insulin, or both" (2). DM is categorized into three primary types, namely type 1, type 2, and gestational diabetes (3). The ADA reports that Type 1 is the predominant type across pediatric age groups (4).

Diabetes type 1 (T1DM), previously known as insulin-dependent, juvenile, or childhood-onset diabetes, is usually characterized by an absolute deficiency or lack of insulin (5). Autoimmune disease, a condition triggered by genetic and environmental factors like virus infections, dietary changes, and toxins, results from a response against pancreatic beta cells (6). T1DM is currently not avoidable; however, it can control and prevent its complications. Otherwise, uncontrolled diabetes over time may lead to major damage to the heart, blood vessels, eyes, kidneys, and nerves (4,7). Complications include immediate issues like hypoglycemia and diabetic ketoacidosis (DKA), as well as long-term issues like retinopathy, nephropathy, neuropathy, and cardiovascular disease (8).

According to the current ADA and International Society of Pediatrics and Adolescent Diabetes (ISPAD) standards, DMs are diagnosed with glycated hemoglobin A1C (HbA1c) levels of ≥6.5%, fast blood sugar (FBS) levels of ≥126 mg/dl, 2-hour plasma glucose ≥200 mg/dl during an oral glucose tolerance test, or random plasma glucose levels of ≥200 mg/dl plus typical symptoms such as polyuria, polydipsia, and unexplained weight loss (4,9). It was known that GC had either optimal or suboptimal control when the mean HbA1c level was <7.5% or ≥7.5% and/or when the average FBS level was between 70 and 145 mg/dl or <70 mg/dl or ≥145 mg/dl, respectively (10,11). The ADA and ISPAD recommend that pediatrics with access to comprehensive DM treatment attempt to fulfill HbA1c targets by age group: 7.5% to 8.5% for <6 years, <8.0% for 6 to 12 years, <7.5% for 13 to 18 years, and <7.0% for >19 years. However, a higher HbA1c target (<7.5%) is reasonable in instances where there is limited access to analog insulins, improved insulin delivery technology, and continuous glucose monitoring (4,9).

Optimal glycemic control (OGC) is crucial in managing children with T1DM. T1DM care has improved with increased insulin, continuous subcutaneous insulin infusion (CSII) therapy, blood glucose monitoring, and education; however, suboptimal glycemic control (SGC) and

complications remain in many patients (12). GC is the strongest modifiable predictor of the risk of acute and chronic DM complications (13). OGC reduces acute and chronic complications, as well as death (14). However, maintaining the glycemic target is difficult for children and adolescents with T1DM, and excessive therapy increases the risk of hypoglycemia (15). Individuals with low glycemic levels may have a different prognosis depending on how long they remain at that level. This indicates that the longer time the patient remains in that SGC state, the higher the risk of complications and death (16). As a result, the number of children and adolescents affected will rise, putting an emotional and financial strain on both clients and families as a whole if efforts to identify the contributing factors for OGC are not made within the given time frame (9).

1.2. Statement of the problem

In the 21st century, diabetes is one of the health crises with the fastest growth and the largest global health concern among non-communicable diseases (NCDs) (17). The International Diabetes Federation (IDF) reported that in 2021 and 2022, approximately 1.2 and 1.52 million children and adolescents were having T1DM, respectively (18). Globally, incidence varies annually from 3% to 4% (9,12). DM-related global direct health expenditures are currently approaching one trillion United States dollars and projected to exceed this amount by 2030 (19). This increment is also noted more alarmingly in developing countries (20,21).

Globally, more than 70% of T1DM patients were unable to maintain their glycemia. Many children have also suffered from T1DM, which is associated with a high morbidity and mortality rate due to SGC (22,23). Both in developed and developing nations, the prognosis for children and adolescents with T1DM is poor (21). As a result, OGC was oscillating from 20.9% to 39.1%. A study conducted in several industrialized countries showed that it was 20.9% in Jordan (24), 36% in Bulgaria (25), and 39.1% in Saudi Arabia (26). According to a different study conducted in low- and middle-income countries, the magnitude of OGC ranges from 2.6% to 28%, which means 2.6–9.8% in Tanzania (27,28), 24% in Cameroon (21), 24% in Sudan (29), and 28% in Kenya (30), respectively. Even though there is no national-level study in our country, however, a systematic and meta-analysis study found that 33.2% to 34.4% of individuals have maintained OGC (31).

According to current evidence, a variety of factors contributing to SGC/longer time to OGC differ between T1DM children and adolescents, including pubertal age and low socioeconomic status (24,26). The Ministry of Health's (MoH) study revealed that DM patients experience SGC due to inadequate healthcare provider training, limited access to essential antidiabetics, and inadequate documentation (32). Concomitant (comorbidity) disease and dietary noncompliance contribute to SGC in industrialized nations (24,26,31). Conversely, risk factors in developing nations were found to include insufficient healthcare resources, fewer than three clinic visits per year, DM duration, type of insulin regimen, adherence, and financial capacity to cover treatment costs (20–22,34).

Uncontrolled glycemic levels can lead to negative effects on the body, potentially causing growth failure and other health issues (9,34). Long-term uncontrolled hyperglycemia causes a variety of macro- and microvascular complications, including neuropathy, nephropathy, retinopathy, cardiovascular disease, amputations, and early mortality (27,31,32). The most common complications in T1DM patients before 3 months include hypoglycemia (21–42%), DKA (31.5–39%), nephropathy (10.5–32.9%), neuropathy (13.6%), convulsions (10.5%), and retinopathy

(10.3%) (35,36). This consequence accounted for the majority of DM morbidity and mortality (37). Sustained abnormal blood sugar fluctuations over two months can increase the disease's burden, increase hospitalization, and negatively affect disease outcomes (28). Similarly, an Ethiopian study demonstrates the challenge of timely GC, leading to early cases of retinopathy and maculopathy in DM youngsters (38). In Ethiopia, research found that 58.5% of T1DM children had DKA, with an incidence rate of 2.27 per 100 children per month (39). In addition to having a large influence on health outcomes, failing to meet OGC can speed up the onset of chronic complications (27).

Nevertheless, strict GC reduces the likelihood and course of a potential consequence (21,31). Studies called the Diabetes Control and Complication Trial (DCCT) and the Epidemiology of Diabetes Interventions and Complications (EDIC) found that OGC slowed the growth of both short-term and long-term problems in children and adolescents with T1DM (15). ADA states that "children are not little adults." Pediatric-onset diabetes is different from adult DMs because of its unique pathophysiology, developmental stages, and treatment response. DM care for children shouldn't be extended from care for adults with DM. Timely anticipatory guidance and care coordination will allow for a smooth transition from childhood to adulthood (40).

To alleviate the burden of SGC, several integrated programs, guidelines, and recommendations have been established, including those from the ADA, ISPAD, and MoH of Ethiopia (9,11,40). New approaches to controlling T1DM are being developed, with the ultimate goals of GC, weight gain restriction, comorbidity mitigation, and improved quality of life (12). Aggressive insulin regimens that coincide with meals and exercise are always used to manage T1DM in youngsters (28,41). These regimens can include multiple daily injections, or CSII (42). The ISPAD recommends routine self-monitoring of blood glucose levels in T1DM pediatrics, either intermittently or continuously, with a HgA1c examination every 2-3 months (20).

Despite continuous improvements and the creation of supported protocols that have been implemented to reduce time to OGC, most pediatrics with T1DM fail to achieve OGC within 3 months of diagnosis, with only 21% of them achieving it (27). A study conducted in Ethiopia found that T1DM children took the longest (8 months) to meet their first glycemic targets (43). Daily T1DM care for children and their parents is difficult due to physiological, developmental, and psychosocial issues (44). Adolescent hormonal changes can lead to insulin resistance (45), and the pubertal growth spurt, which is caused by sex hormones and pubertal growth hormone, can antagonize insulin action. The young age of diagnosis is also cause for concern; children may be unable to detect and/or report early symptoms and early time development of complications (44).

In Ethiopia, some studies have been done regarding the predictors and prevalence of poor or suboptimal GC in T1DM pediatrics. However, little is known about the time of the first OGC and its predictors. The time the patient stayed at that suboptimal glycemic level prior to attaining OGC, which is the first crucial parameter to reduce complications, has not yet been studied in both children and adolescents. Furthermore, even if one study was conducted in Ethiopia, it didn't include an important variable: health insurance, and it also did not involve both children and adolescent age groups. Therefore, this study was to fill the above information gaps and update previous knowledge on the same problem by including both children and adolescents in the pastoralist area. This is a retrospective cohort study that aims to estimate the time to the first OGC and identify its predictors among T1DM children and adolescents following up at public hospitals in the Borena Zone, southern Ethiopia.

1.3. Significance of the study

Thus, the study's findings will provide evidence-based guidance to healthcare facilities and relevant stakeholders, including families and communities in the Borena Zone, enabling them to improve clinical decision-making and enhance the effectiveness of their interventions. The study results will assist health professionals in understanding the duration required to achieve optimal glycemic control, which is crucial for mitigating the risk of both acute and chronic complications related to Type 1 Diabetes Mellitus management. By identifying the predictors that influence the duration of achieving optimal glycemic control, clinicians, stakeholders, and policymakers can customize treatment strategies, intensify interventions as needed, and enhance patient care to accelerate the attainment of optimal glycemic control.

Furthermore, this study will enhance nursing knowledge and practice, as well as promote nursing education and research. It also serves as a reference for future research in this area by taking this study as a preliminary finding.

2. LITERATURE REVIEW

2.1. Survival time to first optimal glycemic control among type 1 diabetes

A retrospective cohort study of under-15-year-old children in Bahir Dar, Ethiopia, demonstrated that the median survival time for first OGC among T1DM children was 8 months. The optimal glycemic achievement rate was 8.2 per 100 people per month observed (43). Also, a study done at public hospitals in Addis Ababa on type 2 diabetes adults reported that the overall median time to first achieve OGC among the study population was 9.5 months (16). In spite of this, the ADA has suggested that children and adolescents diagnosed with T1DMs attain OGC within three months after getting their diagnosis and start treatment (10).

2.2. Predictors of time to first optimal glycemic control among type 1 diabetes

2.2.1. Sociodemographic predictors

Several studies from different parts of the world showed an association between GC and multiple variables. Studies indicated that discrepancies in GC among diabetic children based on their age, gender, and geographic location were still not as certain (46). For instance, a retrospective cohort study done in East London found that individuals diagnosed with T1DM aged 12–18 have five-fold higher longer hazards of OGC than people who were younger (47). This was again supported by a cohort study in Middle East Jordan published in 2019 that also revealed that the age at diagnosis of T1DM among children and adolescents older than 14 years had a high risk of longer time to OGC (24). But this contrasts with a study conducted in Iran, which showed that postpubertal (16–18 years old) children were more likely to have OGC compared to pubertal and prepubertal ages, and it had no significant association with other demographic factors, including sex (48).

Another study in Iran discovered that being female is an independent risk factor for prolonged GC and T1DM-related complications (49). A retrospective study in Taiwan found that GC among T1DM patients was associated with female gender, older age groups (over 14 years), and residents, notably in urban areas (50). A retrospective research analysis from Qatar in 2022 found no significant link between children and adolescents with a family history of diabetes and time to OGC (51).

According to the findings of two Tanzanian research studies, the first study conducted at the diabetic clinic for children and adolescents in 2016 had 75 participants. Those under the age of ten had significantly lower mean HbA1c levels (9.8%) than those aged 10 to 14 (11.5%) or older (11.4%) (28). The second study, which was conducted in 2021, found that patients above the age of

ten were at a higher chance of having poor GC (27). In other words, a retrospective cohort study of 188 Tunisian participants found that mean HbA1c was greater in T1DM patients, with a negative connection between age at onset of diabetes (22). A meta-analysis conducted in Africa found that HbA1c levels were <7.5% in those under 15 years, and females were 9% less likely to have OGC than males (52). However, a study in Kenya found no significant difference in age at diagnosis for OGC (30).

A retrospective cohort study in Bahir Dar, Ethiopia, found a 67.6% lower rate of obtaining OGC among patients aged >10–14 years compared to those aged ≤5 years. This suggests it takes a longer time to reach the first OGC compared to patients aged ≤5 years (43). Whereas, in Ethiopia, specifically in Gojjam, age <5 years among T1DM children, the hazard of occurrence of acute complications was 3.52 times higher in children age >10 years (39). A study carried out at the Wollega University referral and the Nekemte specialized hospitals found that the risk of SGC in females was nearly twice that of males (53). A study in southern Ethiopia found that having SGC was linked to coming from a family that can't afford insulin when it's not available for free (health insurance). The study also found that there was no significant difference in residence for OGC (54).

2.2.2. Clinical/Medical-related predictors

Multiple clinical conditions are associated with glycemic control. A study done in India found that children and adolescents with T1DM under 24 months duration of diabetes had better OGC compared to those with 25–60 months and over 60 months (55). A study conducted in Iraq demonstrated that >3 years of diabetes duration and the presence of hypertension as a comorbid illness were associated with an increased risk of poor GC (56). However, it contradicted to a study conducted in southwestern Saudi Arabia, which reported that children with a duration of DM ≤3 years had a higher risk of SGC compared to children with a duration of DM exceeding 3 years (57). But a report from Thailand in 2022 also found that the duration of DM was not significantly associated with OGC (58). A study conducted in Isfahan, Iran, indicated that underweight body mass index (BMI) children had an increase of 74% in the risk of SGC/longer time compared with normal-weight children (48).

In sub-Saharan Africa, the chronic care health system has significantly developed in the last decade, but the potential for managing and approaching diabetes cases remains unsatisfactory. For instance, a study revealed that those with ≥2 years of DM duration had a 93% higher likelihood of OGC compared with those with <2 years of diabetes duration (59). However, in Tanzania, children with diabetes for less than one year had a mean HbA1c that was 2% lower than those with DM for a longer duration associated with better GC (28). Also, another study conducted in Tanzania in

2021 indicated that children and adolescents with an overweight BMI had better OGC as compared to those with a normal weight BMI (27). Another study in Sudan revealed that a relationship was not observed between nutritional status and GC (29). A study carried out in Kenya demonstrated that a significant association between OGC and infection is risky for a longer time of OGC (60).

Furthermore, a study done at the Bahir Dar City Hospital demonstrated that patients with DMs living for ≥4 years, a history of comorbid illness, and increased weight, the hazard of reaching OGC was 35.8%, 27.8%, and 3.6%, respectively, lower than that of counterparts (43). A survival study conducted in Ethiopia found that patients with T1DMs had a high risk of death, with the main predictive factors for diabetic patients' survival time being hypertension, diabetic complications, overweight, and high blood cholesterol level-related behaviors, particularly in adolescents, with the recommendation of regular blood glucose level checks and proper insulin use to achieve OGC in a short period of time (61). Another study conducted in Addis Ababa found that having a comorbid illness is a significant predictive factor that influences the time to OGC. Patients with hypertension, dyslipidemia, and cardiovascular disease were 38.9%, 39.1%, and 33.0% less likely to reach OGC than those without such disorders (16). However, a study in Gondar, Ethiopia, found that infection was not significantly associated with OGC (62).

