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# Prevalence and associated factors of lipodystrophy in type 1 diabetic children and adolescents at Ayder Comprehensive Specialized Hospital, Tigray, Ethiopia

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## Abstract

**Introduction** Lipodystrophy can cause poor glycemic control in addition to cosmetic problems in children and adolescents with type 1 diabetes mellitus. However, data on its prevalence and associated factors is scarce among children and adolescents who live in developing countries like Ethiopia.

**Objective** To determine the prevalence and identify associated factors of lipodystrophy in children and adolescents with type 1 diabetes mellitus who visited the endocrinology clinic of Ayder Comprehensive Specialized Hospital between May 1 and July 31, 2020.

**Method** This was an institution-based cross-sectional study conducted on 57 children and 65 adolescents with type 1 diabetes mellitus who had been taking insulin injections for a year or more. The dependent variable was lipodystrophy. A pretested, structured questionnaire was used to collect data related to lipodystrophy and other characteristics. The principal investigator oversaw the data collection, which was done by pediatric and child health specialty residents with training. Data was subjected to descriptive statistics, and predictors of lipodystrophy were identified by fitting a multivariable logistic regression model. Statistical significance was declared at $p < 0.05$.

**Results** More than half (53.3%) of patients were in the age range of 13 to 17. The male-to-female ratio was almost 1:1. Educational status for 63.1% of patients was primary school. Four-fifths of patients were residing in urban areas. Of the 122 participants, 60 (49.2%) had lipodystrophy (48.3% lipohypertrophy and 0.8% lipoatrophy), with grade II lipohypertrophy being the most common type at 81.7%. The thigh was the most common site of lipodystrophy. In multivariable regression analysis, the long duration of insulin injection (AOR = 3.6, 95% CI, 1.5 to 9.0, $p = 0.005$) and inappropriate rotation of the injection site (AOR = 9.0, 95% CI, 2.2 to 37.0, $p = 0.002$) were significantly associated with lipodystrophy. HbA1c testing was conducted for 70 patients, and poor glycemic control (HbA1c ≥ 7%) was found in 43 (61.4%) of them. Patients with lipodystrophy were more likely to have poor glycemic control (75%) than those without lipodystrophy (47.1%) ($p = 0.016$).

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**Conclusion** The prevalence of lipodystrophy was comparable with other studies. Long duration of insulin injection and improper rotation of the injection site are associated with an increased risk of lipodystrophy. Patients with lipodystrophy were more likely to have poor glycemic control, defined by higher HgA1c, than those without lipodystrophy. Proper education of patients and their parents must include correct injection techniques, rotating injection sites, and changing injection sites intermittently to lessen the risk of developing lipodystrophy.

**Keywords** Children, Diabetes mellitus, Lipodystrophy

## Introduction

Type 1 diabetes mellitus is a chronic condition that affects millions of children and adolescents worldwide. Patients with type 1 diabetes mellitus rely on exogenous insulin, either by continuous infusion or multiple daily injections, to control their blood glucose levels [1, 2]. However, one of the long-term complications of insulin therapy is the development of lipodystrophy, a condition characterized by abnormal distribution of body fat. This can be a thickening of the subcutaneous fat (lipohypertrophy) or a loss of fat (lipoatrophy) at the insulin injection site.

The lipodystrophy area loses its sensitivity. Despite being aware that it is necessary to rotate sites, patients often stick to their injection site once they experience pain while injecting anywhere other than the lipodystrophy area [3]. Insulin injected into a lipodystrophy area may cause irregular insulin absorption, which could result in unpredictable hypoglycemia and poor glycemic control [4].

Even though the prevalence of lipodystrophy is high [3], there is a dearth of study and information about lipodystrophy in low- and middle-income countries, especially in Ethiopia. This study aims to explore the prevalence and associated factors of lipodystrophy in Type 1 diabetic children and adolescents at Ayder Comprehensive Specialized Hospital in Tigray, Ethiopia. The relevance of this research lies in the fact that lipodystrophy is a relatively understudied complication of Type 1 diabetes mellitus in children and adolescents, particularly in low-resource settings such as Ethiopia. Therefore, the reason for conducting this study was to determine the prevalence and identify associated risk factors for the development of lipodystrophy in children and adolescents. Understanding these factors can help improve diabetes management and quality of life for these patients.