2.2.3. Treatment and Personal behavior-related predictors

Insulin dose has been linked to GC levels. Several factors affect the initial daily insulin dose per kilogram of body weight. In pubertal children, the dosage is typically higher. Most youngsters with new-onset diabetes have residual βeta cell activity (the honeymoon phase), reducing the need for exogenous insulin. Children with long-term diabetes and no insulin reserve require around 0.7 international units (IU)/kilogram (kg)/day when prepubertal, 1.0 IU/kg/day at mid-puberty, and 1.2 IU/kg/day at the end of puberty. An appropriate dose for a newly diagnosed child is around 60-70% of the full replacement dose based on pubertal status (1). A retrospective observational study of 58 Thailand teenagers found that those with early OGC used significantly fewer insulin IU/kg/day than those with late OGC (58). The T1DM exchange database from diabetes clinics in the USA revealed that children and adolescents with excellent GC had improved diabetes outcomes, including fewer treatment discontinuations and a lower mean total daily insulin dose (63).

A study conducted in Shantou, China, found that the type of insulin injection regimen was an independent predictor of OGC (64). According to results from a different study conducted in Qatar and Japan, compliant adolescents had an optimal GC rate of 78% and 19% compared to non-compliant adolescents, respectively (51,65). A retrospective cohort study of 2463 patients managed in Singapore demonstrated that the medication noncompliance patients were 2.6 times more likely

to have hospitalization or emergency department visits and were 2.4 times more likely to have SGC compared with the fully adherent patients (66).

Comparably, a Tanzanian study found that children and adolescents who used non-premixed actrapid (Regular) and insulatard (Neutral Protamine Hagedorn (NPH)) insulin regimes were 1.3 times more likely to achieve OGC than those who used premixed NPH + Regular or NPH alone (27). Similar findings reported by Yazidi et al. showed that good compliance with insulin treatment (mean HbA1c, 8.9%) was more likely to lead to OGC than poor compliance (mean HbA1c, 11.1%) (22). Also, a study undertaken in northwest Cameroon found that good insulin compliance during follow-up was 97% more likely to lead to OGC than those who had non-compliance (21). However, a study in Kenya indicated that non-compliance with insulin and insulin dose (<0.6 or ≥0.6 IU/kg/day) was not substantially linked with OGC (30). Another report from Nairobi, Kenya, also found that keeping regular appointments at DM care was insignificantly associated with time to OGC (60). According to a study in La Rabta Hospital, Tunisia, children and adolescents who had ≥3 clinic visits per year (mean HbA1c, 8.9%) were more likely to have OGC than those who had < 3 clinic visits (mean HbA1c, 10.5%) (22).

However, a study conducted in Bahir Dar public hospitals found that increasing the dose of insulin at the start of treatment increased the time to the first OGC achievement rate by 1.053 times for every one-unit increase. Furthermore, the initial OGC rate was 9.7 times greater in individuals who followed DM treatment recommendations than those who did not (43). Correspondingly, a facility-based retrospective study conducted at the University of Gondar on poor GC and associated factors among pediatric DM reported that the risk of suboptimal GC for poor treatment adherence or treatment discontinuation during follow-up was 2.42 times higher compared to those who took their treatment properly, but increasing the insulin dose by one IU reduced the risk of SGC by 4% (62).

2.2.4. Diabetes-related complications predictors

According to several research studies, complications are the leading cause of SGC/longer OGC in children and adolescents. For example, a 2019 data synthesis in Brazil recognized that, in addition to the usual communicable disease, other types of infections have occurred predominantly in diabetic patients, particularly when GC is inadequate, and that majority of these infections can be severe and interfere with glucose control, with a high risk of leading to DM-related complications (67). For instance, a retrospective review research study conducted in India on GC and factors influencing it in children with T1DM discovered that those who had an episode of DKA in the previous 12 months had a higher HbA1c and/or mean FBS than those who had not had an episode of DKA (55). Other research at Egypt's Assiut University found that having DKA more than once

increased the likelihood of SGC, as did having a history of hypoglycemia. Furthermore, DKA was responsible for 28.9% of hospital admissions, while hyperglycemia accounted for 55% (68).

According to a study done in our country, Southwest Ethiopia, on GC and associated factors among children and adolescents with T1DM, DM-related hospitalization in the past 6 months was eight times more likely to increase the risk of SGC than those not admitted to the hospital (69). However, in contrast to the findings reported by Abdelaty et al., DM-related hospitalizations were not statistically significantly associated with time to OGC (68).

Similarly, according to a cohort study conducted in Northwest Ethiopia on the time to first OGC and its predictors in children with T1DM under the age of 15, patients without a history of diabetes-related complications had a higher percentage of OGC (76.6%) than patients with a history (70.7%) (43). In line with a study done in Addis Ababa, patients who have more than one acute or chronic diabetes-related problem, especially neuropathy, are at a considerable predicted risk. The OGC rates of patients with neuropathy and multiple complications are 49.8% and 62% lower, respectively, than those of those without neuropathy and no more than one complication (16).

2.3. Conceptual framework

After reviewing different literature (16,21,27,39,43,55,68,70) about predictors of time to first optimal glycemic control and/or glycemic control among T1DM children and adolescents, the following conceptual framework is adapted. By incorporating sociodemographic, clinical/medical-related, treatment and personal behavior-related, and diabetes-related complications predictors and the outcome variable.

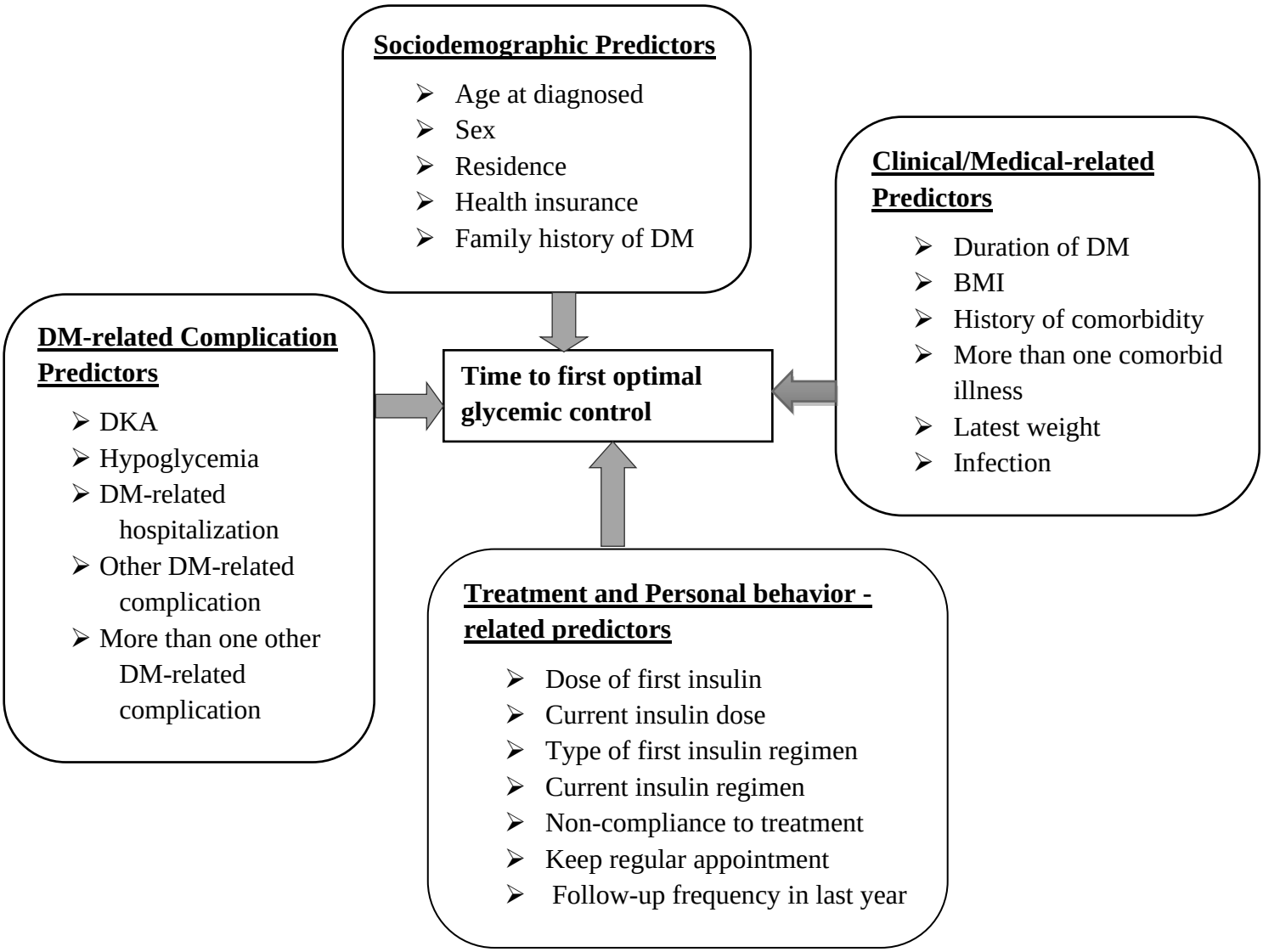


Figure 1: Conceptual framework for the time to first optimal glycemic control and its predictors among type 1 diabetes children and adolescents, 2024.

3. OBJECTIVES

3.1. General objective

To determine the time to first optimal glycemic control and its predictors among type 1 diabetes children and adolescents follow-up at public hospitals in the Borena zone, Oromia, Southern Ethiopia, 2024.

3.2. Specific objectives

To determine the time to first optimal glycemic control among type 1 diabetes children and adolescents follow-up at public hospitals in the Borena Zone, Oromia, Southern Ethiopia, 2024.

To identify predictors of time to first optimal glycemic control among type 1 diabetes children and adolescents follow-up at public hospitals in the Borena Zone, Oromia, Southern Ethiopia, 2024.

4. METHODS AND MATERIALS

4.1. Study area and Period

This study was conducted at public hospitals in the Borena zone. Borena Zone is one of Oromia Regional State's 22 zones. Yabelo is the administrative center of the Borena zone, which is located in southern Oromia and 570 kilometers (km) from Addis Ababa, Ethiopia's capital city. The Borena Zone is bordered by the Somali regional state in the east, the southwestern Ethiopian region in the west, the Guji Zone in the north, and Kenya in the south. It is divided into 11 administrative woredas and two town administrations. The Borena Zone is among the most severely drought-stricken and has experienced consecutive drought seasons in Oromia, where pastoralism is a mainstay for communities. In the Borena zone, pastoralism and agro-pastoralism serve as the primary sources of income and livelihood for the communities.

The zone has five public hospitals (one general hospital and four primary hospitals) and 44 health centers. All of the hospitals have provided chronic illness care for diabetes patients. Yabelo Hospital is the only general hospital in the Borena Zone, which is found in Yabelo Town. Moyale Hospital is one of the primary hospitals in the Borena Zone, which is found in Moyale town in the Oromia regional state. Yabelo General Hospital and Moyale Primary Hospital are found 570 and 770 km from Addis Ababa, respectively. According to information obtained from those hospitals' administrative offices, they have been serving 1,273,701 and 673,901 estimated populations in their catchment area, respectively. This study was conducted at the DM clinics in those hospitals. The study period was conducted from June 25, 2024, to July 25, 2024.

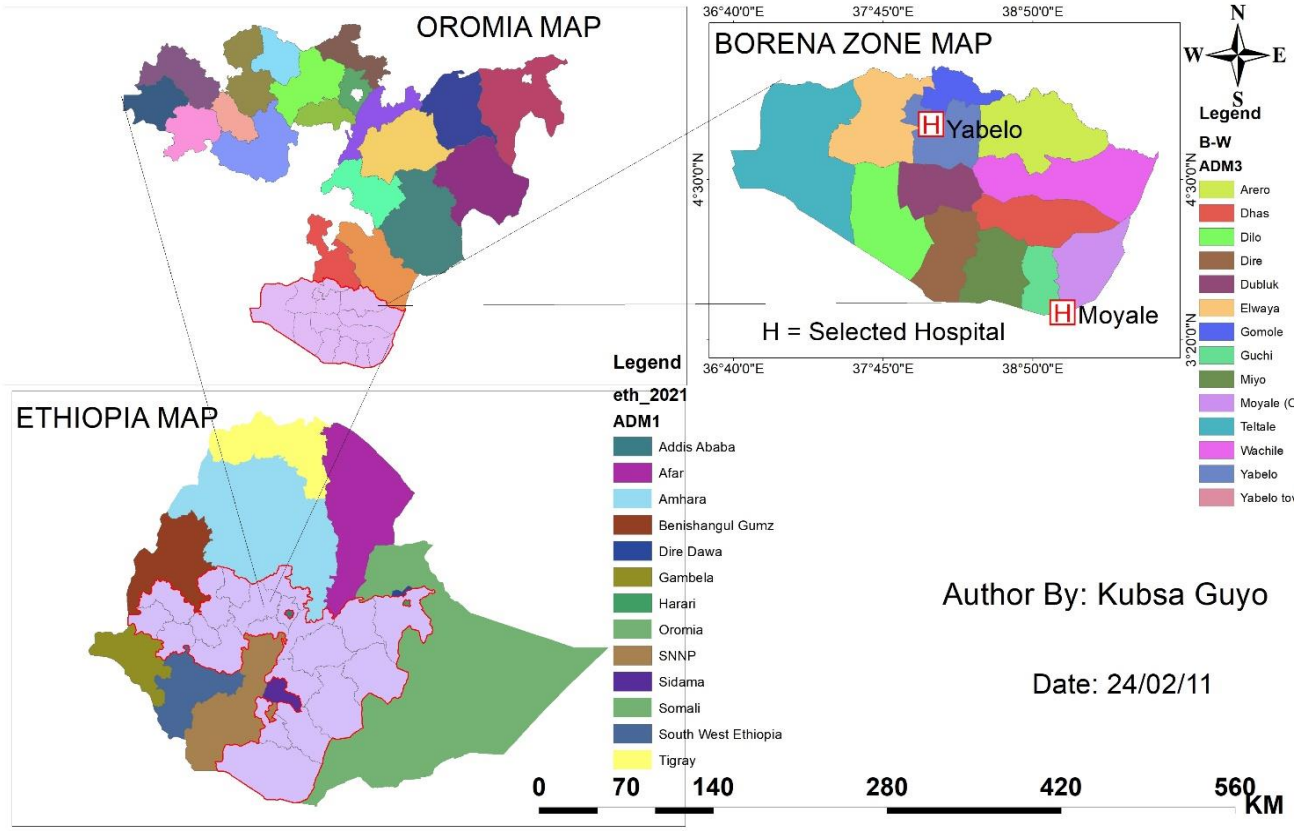


Figure 2: Map of study area of selected public Hospital in Borena zone, Oromia Regional state, Southern Ethiopia, 2024.

4.2. Study Design

A hospital-based retrospective cohort study design was conducted.

4.3. Populations

4.3.1. Source of Population

All type 1 diabetes children and adolescents aged ≤18 years old who had been registered (diagnosed) and followed up at the diabetes clinics of public hospitals in the Borena Zone.

4.3.2. Study population

All type 1 diabetes children and adolescents aged ≤18 years old who had registered and followed up (started treatment) at selected public hospitals in the Borena Zone from January 1st, 2019 to January 31st, 2024.

4.3.3. Study unit

All randomly selected type 1 diabetes children's and adolescents' charts ≤18 years old that had been registered and followed up at the diabetes clinics of the selected public hospitals in the Borena Zone from January 1st, 2019 to January 31st, 2024, and who fulfilled the inclusion criteria.

4.4. Eligibility Criteria

4.4.1. Inclusion criteria

All charts of type 1 diabetes children's and adolescents' aged ≤18 years old who had been registered and started treatment and had at least one HbA1c and/or three months of consecutive measurements of FBS with a clear date of diagnosis from January 1st, 2019 to January 31st, 2024 at public hospitals in the Borena Zone were included in the study.

4.4.2. Exclusion criteria

Children's and adolescents' medical records or charts with incomplete information (such as charts that missed registering at least the following data: age with date of diagnosis, sex, treatment modality, frequency of follow-up visit, and date of outcome status occurrence) were excluded from the study. Additionally, charts that were lost from the shelf (misplaced) during data collection, those with less than three months of follow-up during the study period, and cases transferred from another health institution with an unclear date of diagnosis were also excluded.

4.5. Sample Size determination

For the 1st objective, the sample size was calculated based on the assumption that the 95% confidence interval (CI), power of 80%, and the median survival time for exposed people with a history of comorbidity were 8.9 months, and the median survival time for unexposed people without a history of comorbidity was 6.3 months. The median survival times were obtained from a previous study conducted in Bahir Dar, Ethiopia (43). Assuming that patients enter the study at a uniform rate over a time period (T) of 60 months (5 years), using a two-sample comparison of survivor functions the formula, which depends on the separate median survival times for exposure and non-exposure.

The number of required children and adolescents in each group was calculated as follows:

$$\mathbf{n} = \frac{\left[\mathbf{Z}\frac{\boldsymbol{\alpha}}{\mathbf{2}} + \mathbf{Z}\boldsymbol{\beta}\right]^{\mathbf{2}}[\boldsymbol{\Phi}(\boldsymbol{\mu}_{\mathbf{E}}) + \boldsymbol{\Phi}(\boldsymbol{\mu}_{\mathbf{C}})]}{(\boldsymbol{\mu}_{\mathbf{E}}^{-\mathbf{1}} - \boldsymbol{\mu}_{\mathbf{C}}^{-\mathbf{1}})^{\mathbf{2}}}$$

Where: $\boldsymbol{\Phi}(\boldsymbol{\mu}_{\mathbf{i}}) = \frac{\frac{\mathbf{T}}{\boldsymbol{\mu}_{\mathbf{i}}^{\mathbf{3}}}}{\left[\frac{\mathbf{T}}{\boldsymbol{\mu}_{\mathbf{i}}} - \mathbf{1} + \mathbf{e}^{\left(-\mathbf{T}/\boldsymbol{\mu}_{\mathbf{i}}\right)}\right]}$, i = C, E

C = median survival time for the non-exposed group (6.3 months)

E = median survival time for the exposed group (8.9 months)

T = total time in which study subjects were recruited or entered into the study (60 months)

e = the exponential constant value is approximately 2.7182

Zα/2 = two-sided level of significance (α = 0.05), Zα/2 = 1.96 at 95% CI

Zβ = 80% power (1-β = 1-0.2 = 0.8), which is 0.842, and n = the minimum sample size for each group.

Thus, applying the above formula:

$$\Phi(\mu_C) = \frac{\frac{60}{6.3^3}}{\left[\frac{60}{6.3} - 1 + e^{(-60/6.3)}\right]} = \frac{\frac{60}{250.05}}{\left[9.52 - 1 + e^{(-9.52)}\right]} = 0.028$$

$$\Phi(\mu_E) = \frac{\frac{60}{8.9^3}}{\left[\frac{60}{8.9} - 1 + e^{(-60/8.9)}\right]} = \frac{\frac{60}{704.97}}{\left[6.7 - 1 + e^{(-6.7)}\right]} = \frac{0.085}{5.701231} = 0.0149$$

$$n = \frac{[\,1.96 + 0.842\,]^2[0.028 + 0.0149]}{(8.9^{-1} - 6.3^{-1})^2} = \frac{0.3358}{0.0021} = 159.9 \approx 160$$

For each group, the minimum sample size was 160. After adding 10% for incomplete records, the final sample size was 176 for exposed and 176 for non-exposed (exposed and unexposed in a 1:1 ratio), and the total sample size was 352 for this objective.

For the 2nd objective, sample size was determined by STATA version 15 after taking predictors associated with time to the first OGC from a previous study conducted by retrospective cohort design. Age of patient, adherence with insulin, comorbidity, and duration of diabetes are variables that are found to be significant predictors of time to first OGC among T1DM children based on a study done in Bahir Dar, Ethiopia (43) to calculate the required sample size. Finally, it was calculated using the statistical program STATA version 15 using Schoenfeld, with the following assumptions: a CI of 95%, a power of 80%, an exposure to an unexposed ratio of 1:1 by the general cohort study, a standard deviation, and a correlation of covariates 0.5 and 0, respectively. There was also a 10% proportion of subjects who anticipated withdrawal from the study. Then, the variable that gives the largest sample is used as the independent predictor, which is the history of comorbidity (to decrease the role of chance). The sample size calculation is summarized in the following Table 1.

The Schoenfeld formula is written as follows, with two steps:

Step 1: $$\mathbf{E} = \frac{\left[\mathbf{Z}\frac{\alpha}{2} + \mathbf{Z}\beta\right]^2}{\mathbf{P1P2}(\ln HR)^2}$$

Step 2: Sample size required (n) = $\frac{\textbf{Total number of events (E)}}{\textbf{Probability of an event (PE)}}$ $\mathbf{n} = \frac{\mathbf{E}}{\mathbf{PE}}$

Where:

E = total number of required events (achieved first OGC)

n = sample size

HR = the hazard ratio of selected significant covariates

ln = natural logarithm

P_1 = proportion of subjects in the exposure group, and $P_2 = 1 - P_1$

PE = the probability of an event (achieved first OGC) from a previous study, which is 0.717 (43).

Zα/2 = two-sided level of significance (α = 0.05), Zα/2 = 1.96 at 95% CI, and

Zβ = 80% power (1-β = 1-0.2 = 0.8), which is 0.842.

Table 1: Sample size calculation to determine the time to first OGC and its predictors among T1DM children and adolescents follow-up at public hospitals in the Borena Zone, southern Ethiopia, 2024.

Variables	**AHR**	**P-Event (PE)**	**Event (E)**	**Sample size (n)**	**Reference**
Age of patient (>10-14 years)	0.323	0.717	25	39	(43)
Adherence to insulin (yes)	9.7	0.717	7	10	(43)
History of comorbidity (yes)	0.7	0.717	247	383	(43)
Duration of diabetes (more than four years)	0.64	0.717	158	245	(43)

Therefore, the largest sample size (n = 383) was selected under this objective as the final sample size for the study.

4.6. Sampling technique and Procedure

The study was conducted at public hospitals in the Borena zone. First, the two hospitals, named Yabelo General Hospital and Moyale Primary Hospital, were selected by a simple random sampling technique (lottery method) among the five public hospitals in the zone. Then, the medical record numbers (MRNs) of T1DM children and adolescents who were diagnosed and initiated treatment from January 1st, 2019 to January 31st, 2024, in the two selected hospitals were identified from the diabetic registration logbooks to create a sampling frame. Then, the MRN of the T1DM children and adolescents was used as a sampling frame. The total sample needed is 383.

The total number of children and adolescents enrolled in T1DM treatment was five hundred ninety-two (592), recorded from January 1st, 2019 to January 31st, 2024, on the registration logbooks of both hospitals (332 charts registered at Yabelo and 260 charts registered at Moyale hospital, respectively). The total sample size was proportionally allocated for the charts in each hospital (Yabelo General Hospital = 215 and Moyale Hospital = 168). Then, all of the study participant's MRNs from each selected hospital were entered into Microsoft Excel 2021 version. After entry, the study units from each selected hospital list were selected by a simple random sampling technique using the computer-generated random number system in Excel. Finally, the selected medical charts that fulfill the criteria were reviewed, as shown in Figure 3.

Proportional sample size allocation =

$$\frac{\text{Final sample size of the study } \mathbf{X} \text{ Number of children and adolescents diagnosed with T1DM in each selected hospital}}{\text{Total number of children and adolescents diagnosed with T1DM in the selected hospitals from January 1, 2019 to January 31, 2024}}$$

After the total T1DM children and adolescents from each of the five years of follow-up in each of the two selected hospitals are taken, the final sample was calculated as follows:

$$\mathbf{nj} = \frac{\mathbf{Nj\ x\ n}}{\mathbf{N}} \qquad j = 1, 2$$

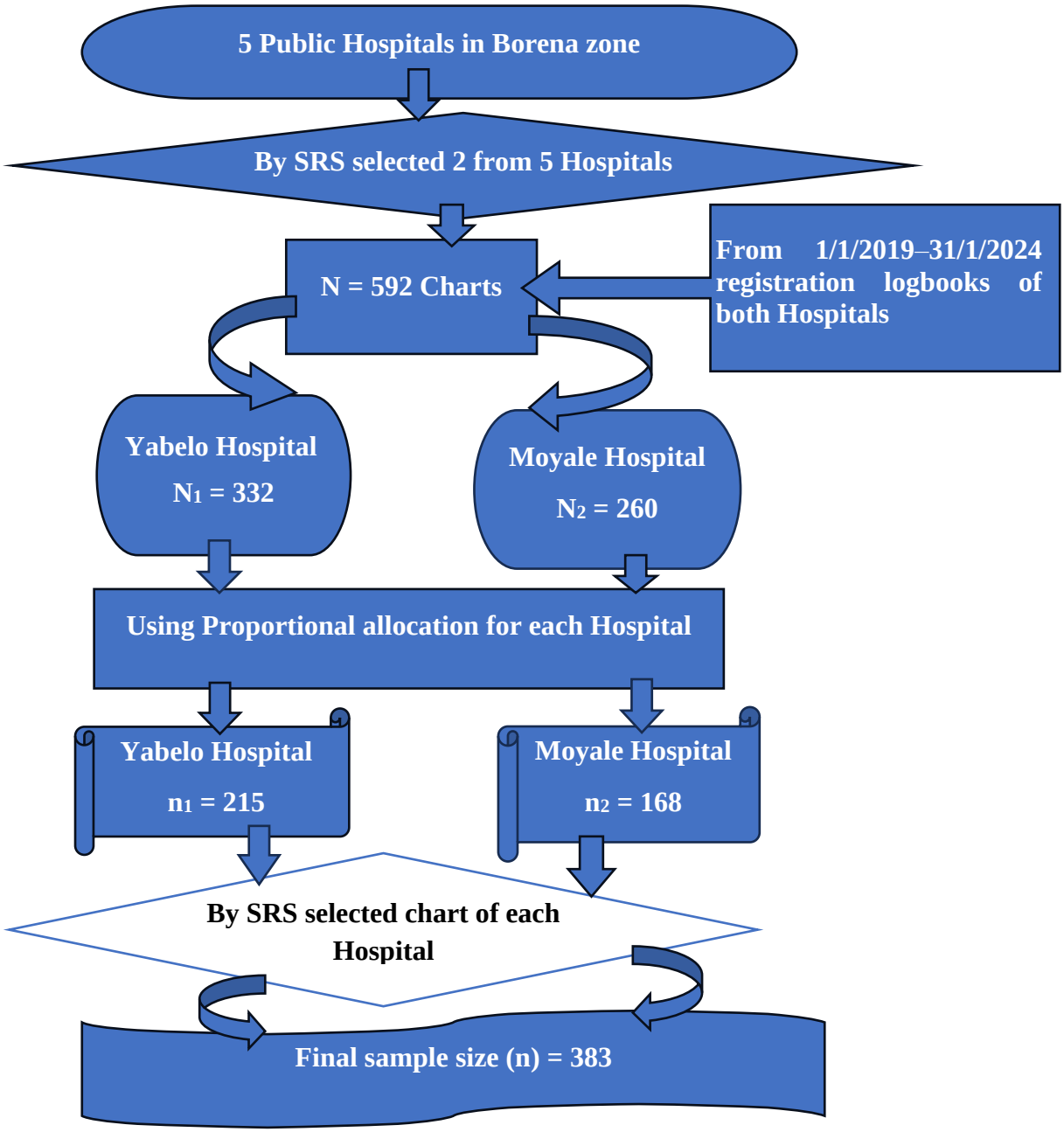
Where:

nj = sample size of T1DM children and adolescents that was selected from each j^{th} hospital

Nj = the number of T1DM children and adolescents in each selected j^{th} hospital from January 1st, 2019 to January 31st, 2024

n = the final sample size of the study ($n = n_1 + n_{2)}$ and

N = total number of children and adolescents diagnosed with T1DM in the selected hospitals from January 1st, 2019 to January 31st, 2024 ($N = N_1 + N_2$).



SRS: Simple Random Sampling

Figure 3: Schematic presentation of sampling procedure to assess the time to first OGC and its predictors among T1DM children and adolescents follow-up at public hospitals in Borena Zone, southern Ethiopia, 2024.

4.7. Data collection tools and procedure

The available information on the patient chart was first checked. The tools were adapted from different related literature and modified and prepared according to the Ethiopian context based on available information on the patient's chart (16,21,27,39,43,55,68,70). The questionnaire was prepared as a checklist in the English language. A structured data extraction tool was adapted by considering study variables such as five items from socio-demographics, six items from clinical/medical, seven items from treatment and personal behavior-related, and five items from diabetes-related complication predictors from patients' charts and the DM registration logbooks collected by two BSc nurses supervised by two senior nurses. The patient's charts were retrieved using the client's MRNs, which were identified in the registration logbooks. The starting point for retrospective follow-up was the time from which the T1DM patient's treatment started, and the end point was the time at which patients achieved the first OGC or were censored. The study participant charts were assessed to exclude ineligible cases before starting the collection of data.