## Methodology

### Study area

This study was conducted at Ayder Comprehensive Specialized Hospital, located in Tigray region, Mekelle town, which is 778 km from the capital city, Addis Ababa. It started as a referral and specialized medical center in 2008. It delivers clinical services to more than 8 million populations in the catchment areas of Tigray, Afar, and the south-eastern parts of the Amara regional state. It provides a broad range of medical services to both inpatients and outpatients of all age groups. It also serves as a teaching hospital for medical and other health science disciplines in both undergraduate and postgraduate programs. The pediatrics and child health department provide services at outpatient clinics, in the emergency department, under-five and above-five wards, pediatric intensive care units, and neonatal intensive care units. One of our outpatient clinics is the diabetic clinic, which provides service to approximately 200 pediatric diabetic patients monthly. There are 2 pediatricians, 2 pediatric residents, and 4 nurses assigned to the diabetic clinic monthly.

### Study design and study period

A facility-based cross-sectional study design was conducted at the pediatric endocrinology follow-up clinic at Ayder Comprehensive Specialized Hospital in Tigray, Ethiopia. The study period was from May 1 to July 31, 2020.

### Eligibility criteria

All children with type 1 diabetes mellitus aged < 18 years old who were taking insulin for at least 1 year during the study period were included in the study.

### Sampling size determination and sampling procedure

We included all children with diabetes mellitus aged < 18 years who had been taking insulin for at least one year during the study period. Out of 233 registered children, 122 met the eligibility criteria (i.e., were aged < 18 years and had been taking insulin for at least one year during the study period) and were included in the study.

### Study variables

The dependent variable was lipodystrophy, which was categorized as absent or present. Independent variables were age, sex, educational status, BMI, RBS, FBS, hypoglycemia, insulin type, needle size, injection site, needle reuse, injection site rotation, DKA, and injection to the lipohypertrophy area.

### Data collection tool and procedure

After reviewing related research, a questionnaire was developed, and an arrangement was made that fits our setup. This was information on the objective of the

study, translated into Tigrigna and pretested for a week before actual data collection. Following the pretest, we rephrased some of the questions and corrected some language errors. It was altered to better suit the context of the native language. Both the English and Tigrigna versions of the questionnaire were evaluated by experts (pediatrics and child health specialists).

Six pediatric and child health specialty residents were designated as data collectors. They underwent a comprehensive one-day training program that encompassed the following aspects:

- Interview Techniques: Ensuring proper interview conduct and participant comfort.
- Lipodystrophy Assessment: Detailed training on evaluating injection sites for lipodystrophy.
- Consistency in Data Collection: Strategies to achieve uniformity and minimize inter-observer variability.
- Ethical principles.

Weekly oversight by the principal investigator was made to maintain data quality. Lipodystrophy was diagnosed as present or absent by visual inspection and palpation by pediatric resident physicians. The presence of a noticeable or palpable lump at the injection site indicated that lipodystrophy was present. Accordingly, lipodystrophy was defined as having different grades based on morphology and pathogenesis.

### Data analysis

Data were entered, processed, cleaned, coded, classified, and computer-entered and analyzed using the Windows Statistical Package for Social Scientists (SPSS) version 25.0 software. A descriptive analysis was used to describe the prevalence of lipodystrophy and other characteristics. Results were presented using tables, graphs, and text based on the data type. A Chi-squares test of association was used to show the relationship between categorical variables and lipodystrophy. Variables with the crude odds ratio's p-value less than 0.25 during pairwise binary logistic regression were candidate variables for multivariable logistic regression. The adjusted odds ratio (AOR), with its 95% confidence interval and significance, is reported to show an association of predictors with the dependent variable (i.e., lipodystrophy). Those variables with a p-value less than 0.05 during multivariable analysis were considered significant predictors of lipodystrophy. Model fitness was tested using the Hosmer-Lemeshow test. A model was considered good-fit if the Hosmer-Lemeshow test result was insignificant (i.e., p value greater than or equal to 0.05). The final multivariable model was a good fit for the data (Hosmer-Lemeshow test: $p=0.286$).