Two BSc nurses were data collectors who retrospectively reviewed the children's and adolescents' medical records that fulfilled the inclusion criteria and were followed up at Yabelo General Hospital and Moyale Primary Hospital during the study period. The time to the first OGC of patients and predictors was obtained from the medical record/chart and registration logbooks. Survival time was calculated as the time between the date of starting treatment and the date of the first OGC or censored. To confirm OGC, the value of at least one month's HbA1c and/or the average of three consecutive months' FBS levels of T1DM children and adolescents in the medical records were reviewed.

4.8. Study Variables

4.8.1. Dependent Variable

- Time to first optimal glycemic control

4.8.2. Independent Variables

Sociodemographic variables;

- Age at DM diagnosis, sex, place of residence, health insurance, family history of diabetes.

Clinical/Medical-related variables;

- Duration of diabetes, history of comorbidities, history of more than one comorbidity, latest weight, BMI, infection.

Treatment and personal behavior-related variables;

- Type of first/initial insulin regimen, type of current insulin regimen, dose of first/initial insulin, dose of current insulin, non-compliance to treatment, follow-up frequency in last year, keep regular appointments.

Diabetic-related complications variables;

- DKA, hypoglycemia, DM-related hospitalization, other DM-related complications, more than one other DM-related complications.

4.9. Operational and Term definitions

Optimal glycemic control: HbA1c is less than 7.5% and/or the average of three consecutive months of the FBS level is between ≥70 and <145 mg/dl (10,71).

Suboptimal glycemic control: HbA1c being more than or equal to 7.5% and/or the average of three consecutive months of FBS level being either <70 or ≥145 mg/dl (10,71).

Fasting blood sugar: blood sugar measured from blood no caloric intake for at least 8 hours (72).

Censored: A child or adolescent has died, lost follow-up, transferred out, and completed the follow-up period without first achieving optimal glycemic control.

Event: A child or adolescent achieved first optimal glycemic control during the follow-up period.

Time to event/time to first optimal glycemic control: time between initiation of treatment up to achieved first optimal glycemic control (event) with a measure in months.

Survival time: the measure of the follow-up time (in months) from the date of diagnosis with the initiation of treatment up to the date of first optimal glycemic control or censored.

Time origin: enrollment of T1DM children and adolescents in antidiabetic treatment.

Time scale: months from diagnosis with initiation of treatment for T1DM children and adolescents.

Loss to follow-up: when the child or adolescent withdrawal from study during the follow-up period without first achieving optimal glycemic control.

Transferred out: when a child or adolescent is transferred to another health facility.

Incomplete charts: children's and adolescents' charts with incomplete information, such as charts that missed to register at least the following data: age with date of diagnosis, sex, treatment modality, frequency of follow-up visit, and date of outcome status occurred (43).

Children: are a group of people under the age of 12 years (73).

Adolescents: are a group of people aged between 12 and 18 years (73).

Comorbidity: was assessed by 'Yes' or 'No' questions, which were considered present if a child or adolescent had at least one history of comorbidity like tuberculosis, cardiovascular disease, hypertension, kidney disease, the human immunodeficiency virus (HIV), epilepsy, or other chronic illnesses that were previously diagnosed (69).

Other diabetes-related complications: a child or adolescent had at least one diabetes-related complication that was physician-diagnosed after being diagnosed with T1DM, like neuropathy, nephropathy, retinopathy, cardiovascular disease, or other complications during the follow-up period (74).

Non-compliance with treatment: dose omission, treatment discontinuation, skipping treatments for a minimum of one day, including skipping even a single dose of treatment (43).

DKA: was considered in the context of hyperglycemia (blood glucose measurement >200 mg/dl) and any of the following: a blood bicarbonate level < 15 mmol/L and/or a pH < 7.30, and/or a DKA diagnosis mentioned in the medical records and/or a ketone body in the urine (75).

Hypoglycemia: at least one documented measured blood glucose level <70 mg/dL (3.9 mmol/L) is considered hypoglycemia in children and adolescents with diabetes on treatment (72).

Body mass index (BMI): a person's weight in kilograms divided by the square of their height in meters. For children and adolescents, BMI is age- and sex-specific and is often referred to as BMI for age. BMI-for-age weight status categories and the corresponding percentiles were based on age- and sex-specific interpretations using WHO standard growth charts (76), as shown in the following Table 2.

Table 2: BMI-for-age weight status categories and the corresponding percentiles.

Weight status category	**Percentile range**
Underweight	Less than the 5^{th} percentile
Healthy Weight (Normal Weight)	5^{th} percentile to less than the 85^{th} percentile
Overweight	85^{th} to less than the 95^{th} percentile
Obesity	Equal to or greater than the 95^{th} percentile

4.10. Data Quality Control

To ensure the quality of the data, the checklist was pretested among 5% (19 charts) of the study sample size at Nagele Borena General Hospital, found in East Borena Zone, Oromia regional state, two weeks prior to the actual data collection date. The data abstraction format was reviewed in the

hospital documentation system to confirm its alignment with the study's variables. Any error found during the process of checking was corrected and modified by the principal investigator. Then crucial modifications were made to warrant the comprehensiveness and ensure the validity of the final version of the data collection tool (checklist).

The data collectors and supervisors were senior, experienced BSc nurses who have been trained in diabetes care and are currently working in another hospital's diabetes clinic (two supervisors and two data collectors were recruited). A one-day training (orientation) was given to data collectors and supervisors before actual data collection on the purpose of the study, the data collection tool, data collection methods, and ethical concerns during data collection. In each hospital, one supervisor was assigned to closely supervise the entire data collection process of the data collector.

During the data collection period, close and ongoing supervision and monitoring were done by supervisors to ensure the quality of the data. On each day of data collection, all collected data was examined for completeness and consistency by supervisors and the principal investigator. Consistency was examined through a random selection of the study sample’s charts by the principal investigator and cross-checked for similarity. After data collection, the principal investigator was carefully double-checking the data entry using Epi-data 4.6.0 software and cleansing the data before starting the analysis using Stata version 15 statistical software.

4.11. Data Processing and Analysis

The collected data was coded, entered into Epi-data version 4.6.0, and then exported into STATA version 15 statistical software for cleaning, categorizing, and analysis. Descriptive statistics were presented with a central tendency (mean or median) and dispersion (standard deviation or interquartile range) for continuous data and a frequency distribution for categorical data. Months are used as a time scale to calculate the time to the first OGC. The outcome status of study participants was dichotomized as either an event or censored. The Kaplan-Meier curve was used to estimate the median survival time and compare the survival differences between the different covariates using survival curves. A log-rank test was also used to compare statistically significant survival differences between categories of different explanatory variables.

The Cox proportional hazard (PH) regression model was used to analyze the relationship between independent and outcome variables. Before running the Cox PH regression model, multicollinearity was checked using the variance inflation factor (VIF) (mean of VIF = 1.83) (Table 10). Bivariate Cox PH regression model analyses were fitted for each explanatory variable to identify candidate variables for the multivariable Cox PH regression model. Variables with a p-value ≤ 0.25 in the

bivariate analysis were entered into the final model to determine the predictors of time to the first OGC. After performing the Cox PH regression, assumptions were checked using both the Schoenfeld residual test (global test) with a p-value = 0.5286 (Table 9) and graphically using the log-log plot of survival curves. Also, Cox PH model goodness-of-fit to the data was checked by using Cox Snell residuals, in which the hazard function follows the 45-degree baseline (Figure 11). In conclusion, the final model fitted the data successfully. The association between the independent variables and the time to the first OGC was assessed using the multivariable Cox PH regression model with a 95% CI, and a P-value < 0.05 was considered statistically significant. The adjusted hazards ratio (AHR) with 95% CI and p-values was used to measure the strength of the association, identify statistically significant results, and interpret the results. Lastly, the results were organized and presented in texts, tables, and graphs.

4.12. Ethical Considerations

An ethical clearance letter with reference number SLU-IRERC-270/2016 was obtained from the Institutional Review Board (IRB) of Salale University College of Health Science. A formal or supportive letter was obtained from the Salale University College of Health Science. A copy of the ethical clearance and supportive letters was submitted to the administrative bodies of both Yabelo General Hospital and Moyale Primary Hospital for data collection. Then informed, voluntary, written, and signed consent was obtained from the heads of both hospitals and all concerned staff who are working in the diabetic clinic. Since the study was done through the review of medical records, individual patients may not be harmed as long as confidentiality is maintained. Confidentiality was maintained by omitting their name and personal identification from the data collection format. Finally, all collected data was coded and locked in an isolated room before entering the computer, and once entered, the computer was locked by password. The collected data was not disclosed to any person other than the principal investigator.

4.13. Dissemination of the result

The result of this study will be submitted and presented to Salale University, College of Health Science, Department of Nursing. The findings will also be submitted to the Zonal Health Department, all public hospitals in the Borena Zone, and other concerned bodies. For students and other readers, hard and soft copies will be available in Salale University's library. Further effort will be made to present the findings at different seminars, conferences, and workshops. Lastly, an attempt will be made to publish the findings of this study in scientific and peer-reviewed international journals.

5. RESULTS

5.1. Socio-demographic characteristics of the Study participants

Among 383 T1DM children and adolescents, records were reviewed, and of those 373 (97.3% in response rate) records, they met inclusion criteria in the final analysis. Ten charts were excluded (5 charts with incomplete data, 2 charts with less than 3 months of follow-up during the study period, and 3 of the charts were not available at the time of data collection).

Out of 373 children and adolescents, 209 (56%) came from Yabelo General Hospital. The median age of the study participants was 13.0 ± 4 SD years old. Approximately one-third of them, 132 (35.4%), are between the ages of 10-14 years, and the majority of 73 (61.9%) achieved OGC, which concentrated in the age groups of 14-18 years. More than half of the study's participants, 215 (57.6%), were males, and 131 (60.9%) of them achieved OGC during the follow-up period. The majority of the patients, 206 (55.2%), were from rural areas. However, the proportion of rural patients who obtained first OGC is 43.7%, which is lower than that of urban residents (62.3%). (Table 3).

Table 3: Baseline socio-demographic characteristics of T1DM children and adolescents follow-up at public Hospitals in Borena zone, Southern Ethiopia, 2024.

Covariates	**Category**	**Event and Censored Status**		**Total**
		Event n (%)	**Censored n (%)**	
Age	<=5 years	35 (92.1%)	3 (7.9%)	38 (10.2%)
	>5-10 years	34 (40.0%)	51 (60.0%)	85 (22.8%)
	>10-14 years	52 (39.4%)	80 (60.6%)	132 (35.4%)
	>14-18 years	73 (61.9%)	45 (38.1%)	118 (31.6%)
Sex	Male	131 (60.9%)	84 (39.1%)	215 (57.6%)
	Female	63 (39.9%)	95 (60.1%)	158 (42.4%)
Residence	Urban	104 (62.3%)	63 (37.7%)	167 (44.8%)
	Rural	90 (43.7%)	116 (56.3%)	206 (55.2%)
Presence of health Insurance	Yes	155 (55.2%)	126 (44.8%)	281 (75.3%)
	No	39 (42.4%)	53 (57.6%)	92 (24.7%)
Family history of DM	Yes	39 (65.0%)	21 (35.0%)	60 (16.1%)
	No	155 (49.5%)	158 (50.5%)	313 (83.9%)

5.2. Clinical/Medicals characteristics of type 1 diabetic children and adolescents

Among the total participants, 33 (8.8%) of T1DM children and adolescents had an overweight BMI, and 29 (87.9%) of them achieved their first OGC during follow-up. The median weight of patients was also found to be 35.9 ± 10.8 SD Kgs, while 9.8 Kgs was the minimum weight and 60.0 Kgs was the maximum weight during the last follow-up. More than half, 198 (53.1%) of T1DM children and adolescents had less than 2 years of DM; of those, 111 (56.1%) achieved their first OGC during the follow-up period. More than one-third, 137 (36.7%) of the study participants had a history of comorbidity; however, among those, 38 (27.7%) had more than one history of comorbidity. This study also showed that T1DM children and adolescents who had no history of infection were more likely to achieve a first OGC of 151 (70.2%) than their counterparts, 43 (27.2%) (Table 4).

Table 4: Clinical/Medicals characteristics of T1DM children and adolescents follow-up at public Hospitals in Borena zone, Southern Ethiopia, 2024.

Covariates	**Category**	**Event and Censored Status**		**Total**
		Event n (%)	**Censored n (%)**	
Duration DM category (years)	<2	111 (56.1%)	87 (43.9)	198 (53.1%)
	[2-4)	65 (50.4%)	64 (49.6%)	129 (34.6%)
	>=4	18 (39.1%)	28 (60.9%)	46 (12.3%)
BMI-Age weight status	Healthy Weight	112 (52.6%)	101 (47.4%)	213 (57.1%)
	Underweight	27 (30.3%)	62 (69.7%)	89 (23.9%)
	Overweight	29 (87.9%)	4 (12.1%)	33 (8.8%)
	Obesity	26 (68.4%)	12 (31.6%)	38 (10.2%)
History of comorbidity	Yes	68 (49.6%)	69 (50.4%)	137 (36.7%)
	No	126 (53.4%)	110 (46.6%)	236 (63.3%)
More than one history of co-morbidity	Yes	22 (57.9%)	16 (42.1%)	38 (27.7%)
	No	46 (46.5%)	53 (53.5%)	99 (72.3%)
Infection	Yes	43 (27.2%)	115 (72.8%)	158 (42.4%)
	No	151 (70.2%)	64 (29.8%)	215 (57.6%)

5.3. Treatment and Personal behavior characteristics of the study participants

The median dose of the current insulin regimen among type 1 diabetic children and adolescents was found to be 24.0 ± 9.8 SD IU/Kg/Day. T1DM children and adolescents currently on the NPH alone insulin regimen were given for the majority of the patients, 53.1%, during the follow-up of treatment, as compared to other regimens such as NPH with regular and premixed insulin (30/70 mixed insulin) (18%, 28.9%), respectively. Compliance with diabetic care was the most common (76.9%). Approximately three-fifths of the study individuals (57.1%) had less than or equal to four follow-up frequencies in the last year, with the median being 4.0 ± 1.5 SD frequencies of clinic visits (Table 5).

Table 5: Treatment and Personal behavior characteristics of T1DM children and adolescents follow-up at public Hospitals in Borena zone, Southern Ethiopia, 2024.

Covariates	Category	Event and Censored Status		Total
		Event n (%)	Censored n (%)	
Type of first insulin regimen	Non-premixed NPH and RI	16 (25.8%)	46 (74.2%)	62 (16.6%)
	Premixed NPH and RI	66 (68.0%)	31 (32.0%)	97 (26%)
	NPH alone	112 (52.3%)	102 (47.7%)	214 (57.4%)
Type of current insulin regimen	Non-premixed NPH and RI	11 (16.4%)	56 (83.6%)	67 (18%)
	Premixed NPH and RI	73 (67.6%)	35 (32.4%)	108 (28.9%)
	NPH alone	110 (55.6%)	88 (44.4%)	198 (53.1%)
Non-compliance to treatment	Yes	60 (69.8%)	26 (30.2%)	86 (23.1%)
	No	134 (46.7%)	153 (53.3%)	287 (76.9%)
Keep regular appointment	Yes	109 (44.7%)	135 (55.3%)	244 (65.4%)
	No	85 (65.9%)	44 (34.1%)	129 (34.6%)
Follow-up frequency	<=4	140 (65.7%)	73 (34.3%)	213 (57.1%)
	>4	54 (33.8%)	106 (66.2%)	160 (42.9%)

(Note: RI: Regular insulin)

5.4. Diabetes-Related complications characteristics of the study participants

Regarding complications, 56.6% of the patients had experienced more than one diabetes-related problem. The proportion of patients who achieved OGC is relatively higher among those with no more than one history of diabetes-related complications (71.7%) as compared to those with more

than one history of complications (70%). The majority of patients experienced DKA, 248 (66.5%), including episodes at diagnosis and during follow-up, followed by hypoglycemia (24.4%). Nearly three-fifths of 219 (58.7%) T1DM children and adolescents were hospitalized for DM-related reasons, with 100 (45.7%) achieving first OGC during the follow-up period (Table 6).

Table 6: Diabetes-related complications characteristics of T1DM children and adolescents follow-up at public Hospitals in Borena zone, Southern Ethiopia, 2024.

Covariates	**Category**	**Event and Censored Status**		**Total**
		Event n (%)	**Censored n (%)**	
DKA	Yes	112 (45.2%)	136 (54.8%)	248 (66.5%)
	No	82 (65.6%)	43 (34.4%)	125 (33.5%)
Hypoglycemia	Yes	54 (59.3%)	37 (40.7%)	91 (24.4%)
	No	140 (49.6%)	142 (50.4%)	282 (75.6%)
DM-related Hospitalization	Yes	100 (45.7%)	119 (54.3%)	219 (58.7%)
	No	94 (61.0%)	60 (39.0%)	154 (41.3%)
Other DM-related complications	Yes	73 (68.9%)	33 (31.1%)	106 (28.4%)
	No	121 (45.3%)	146 (54.7%)	267 (71.6%)
More than one other DM-related complications	Yes	42 (70.0%)	18 (30.0%)	60 (56.6%)
	No	33 (71.7%)	13 (28.3%)	46 (43.4%)

5.5. Time to first optimal glycemic control and Overall Kaplan-Meier survivor function of the study participants

A total of 373 children and adolescents with T1DM were enrolled in treatment and followed, of which 194 (52.01%) (95% CI: 46.9-57.1) achieved the first OGC during the follow-up period. In the analysis of children and adolescents with T1DM, 179 (47.99%) were censored. Among these, 116 (64.8%) completed the follow-up without achieving the first OGC, 3 (1.7%) died, 29 (16.2%) transferred to another health facility, and 31 (17.3%) were lost to follow-up by the end of the study period.

The total person-time risk of follow-up was 4389.26 person-months, with an incidence rate of the overall achieved first OGC rate of 4.42 (95% CI: 3.8-5.1) per 100 person-month observation. As shown in figure 4, the overall median survival time to first OGC was 14.3 (95% CI: 13-17) months with an interquartile range (IQR) of 7-33.7 months and a minimum and maximum follow-up time of 3 and 43.9 months. The median length of follow-up at hospitals was 7.9 months. On the Kaplan-Meier (KM) survival curve for time to first OGC of the children and adolescents on antidiabetics, the probability of survival decreases as the follow-up time increases. The overall KM estimate showed that the probability of survival among T1DM children and adolescents is high in the first ten months of diagnosis, which relatively falls as follow-up time increases (Figure 4).

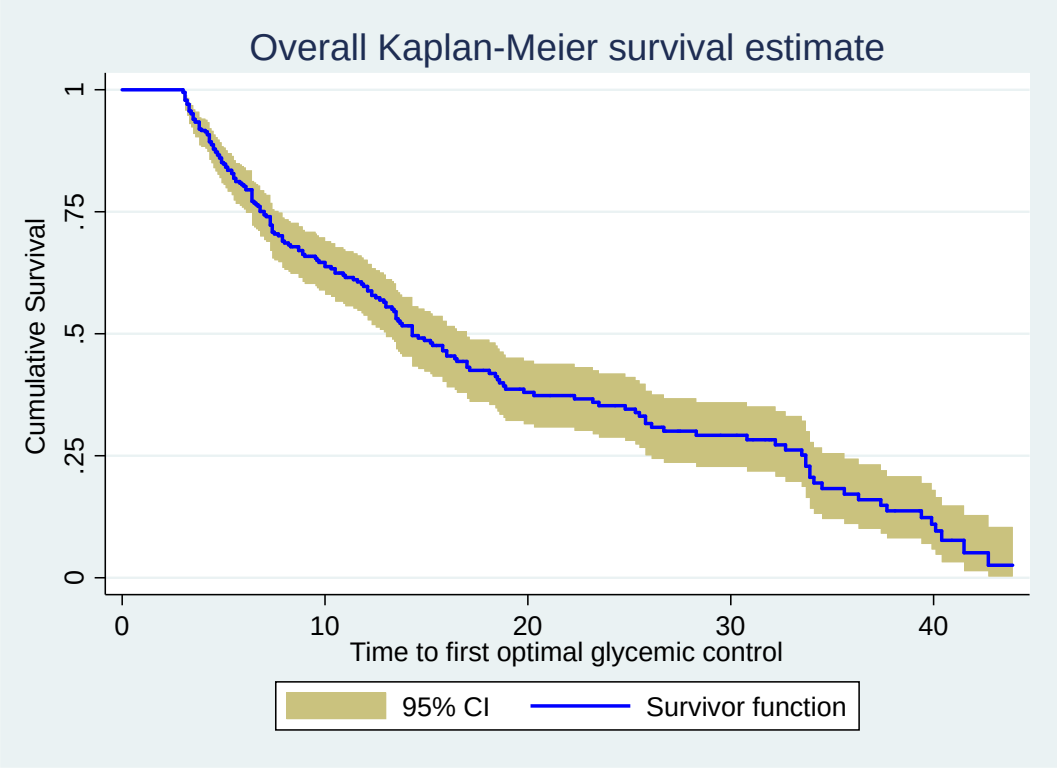


Figure 4: Overall KM estimation of survivor functions of T1DM children and adolescents follow-up at public Hospitals in Borena zone, Southern Ethiopia, 2024.

5.5.1. Comparison of Survivorship Functions for different categorical variables

The KM estimator survival curve provides an estimate of the survivor function among different categories of a covariate for comparison purposes. Separate graphs of the estimates of the KM survivor functions were created for each category covariate, as detailed below. The statistical question is whether the observed difference on the graph is significant or not. A log-rank test can help demonstrate this. The test statistics derived from the log-rank test revealed significant differences in the survival function (curve) for different categorical variables, as illustrated in Table 7. The graph below shows that survival rates differ significantly among the various categories.

In this study, the median time to achieve the first OGC varied across independent categorical variables. As shown in Figure 5, the median time to achieve the first OGC of female T1DM children and adolescents was longer than that of male T1DM: 25.8 months (95% CI: 14.9-33.5) and 12.9 months (95% CI: 10-14.3), respectively. This difference was statistically significant with a p-value of 0.0001.

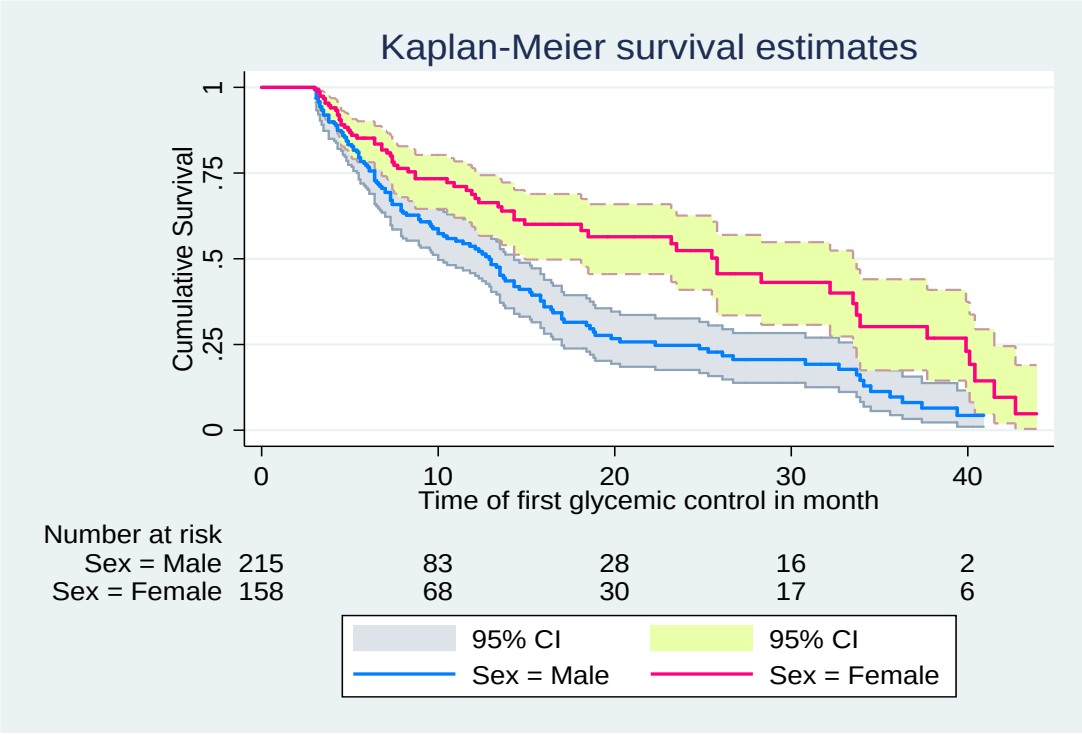


Figure 5: KM survival estimate for time to first OGC among T1DM children and adolescents with categories of sex at public hospitals in Borena zone, Southern Ethiopia, 2024.

Similarly, the median survival time to achieve the first OGC for those T1DM children and adolescents who lived in rural residence had a longer median survival time (15.8 months, 95% CI: 12.3-25.3) than those who lived in rural residence (13.6 months, 95% CI: 11.4-16.5). The difference was statistically significant at p = 0.0285 (Figure 6).

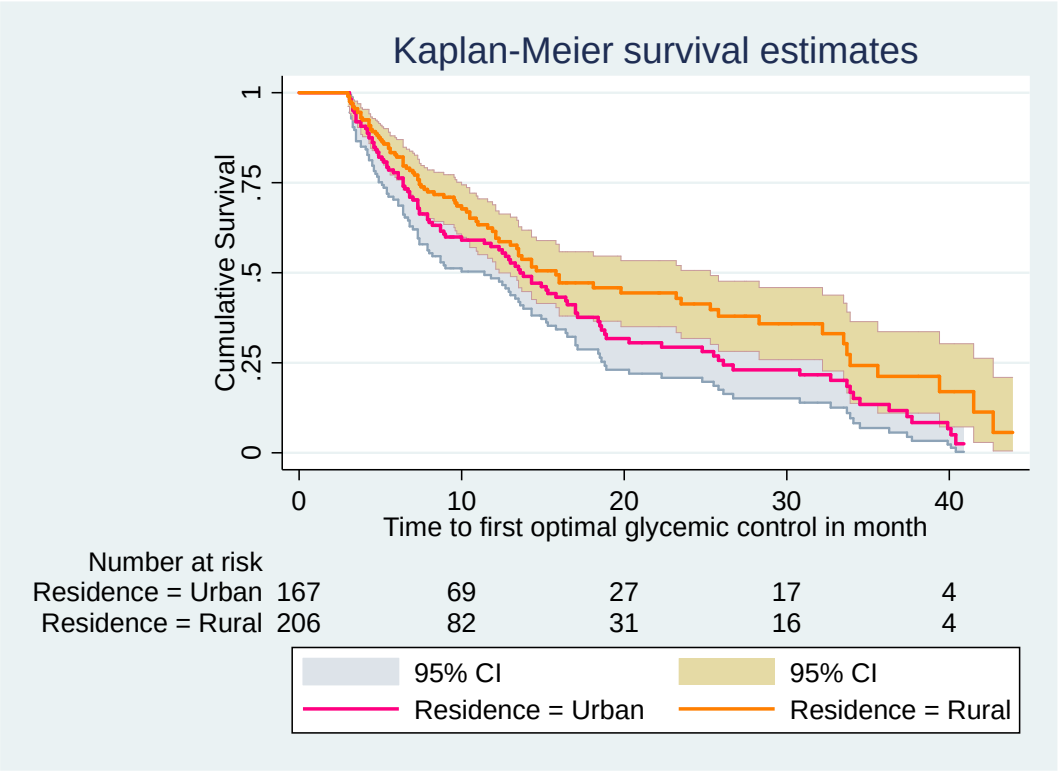


Figure 6: KM survival estimate for time to OGC among T1DM children and adolescents with categories of residency at public hospitals in Borena zone, Southern Ethiopia, 2024.

This study also revealed that T1DM children and adolescents who don't have health insurance had a longer median survival time to achieve first OGC than those who do (33.9 months, 95% CI: 14.9–37.7) and (13.4 months, 95% CI: 11.6–15.3), with p-values of <0.0001, respectively, as shown in the figure below (Figure 7).

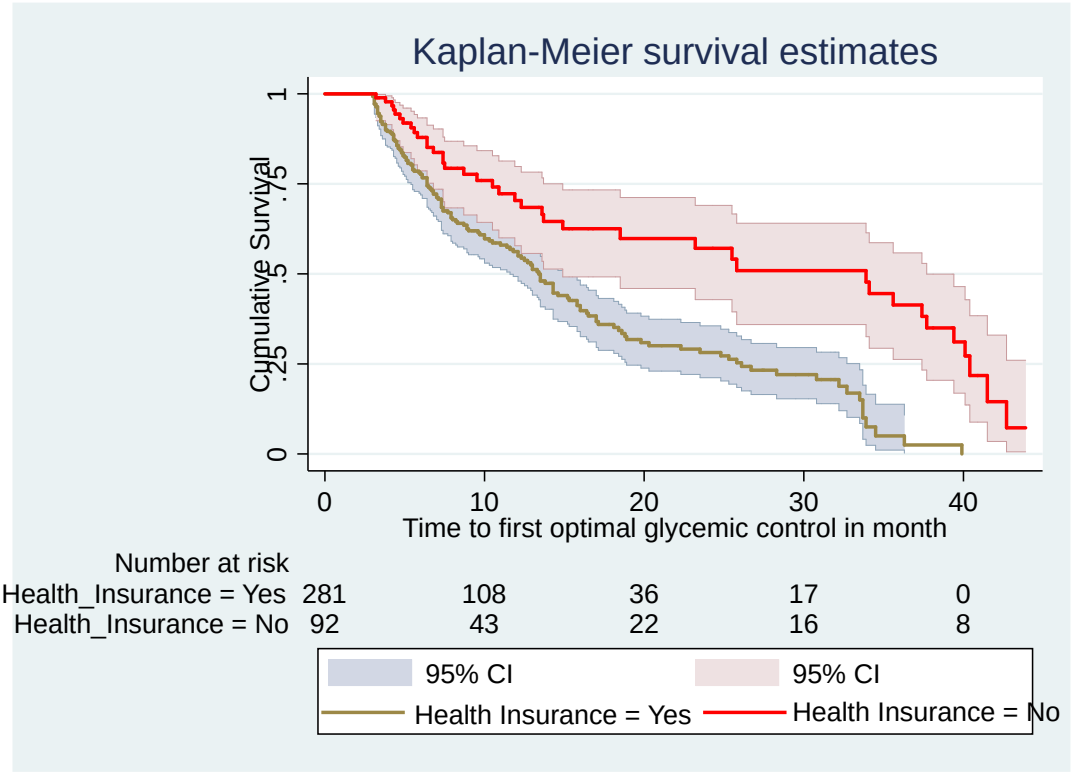


Figure 7: KM survival estimate for time to OGC among T1DM children and adolescents with categories of health insurance at public hospitals in Borena zone, Southern Ethiopia, 2024.

For T1DM children and adolescents with DKA during the follow-up period, the median survival time to attain first OGC was 17 months; for those without DKA during the follow-up period, it was 12.1 months. A p-value of 0.0008 indicated that the variance was significant (Figure 8).

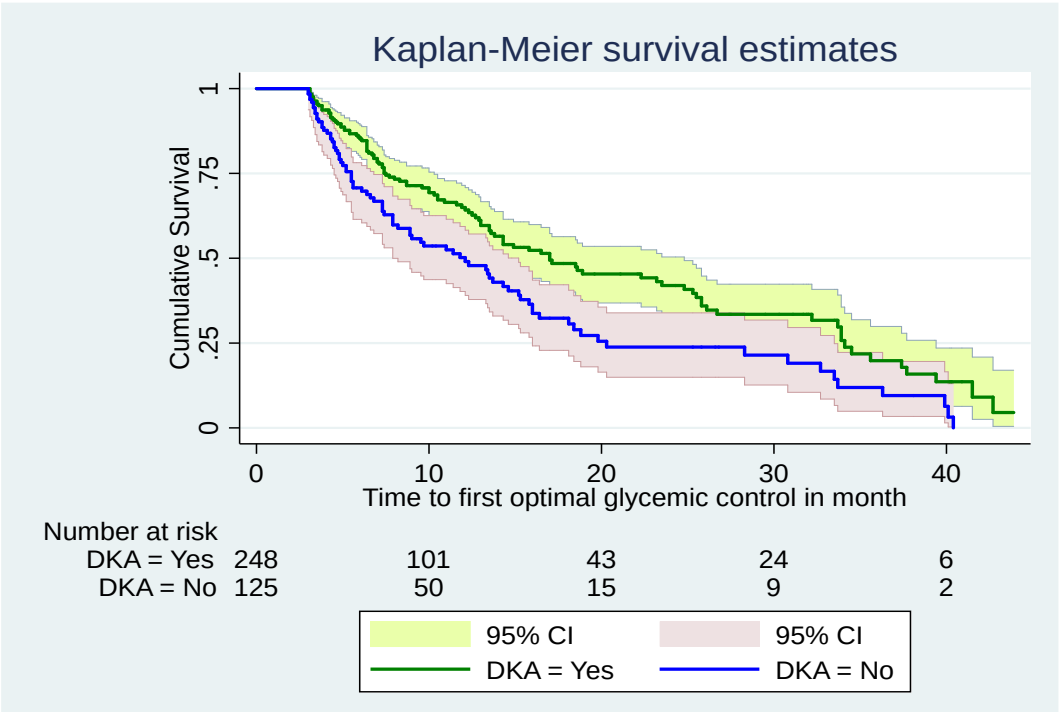


Figure 8: KM survival estimate for time to OGC among T1DM children and adolescents with categories of DKA at public hospitals in Borena zone, Southern Ethiopia, 2024.

Regarding the form of the current insulin regimen, there was also variation in the median time to attain first OGC among children and adolescents with type 1 diabetes. Non-premixed NPH and regular insulin were not observed at 0.5 median survival time, and children and adolescents with premixed NPH and regular insulin had a shorter median OGC time (12.3) than those with NPH alone (14.6 months) (Figure 9).

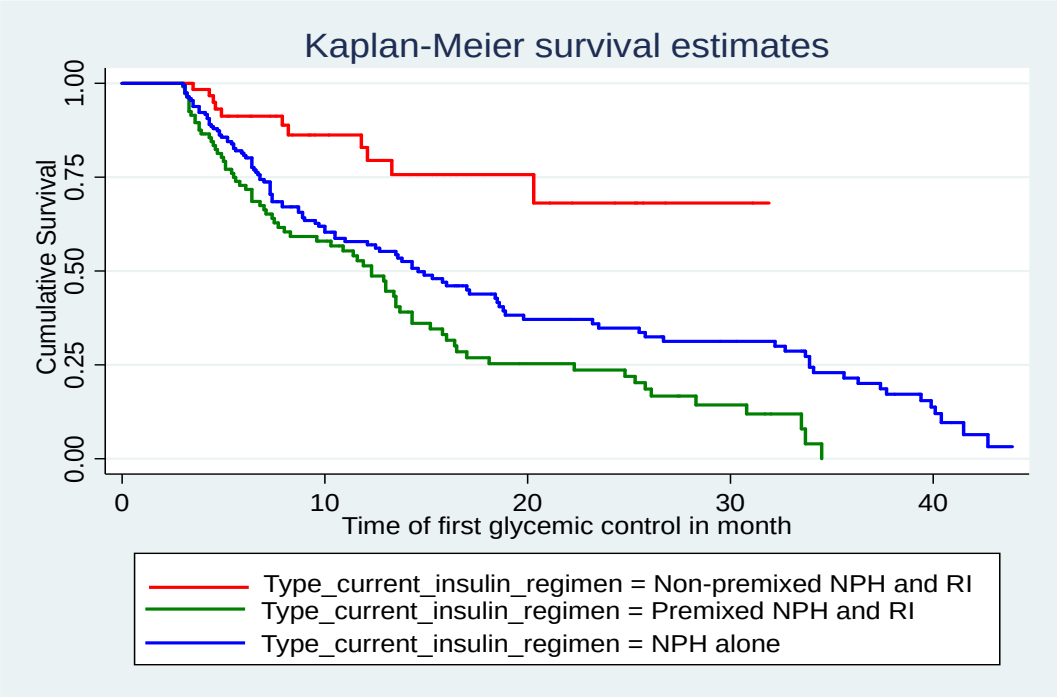
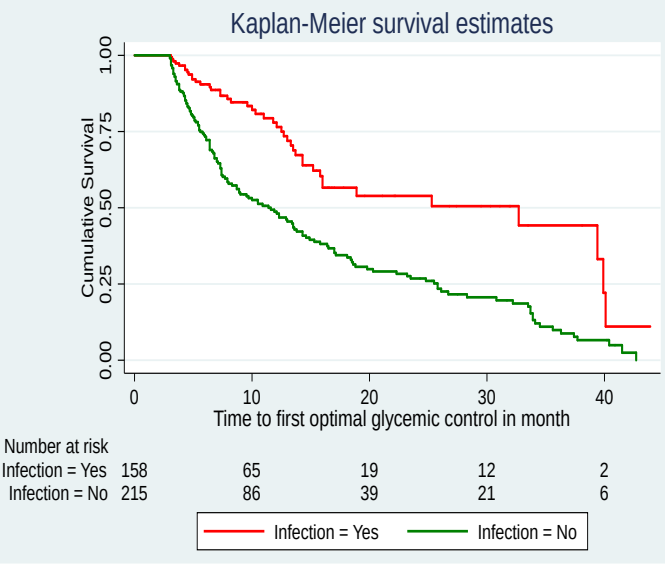


Figure 9: KM survival estimate for time to OGC among T1DM children and adolescents with categories of current insulin regimen at public hospitals in Borena zone, Ethiopia, 2024.

Similarly, children and adolescents with an infection diagnosis and fewer than or equal to four follow-up frequencies had a higher median survival time to OGC than those without an infection diagnosis and with more than four follow-up frequencies; this difference in survival time was statistically significant (p-value = <0.0001 and 0.0007, respectively) (Figure 10).



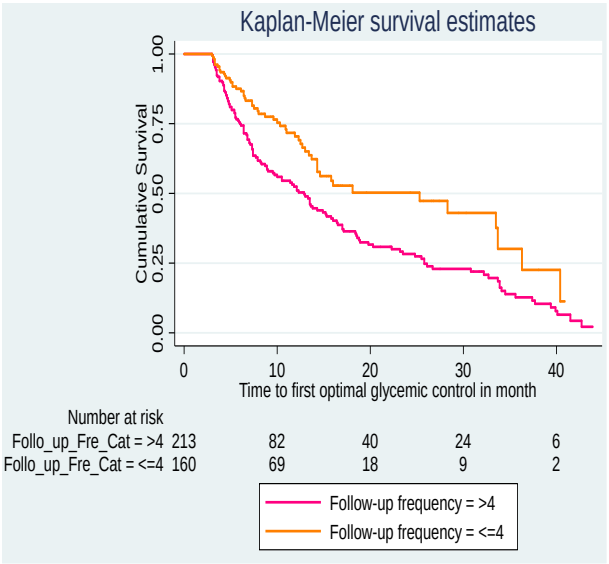


Figure 10: KM survival estimate for time to OGC among T1DM children and adolescents with categories of infection and follow-up frequency at hospitals in Borena zone, Ethiopia, 2024.

Accordingly, the KM analysis indicated significant evidence of differences in survival times in the categories, and the log-rank test is statistically significant (p-value <0.05). This indicates that there is sufficient data to conclude that, with respect to categories of significant covariates, the enrollment of T1DM children and adolescents in antidiabetic survival curves (KM curves) differs significantly. Table 7 below shows that the smallest median time to achieve first OGC was 8.9 months (95% CI: 5.5-18.6) for children and adolescents with an obese BMI, with a p-value of 0.0044, and the highest median time to achieve first OGC was 33.9 months for those who had an absence of health insurance (Table 7).

Table 7: Median and Mean survival time and log-rank test for equality of survivor functions among T1DM children and adolescents follow-up at hospitals in Borena zone, Southern Ethiopia, 2024.

Covariates	**Category**	**Survival time to first OGC**		**Log-rank test**	
		Median (95% CI)	**Mean (95% CI)**	**X^2**	**P-value**
Sex	Male	12.9 (10,14.3)	16.0 (14.1,17.9)	16.12	0.0001
	Female	25.8 (14.9,33.5)	24.0 (20.9,27.0)		
Residence	Urban	13.6 (11.4,16.5)	17.1 (14.9,19.4)	4.80	0.0285
	Rural	15.8 (12.3,25.3)	21.2 (18.5,23.9)		
Presence of health Insurance	Yes	13.4 (11.6,15.3)	16.4 (14.7,18.1)	21.25	<0.0001
	No	33.9 (14.9,37.7)	26.2 (22.3,30.0)		
Duration DM	<2	13.3 (10,15.3)	17.7 (15.3,20.2)	3.05	0.2178

(years)	[2-4)	17.0 (13.5,25.8)	20.6 (17.7,23.5)		
	>=4	18.9 (7.5,33.7)	21.1 (15.6,326.6)		
BMI-Age Weight status	Healthy Weight	13.5 (12.1,16.5)	17.5 (15.4,19.6)	13.13	0.0044
	Underweight	25.8 (14.6.)	25.9 (21.2,30.6)		
	Overweight	12.7 (7.3,23.5)	18.9 (14.0,23.8)		
	Obesity	8.9 (5.5,18.6)	14.6 (10.1,19.1)		
History of comorbidity	Yes	17.0 (12.7,26.7)	21.5 (18.5,24.5)	3.70	0.0543
	No	13.6 (10.5,16)	17.7 (15.6,19.8)		
Infection	Yes	32.7 (15.8,39.9)	26.0 (22.5,29.6)	26.91	<0.0001
	No	11.6 (8.3,13.8)	15.9 (14.1,17.8)		
Type of first insulin regimen	Non-premixed NPH and RI	32.7 (14.6.)	25.8 (20.3,31.2)	7.82	0.0200
	Premixed NPH and RI	13.5 (11,16)	17.4 (14.6,20.3)		
	NPH alone	13.6 (10.5,17.13)	18.5 (16.1,20.9)		
Type of current insulin regimen	Non-premixed NPH and RI	NA	25.4 (22.0,28.8)	24.52	<0.0001
	Premixed NPH and RI	12.3 (8,13.7)	14.4 (12.2,16.6)		
	NPH alone	14.6 (11,18.6)	19.5 (17.0,21.9)		
Keep regular appointment	Yes	16.0 (13.6,23.2)	20.4 (18.1,22.8)	4.11	0.0427
	No	12.3 (8.2,15.8)	17.0 (14.4,19.7)		
Follow-up frequency	>4	12.9 (9.5,15.2)	16.9 (14.9,18.9)	11.48	0.0007
	<=4	25.3 (14.3,33.7)	23.1 (19.9,26.3)		
DKA	Yes	17.0 (13.6,24.8)	21.0 (18.7,23.4)	11.23	0.0008
	No	12.1 (7.9,15.2)	15.7 (13.1,18.2)		
Other DM-related complications	Yes	13.5 (8.7,17)	17.6 (14.7,20.5)	1.44	0.2297
	No	15.3 (13,18.8)	19.7 (17.5,22.0)		

(Note: X^2: chi-square; CI: confidence interval; P-value: level of significance at <0.05; NA: not applicable)

5.6. Predictors of time to first optimal glycemic control among type 1 diabetes

The relationship between the independent and outcome variables was analyzed using the Cox PH regression model. In the bivariate Cox PH regression analysis, the sex, residence, presence of health insurance, BMI, history of comorbidity, infection, type of initial insulin regimen, type of current insulin regimen, keeping regular appointments in the last year, DKA, other DM complications, duration of DM, and follow-up frequency/clinic visits in the last year were significantly associated with time to first OGC at p-value ≤0.25. In multivariate Cox PH regression analysis, those variables with p-values ≤0.25 in the bivariate analysis and non-collinear independent variables were included. But the presence of health insurance, history of comorbidity, type of current insulin regimen, DKA, and follow-up frequency/clinic visits in the last year showed statistical significance and were declared to be independent predictors of time to first OGC among T1DM children and adolescents in a multivariable Cox PH regression model with less than 5% level of significance.

In the multivariable Cox PH model, five variables were associated with time to first OGC for children and adolescents on antidiabetic care. Accordingly, after adjusting for other predictors, the rate of achieving first OGC among the patients without health insurance was 43.4% lower than among patients with health insurance (AHR: 0.566, 95% CI: 0.356-0.902). Similarly, the hazard of achieving first OGC among patients with a history of comorbid illness was lower by 34.6% compared to patients with no history of comorbid illness (AHR: 0.654, 95% CI: 0.451–0.949). This study found that T1DM children and adolescents currently taking a pre-mixed NPH and regular insulin regimen (30/70 mixed insulin) had a 3.76-times earlier first OGC as compared to those currently taking a non-premixed NPH and regular insulin regimen (AHR: 3.76, 95% CI: 1.48–9.565). In addition, T1DM children and adolescents who had follow-up frequencies less than or equal to four in the last year had a 36.7% lower rate of first OGC as compared to those with more than four follow-up frequencies (AHR: 0.633, 95% CI: 0.421-0.953). Furthermore, the rate of achieving first OGC among T1DM children and adolescents with DKA was 46.2% lower than those without DKA (AHR: 0.538, 95% CI: 0.370-0.782) (Table 8).

Table 8: Results of bivariate and multivariable Cox PH regression model among T1DM children and adolescents follow-up at public hospitals in Borena Zone, Southern Ethiopia, 2024 (n=373).

Covariates	Category	CHR (95%CI)	P-value	AHR (95%CI)	P-value
Sex	Male®	1			
	Female	0.540 (0.398,0.734)	<0.0001	0.721 (0.467,0.902)	0.140
Residence	Urban®	1			
	Rural	0.729 (0.549,0.969)	0.030	0.949 (0.668, 1.348)	0.771
Presence of health Insurance	Yes®	1			
	No	0.407 (0.275,0.603)	<0.0001	**0.566 (0.356, 0.902)**	**0.017**
Duration DM (in years)	<2®	1			
	[2-4)	0.767 (0.564,1.04)	0.092	0.919 (0.656, 1.288)	0.626
	>=4	0.818 (0.497,1.35)	0.432	0.940 (0.545, 1.622)	0.826
BMI-Age Weight status	Healthy Weight®	1			
	Underweight	0.519 (0.341,0.793)	0.002	0.644 (0.412, 1.008)	0.054
	Overweight	0.859 (0.561,1.32)	0.487	1.31 (0.771, 2.221)	0.319
	Obesity	1.29 (0.841,1.98)	0.243	1.24 (0.685, 2.243)	0.478
History of comorbidity	Yes	0.747 (0.554,1.01)	0.056	**0.654 (0.451, 0.949)**	**0.025**
	No®	1			
Infection	Yes	0.419 (0.299,0.589)	<0.0001	0.660 (0.428, 1.018)	0.060
	No®	1			
Type of first insulin regimen	Non-premixed NPH and RI®	1			
	Premixed NPH and RI	2.14 (1.24,3.71)	0.006	0.771 (0.331, 1.792)	0.545
	NPH alone	1.89 (1.12,3.19)	0.018	0.949 (0.404, 2.229)	0.905
Type of current insulin regimen	Non-premixed NPH and RI®	1			
	Premixed NPH and RI	4.14 (2.19,7.80)	<0.0001	**3.76 (1.482, 9.565)**	**0.005**
	NPH alone	2.67 (1.42,4.99)	0.002	2.22 (0.868, 5.719)	0.096
Keep regular appointment	Yes®	1			
	No	1.34 (1.01,1.78)	0.044	0.909 (0.581, 1.424)	0.678

Follow-up Frequency	>4®	1			
	<=4	0.583 (0.425,0.801)	0.001	**0.633 (0.421, 0.953)**	**0.029**
DKA	Yes	0.617 (0.463,0.821)	0.001	**0.538 (0.370, 0.782)**	**0.001**
	No®	1			
Other DM-related complications	Yes	1.2 (0.892, 1.60)	0.232	1.35 (0.943, 1.924)	0.101
	No®	1			

(Note: Those bold numbers above showed significantly associated predictors of time to first OGC; AHR: adjusted hazard ratio; CHR: crude hazard ratio; ®: Reference group; CI: confidence interval; P-value: level of significance at <0.05).

5.7. Test of Proportional Hazard Assumption

Based on binary and multicollinearity outcomes, testing proportional hazard assumptions is vital for the interpretation and use of fitted proportional hazard models and accepting multivariate analysis results. Therefore, in this study, goodness-of-fit (GOF), particularly the Schoenfeld residuals proportional hazard assumption test for the individual covariates, and global tests were done after running a multivariable Cox regression model. If the P-value < 0.05, then the proportional hazard assumption is rejected. From Table 9, observe that each covariate (p-value > 0.05) and all of the covariates simultaneously (global test for Cox PH p-value = 0.5286 > 0.05) met the PH assumption (Table 9).

Table 9: Schoenfeld Residuals test for Cox PH Regression model assumption of each variable for T1DM children and adolescents follow-up at public hospitals in Borena Zone, Ethiopia, 2024.

Covariates	***RHO***	***X^2***	***DF***	**P-value**
Sex	-0.04113	0.31	1	0.5756
Residence	-0.04222	0.38	1	0.5399
Health Insurance	-0.13271	3.38	1	0.0659
Duration DM category	0.11088	2.47	1	0.1159
BMI	-0.04202	0.35	1	0.5524
History of comorbidity	-0.00944	0.02	1	0.8882
Infection	0.00006	0.00	1	0.9993
Type of first insulin regimen	-0.07426	0.93	1	0.3342
Type of current insulin	0.06792	0.67	1	0.4134

regimen				
Keep regular appointment	-0.04427	0.33	1	0.5666
Follow-up frequency	-0.03770	0.28	1	0.5998
DKA	-0.01254	0.03	1	0.8591
Other DM-related complications	0.04618	0.39	1	0.5315
Global Test		11.99	13	**0.5286**

(Note Rho: Rho is the correlation coefficient between the residuals and time, X^2: Chi square, DF: Degree of freedom).

5.8. Multicollinearity Test

The predictor variable in a multiple Cox regression model can be linearly predicted by the others with a considerable degree of accuracy. Multicollinearity occurs when predictor covariates in the Cox regression model are correlated. This correlation is a problem because the relationship between each predictor variable and the outcome variable should be independent. Multicollinearity can be checked by calculating the VIF for each predictor variable (based on binary Cox regression outcome). According to some guidelines, a VIF value less than 10 is considered an acceptable collinearity level. However, a VIF value greater than 4 needs further investigation. In this study, the maximum VIF value was 3.80, with a mean VIF of 1.83. Therefore, there was no multicollinearity, and it can interpret the results of this study (Table 10).

Table 10: Multicollinearity check for each variable based on binary outcome (p-value <0.25) to T1DM children and adolescents follow-up at public hospitals in Borena Zone, Ethiopia, 2024.

Covariates	***VIF***	***1/VIF (Tolerance)***
Type of first insulin regimen	3.80	0.262880
Type of current insulin regimen	3.59	0.278211
Keep regular appointment	1.76	0.567130
Follow-up frequency	1.71	0.583960
Other DM-related complications	1.52	0.659804
BMI	1.51	0.661858
Infection	1.50	0.668451
History of co-morbidity	1.44	0.696718
DKA	1.43	0.700614

Residence	1.34	0.745123
Health Insurance	1.26	0.793421
Duration DM category	1.04	0.959647
Mean of VIF	**1.83**	

5.9. Cox-Snell residuals Test

The Cox-Snell residuals test is used to assess the overall goodness of fit in survival models. It is done graphically with the usual graphs of Cox-Snell, and it is observed that residuals from a correctly fitted model follow an exponential unit distribution along the 45-degree slope (baseline). It is used to identify extreme observations that need additional investigation. In this study, the hazard function follows the 45-degree line close to the baseline. It showed that the multivariable Cox regression model is well fitted for the analysis and interpretation of the results of this study (Figure 11).

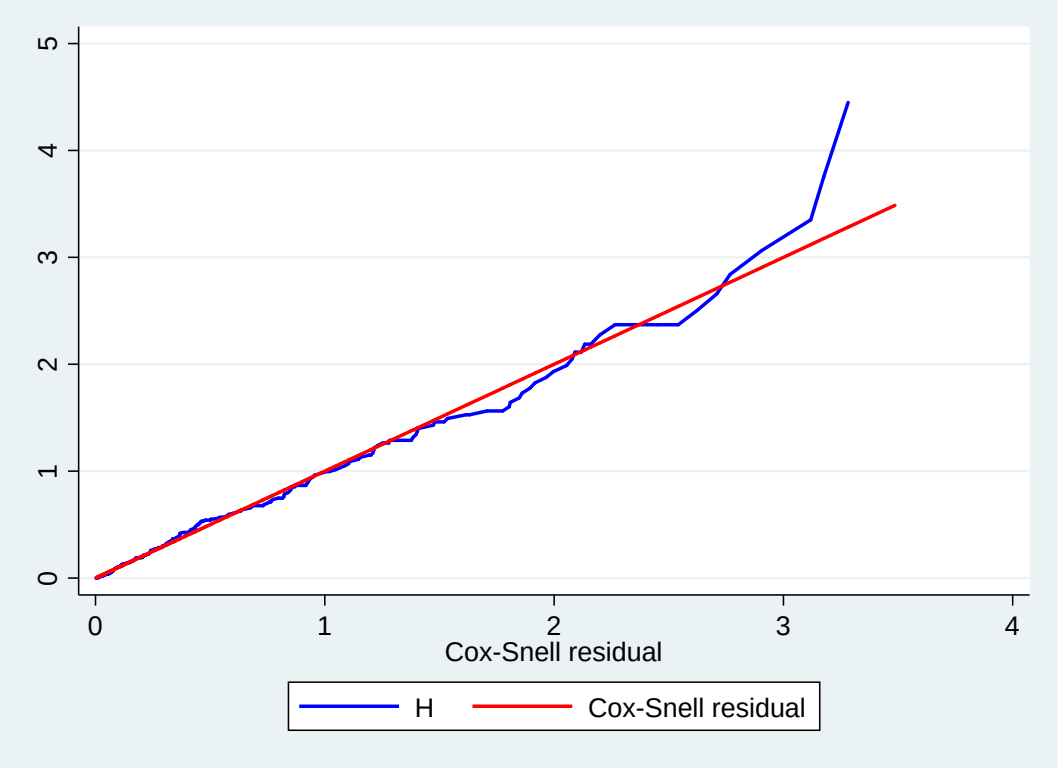


Figure 11: Cox-Snell residual Nelson-Aalen cumulative hazard graph on T1DM children and adolescents follow-up at public hospitals in Borena Zone, Southern Ethiopia, 2024.

6. DISCUSSION

This retrospective follow-up study aimed to determine the time to first optimal glycemic control and its predictors among type 1 diabetes children and adolescents followed up at public hospitals in the Borena zone, Southern Ethiopia. This study revealed that the overall median survival time for achieving first OGC among T1DM children and adolescents during the follow-up period was 14.3 months, with an IQR of 7–33.7 months. Furthermore, the time to first OGC of type 1 diabetic children and adolescents was significantly associated with predictors such as health insurance, having comorbid illness, type of current insulin regimen, follow-up frequency to diabetic care, and DKA.

The current study found that the median survival time to achieve first OGC among T1DM children and adolescents was 14.3 months, significantly higher than the previous study conducted in Bahir Dar and Addis Ababa, Ethiopia, which reported median survival times were 8 months (43) and 9.5 months (16), respectively. The disparity in results could be attributed to the Borena zone, which is a rural area, and pastoralists having less access to specialized diabetes care facilities and resources than the more urban settings of Addis Ababa and Bahir Dar, Ethiopia. Another possible explanation for this discrepancy is that the availability and quality of diabetes care services, such as access to specialized healthcare providers (pediatricians and pediatric residents), diagnostic tools, availability of comorbidity screening tools, and treatment options, may differ between study settings, leading to variations in time to achieve OGC. There was also a variation in the age of the study participants; currently, the study included both children and adolescents.

The present study showed that the time needed to reach first OGC is longer among patients with absence of health insurance as compared to patients having health insurance, indicating that for T1DM patients, the rate of achieving OGC decreases by 43.4% for those with absence of health insurance. This finding is in line with the previous study conducted in southern Ethiopia (54). The possible reason might be that patients without health insurance may face significant barriers in accessing the necessary diabetes care, including regular check-ups, blood glucose monitoring supplies, and other essential medications. This could be attributable to the lack of health insurance coverage, which means that patients have to bear the full out-of-pocket costs for their diabetes care, including the expenses for medications, devices, and healthcare visits. This could be linked to the financial burden, which can be a significant deterrent, leading to delayed or skipped treatments, which ultimately affects their ability to reach and sustain glycemic targets. Furthermore, disruptions

in care continuity and irregular follow-up visits can make it more difficult to closely monitor and adjust the treatment plan to achieve OGC (77).

According to the current study, the hazard of achieving first OGC among T1DM patients with a history of comorbid illness is reduced by 34.6% compared with T1DM patients without such a history. This result is consistent with a study carried out in Bahir Dar, Ethiopia, which discovered that those with a history of comorbid illness were 27.8% less likely to achieve OGC than patients without such a history (43). Also, a study conducted in Addis Ababa revealed that patients with a history of comorbid conditions such as cardiovascular disease, hypertension, and dyslipidemia were less likely to reach OGC than those without such disorders by 38.9%, 39.1%, and 33.0%, respectively (16). This is due to the fact that comorbid conditions influence the course of diabetes, and GC impairment may result from alterations in glucose metabolism. Additionally, taking multiple medications can have the effect of causing drug interactions and decreasing adherence, which can interfere with the effectiveness of medications. Acute comorbid illness may further exacerbate diabetes by increasing counterregulatory hormone levels, which prevent insulin from lowering blood sugar levels via gluconeogenesis and glycogenolysis (73).

In regard to insulin regimens, T1DM children and adolescents currently using premixed NPH and regular insulin regimens are another important predictor that can affect time to OGC. The rate of achieving OGC among patients currently using premixed NPH and regular insulin (30/70 mixed insulin) was 3.76 times more likely as compared with patients currently using non-premixed NPH and regular insulin, which is comparable with a study done in Shantou, China (64). This might be because premixed insulin formulations (30/70 Regular/NPH) combine long-acting and short-acting components in a single injection; simplifying administration can improve adherence and reduce dosing errors. This is beneficial for children and adolescents, as they are less likely to forget or skip doses. This combination mimics the body's natural insulin secretion patterns; improved insulin pharmacokinetics can lead to better postprandial glucose control and reduced glycemic variability. Minimizing glycemic fluctuations is crucial for maintaining OGC and preventing hyperglycemic and hypoglycemic episodes (78).

However, according to a Tanzanian study, children and adolescents with type 1 diabetes who were currently on non-premixed regular and NPH insulin regimens had a 1.3-fold higher chance of achieving OGC than those who were on premixed NPH plus regular insulin (27). Separate insulin, which offers greater flexibility during mealtimes than combined insulin, could be the cause of the results' variation.

Also, patients with fewer than or equal to four follow-up frequencies to their diabetes care had a 36.7% likelihood of experiencing a decline in their glycemic achievement rate as compared to patients with more than four follow-up frequencies to their diabetic care. This study is supported by a retrospective cohort study done in La Rabta Hospital, Tunisia (22). The possible justifications may be that the frequent follow-up visits may improve healthcare engagement, facilitate timely adjustments to treatment plans, medication doses, and self-management strategies, and give comprehensive diabetes education, counseling, and adherence support. This also allows for closer monitoring of potential complications or disease progression, preventing or delaying the development of acute or chronic complications that can impact glycemic achievement (79).

In addition to the above predictors, the current study revealed that in T1DM children and adolescents with a history of DKA, the rate of achieving first OGC was 46.2% lower than that of those with no history of DKA. This finding is consistent with a study conducted in India (55) and Assiut University in Egypt (68). This may be explained by the fact that DKA is characterized by severe hyperglycemia, metabolic acidosis, and electrolyte imbalances, which can significantly disrupt the body's normal physiological processes. These profound metabolic derangements can impair insulin sensitivity, glucose homeostasis, and overall metabolic regulation. This increased insulin resistance can impair the body's ability to effectively utilize insulin, even with appropriate insulin therapy, making it more challenging to achieve OGC (80). The other justification might be that DKA episodes are associated with an increased risk of developing various acute and chronic complications, such as cerebral edema, renal dysfunction, and long-term microvascular complications. The presence of these complications or the increased risk of their development can further complicate the achievement of OGC (81).

7. STRENGTH AND LIMITATION OF THE STUDY

7.1. Strength

The study includes two randomly selected hospitals, which are multicenter; the finding can have more power in regard to generalizability. The data were collected by nurses who trained for chronic care, including diabetes, which has an essential role in ensuring data quality. The data were gathered from five consecutive years of diagnoses/observations, which might increase the number of events and decrease variability, and it could help to see the long-term effect of the anti-diabetes drugs.

7.2. Limitation

Since the study was conducted using secondary sources, some important covariates that could not be obtained from the medical records were missing. The medical records that were incomplete or lost at the time of data collection were excluded. These possibly introduce selection bias that results in underestimation or overestimation of the findings of the result. But this is to imply that there were only 3 records lost from the hospital's record center, 2 less than 3 months of follow-up during the study period, and 5 incomplete records.

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

8. CONCLUSION AND RECOMMENDATION

8.1. Conclusion

The overall median survival time to first optimal glycemic control among type 1 diabetic children and adolescents in the study area was much longer than what the ADA recommended, implying that children and adolescents diagnosed with T1DMs achieve optimal glycemic control within three months following their diagnosis and start treatment. It indicates that patients are unprotected against both acute and chronic complications of T1DM. This increased risk remains higher for those patients achieving their glycemic control over a long period of time compared to those who achieved optimal glycemic control over a short period of time.

This study also showed that absence of health insurance, having comorbid illness, type of current insulin regimen, follow-up frequency to diabetic care, and DKA were statistically significant predictors of time to first optimal glycemic control among type 1 diabetic children and adolescents in the study area.

8.2. Recommendation

Even though the quality of health care service expanded, especially for chronic care, type 1 diabetes children and adolescents time to first optimal glycemic control is still a concerning issue in the study area as well as in Ethiopia. Based on the findings of this study, the following recommendations were forwarded to the concerned body.

To the federal minister of health and other stakeholders

By promoting health education at the community level and through the use of mass media, implement educational programs for families on how to recognize early signs of DKA and the significance of adhering to follow-up frequency. This will help families and/or caregivers of children, particularly those who are presented with the new onset of DM, recognize the signs and symptoms of DKA and seek healthcare early. T1DM children and adolescents should receive integrated child-adolescent care, particularly in pastoral and agro-pastoral settings like this study area.

Advocate for policies that expand health insurance coverage for children and adolescents with type 1 diabetes. Promoting the adoption of standardized insulin regimens that include premixed NPH and regular insulin by providing clear guidelines can help healthcare providers optimize treatment plans, leading to better GC.

Develop initiatives to ensure that diabetic children and adolescents have at least four follow-up appointments per year. Regular check-ups enable timely adjustments in treatment and better management of diabetes. Create integrated care models that address both diabetes management and comorbid conditions. Comprehensive care can enhance overall health and improve the quality of life for affected children and adolescents with diabetes. Investigate more studies on factors that affect time to the first OGC, ensure proper implementation of developed strategies, establish T1DM treatment guidelines for children and adolescents, and regularly modify them depending on best practices and the latest research findings.

To health care providers

Regardless of how long a patient has had diabetes, healthcare professionals should place a strong emphasis on managing comorbid conditions in an appropriate, integrated way. The diabetes adherence team should take proactive steps to educate patients and/or caregivers about the value of frequent follow-up care, evaluating their status at least four times a year, screening for concomitant conditions at each visit, and managing appropriately.

Effective insulin regimens, including the use of premixed NPH and regular insulin, should be strongly prioritized by healthcare professionals and customized according to the needs of each patient. Make follow-up appointments on regular schedules with at least four visits per year, and motivate families to make these visits as frequently as possible. DKA can be identified and managed early on, improving health outcomes and reducing complications, by enhancing involvement and giving clear direction.

To parents or caregivers of children and adolescents

Children and adolescents should not miss follow-up appointments on a regular basis in order to minimize missing any package of care in diabetes clinics. Parents of children and adolescents should, as much as feasible, enroll in community-based health insurance (CBHI) to receive free treatment and ensure continuity of care.

To future researchers

Conduct further studies through prospective follow-up studies by including additional significant variables that were not included in this study (difficult to access only through patient medical record review).

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ANNEXES

Annex I: Information sheet and informed consent form for public Hospitals medical director/CEO

My name is Kubsa Guyo. I am studying for a Masters' degree in Pediatrics and Child Health Nursing at Salale University, College of Health Science. I kindly request that you give me your attention to explain the study and your health institution being selected as the study setting.

Name of the Organization: Salale University College of Health Science, Department of Nursing.

Title of the study

Time to first optimal glycemic control and its predictors among type 1 diabetes children and adolescents follow-up at public hospitals in Borena zone, Oromia, southern Ethiopia, 2024.

Purpose/aim of the study

The study was conducted through a collection of secondary data already collected on the patient's chart (card) and DM logbook register, and the aim of this study was to write a thesis as a partial requirement for the fulfillment of a Masters' degree program in pediatrics and child health nursing for the principal investigator. The study's findings will help the hospital understand the time to optimal glycemic control gap among type 1 diabetes children and adolescents and its common predictors.

Data collection procedure and duration

I was review records of type 1 diabetes children and adolescents using a data retrieval form to obtain pertinent data that was deemed helpful for the study. There were 30 questions, and I was fill out the data retrieval form by reviewing records. The review of each record may take 15–25 minutes to collect data for a single chart.

Risks and benefit of the study

The risk of reviewing in this study was minimal; the only assumed risk was time loss by data collectors during data collection, which was only take a few minutes from the patient's card or database and follow-up charts being used by hospitals. There was not any direct payment for reviewing this study. The findings from this study might contribute to the body of knowledge that informs hospital and child and adolescent program planners and decision-makers.

Confidentiality

The information collected as explained above will be kept confidential. To assure privacy, the information on the charts were collected by excluding the names of the clients, and the information collected from this study development was kept private and stored in a file cabinet. In addition, it

was not shown to anyone except the investigator, and it has been kept in a locked system with a computer password. The study's findings were general for the study community and was not reflect anything particular about individuals.

Rights

Participation in this study is voluntary. Your hospital has the full right to declare whether or not it is reviewing the records. If you have allowed me to review the records, you also have the full right to withdraw from the study at any time if any problem is perceived.

Contact address

This study's development was revised and approved by Salale University's College of Health Science, Department of Nursing. If there is any question or inquiry about the study or procedures at any time, please contact any of the following individuals (investigator and advisors) using the following addresses:

Principal investigator: Kubsa Guyo Boru

Cell phone: +251-986970406

E-mail: kubsaguyo452@gmail.com

Main Advisor: Mr. Mathewos Mekonnen (Assistant professor) Salale University, College of Health Science, Department of Pediatrics and Child Health Nursing.

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Co-advisor: Mr. Asfaw Getaye (BSc, MSc) Salale University, College of Health Science, Department of Nursing.

Mobile: +251-9_____

E-mail: _____

Declaration of informed voluntary consent

I have read the participant information sheet. I have clearly understood the purpose of the research, the procedures, the risks and benefits, the confidentiality issues, the rights to participate, and the contact address for any queries. I have been given the opportunity to ask questions about things that may have been unclear. I was informed that the hospital has the right to withdraw from the study at any time. I was also informed that the hospital has the right to stop this study from being conducted if any unethical procedures are observed during the data collection process on the hospital's premises. Therefore, I declare my voluntary consent on behalf of _____hospital management to allow this study to be conducted in the hospital with my signature.

Name of medical director/CEO: _____Signature _____ Date_____

Name of data Principal investigator: _____Signature _____ Date_____

Annex II: Checklist

This is a checklist set to collect information on time to first optimal glycemic control and its predictors among type 1 diabetes children and adolescents in Borena zone public hospitals, Oromia, southern Ethiopia, 2024.

Instructions: First, introduce yourself and talk about the objectives of the study, then request that you review the selected records of type 1 diabetes children and adolescents. Finally, fill in all individual information from the patient record on the checklist correctly. Please write the required information clearly and completely.

Data collection date ----------month----------Year----------

Name of the Hospital ----------

Name of data collector ---------- signature----------

Name of supervisor ----------signature----------

Data extraction format ID. No ----------

SECTION I: **Socio-demographic Related Predictors.**

NO.	Questions	Coding and Categories	Remark
101	Date of enrolment to DM care	___/____/___ /DD/MM/YY	
102	Age at enrolment/diagnosed	(_____) year or (_____) month	
103	Sex	1. Male 2. Female	
104	Residence	1. Urban 2. Rural	
105	Presence of Health Insurance	1. Yes 2. No	
106	Family history of diabetes	1. Yes 2. No	
107	Hospital in which the data obtained	1. Yabelo Hospital 2. Moyale Hospital	

SECTION II: Clinical/Medicals Related Predictors.

NO.	Questions	Coding and categories	Remark
201	Duration of DM	_____ in years	
202	Latest follow-up Weight and Height/length	Weight _____ Kg Height/length _____cm	

		or _____m	
203	BMI-Age Weight status in the latest clinic visit (**from WHO growth chart**)	1. Healthy Weight 2. Underweight 3. Overweight 4. Obesity	
204	History of co-morbidity	1. Yes 2. No	
205	If **yes Q204,** more than one history of co-morbidity	1. Yes 2. No	**Skip it,** if No **Q204** to **Q206**
206	Infection	1. Yes 2. No	

SECTION III: Treatment and Personal behavior Related predictions.

NO	Questions	Coding and categories	Remark
301	Dose of insulin regimen at initiation/first of treatment	_____U/Kg/Day	
302	Dose of current insulin regimen	_____U/Kg/Day	
303	Type of first insulin regimen	1. Non-premixed NPH and Regular insulin 2. Premixed NPH and Regular insulin 3. NPH alone	
304	Type of current insulin regimen	1. Non-premixed NPH and Regular insulin 2. Premixed NPH and Regular insulin 3. NPH alone	
305	Non-compliance to treatment	1. Yes 2. No	
306	Follow-up frequency/clinic visits in last year	_____	
307	Keep regular appointment	1. Yes 2. No	

SECTION IV: Diabetes-Related Complication Predictors.

NO	Questions	Coding and categories	Remark

301	DKA	1. Yes 2. No	
302	Hypoglycemia	1. Yes 2. No	
303	DM-Related Hospitalization	1. Yes 2. No	
304	Other DM-related complications	1. Yes 2. No	
305	If **yes Q304,** more than one other DM-related complications	1. Yes 2. No	**Skip it,** if No **Q304** to **Q401**

SECTION V: End of follow-up period participants' information.

NO	Questions		
401	Glycemic value at Final outcome	HbA1c= _____% OR Mean of FBS= _____mg/dl	
402	**Date** of Final outcome occurs----------/--------/--------- DD/MM/YY (If the patient First OGC, lost follow-up, transfer out, death or completed the follow-up without achieved First OGC when was it occurs)		
403	Final outcome	1. First OGC 2. Death 3. Completed the follow-up without achieved First OGC 4. Transfer out 5. Loss to follow-up	
404	Final **Status**	1. Censored 2. Event	
405	Final status **TIME** from enrolment	_____ in month	

Annex III: Approval Sheet

I, the undersigned MSc student, agree to accept responsibility for the scientific, ethical, and technical conduct of the research project entitled Time to first optimal glycemic control and its predictors among type 1 diabetes children and adolescents follow-up at public hospitals in Borena zone, Oromia, southern Ethiopia 2024, and the provision of required progress reports to my advisors. All of the necessary advice and guidance was requested and obtained from my advisors.

Submitted by:

Kubsa Guyo (BSc). _____ 21/5/2024

Name of student Signature Date

This research has been submitted for examination with my approval as an advisor.

ADVISORS:

Mr. Mathewos Mekonnen (Assistant professor) _____ 1/5/2024

Name of main Advisor Signature Date

Mr. Asfaw Getaye (BSc, MSc) _____ _____

Name of co-advisor Signature Date

I, the undersigned below, had examined and accepted the research entitled as in the above as a satisfying thesis in its present form and recommended it to the Salale University, Department of Nursing. This is to verify that his thesis has been accepted in partial fulfillment of the requirements for the degree of master in Pediatrics and Child Health Nursing.