### Operational definitions

- Lipodystrophy was assessed as "present" or "absent." The presence of a noticeable swelling or palpable lump at the injection site indicated that lipodystrophy is present, and if there is no noticeable or palpable lump at the injection site, it indicated that lipodystrophy is absent.
- Lipodystrophy was graded as:
  - Grade 0 = no change.
  - Grade 1 = visible hypertrophy of fat tissue but normal consistency on palpation;
  - Grade 2 = intensive fat tissue thickening but with firm consistency; and.
  - Grade 3 = lipoatrophy [5].
- Glycemic control was defined as optimal and poor glycemic control.
  - Optimal glycemic control was when the recent HbA1c levels were less than or equal to 7.5%, whereas.
  - Poor glycemic control was > 7.5% in children less than 19 years old, according to the American Diabetic Association and the International Society of Pediatric and Adolescent Diabetes [6].
- Children: patients who are diabetic aged 12 years and below.
- Adolescents: patients aged between 13 and 18 years.
- Hypoglycemia: blood glucose level of ≤ 60 mg/dL (3.3 mmol/L) and/or occurrence of one or more symptoms of hypoglycemia (such as palpitation, tiredness, sweating, strong hunger, dizziness, and tremor) [7].
- Optimal insulin injection rotation principles.
  1. Choose an area.
  2. Divide that area into four Sect.
  3. Select an injection site in a section to start injecting. Use one section per week.
  4. Inject one finger width away from your last injection.
  5. Always use a new injection site.
  6. Avoid using a single injection site more than once every four weeks (22).

### Ethical considerations

**Ethical approval** was obtained from the Institutional Review Board (IRB) of the College of Health Sciences at

Mekelle University with IRB number ERC 1720/2020. A letter of approval was also obtained from the ACSH Chief Clinical Director's office before the commencement of the study. Caregivers provided informed consent after receiving a detailed explanation of the study's objectives and purpose. They were also informed of their right to withdraw participation at any time. To protect participant privacy, personal identifiers were replaced with codes during the de-identification process. Collected data remained confidential and securely stored on password-protected computers, with no unauthorized third-party access.

**Table 1** Sociodemographic & clinical characteristics of T1DM children & adolescent in ACSH endocrinology clinic Mekelle, 2020

| Variables | | Number | Percentage |
|---|---|---|---|
| Age of participant | < 5 years | 13 | 10.7% |
| | 5 to 12 years | 44 | 36.0% |
| | 13 years and above | 65 | 53.3% |
| Sex of participant | Male | 63 | 51.6% |
| | Female | 59 | 48.4% |
| Educational status of patient | Not started | 15 | 12.3% |
| | Kindergarten | 8 | 6.6% |
| | Primary school | 77 | 63.1% |
| | Secondary school | 22 | 18.0% |
| Educational status of caregiver | Not started | 27 | 22.1% |
| | Primary School | 34 | 27.9% |
| | Secondary school | 40 | 32.8% |
| | Diploma and above | 21 | 17.2% |
| Residence | Urban | 97 | 79.5% |
| | Rural | 25 | 20.5% |
| Duration of insulin injection | 1–5 years | 83 | 68.0% |
| | 6–10 years | 38 | 31.1% |
| | Above 10 years | 1 | 0.8% |
| Most common site of injection | Abdomen | 8 | 6.6% |
| | Arm | 48 | 39.3% |
| | Thigh | 48 | 39.3% |
| | Equally all | 18 | 14.8% |
| Distance between injection sites | 1 finger | 10 | 8.2% |
| | 2 fingers | 48 | 39.3% |
| | 3 fingers | 2 | 1.6% |
| | I do not measure | 62 | 50.8% |
| Size of needle used | 8 mm | 117 | 95.9% |
| | 12 mm | 3 | 2.5% |
| | Other | 2 | 1.6% |
| Technique of injection | 45 degrees | 34 | 27.9% |
| | 90 degrees | 88 | 72.1% |
| Body mass Index | Underweight | 42 | 34.4% |
| | Normal | 78 | 63.9% |
| | Overweight | 2 | 1.6% |
| Fasting blood sugar | ≤ 60 mg/dl | 6 | 4.9% |
| | 61 to 126 mg/dl | 59 | 48.4% |
| | > 126 mg/dl | 57 | 46.7% |
| Random blood sugar | ≤ 60 mg/dl | 1 | 0.8% |
| | 61 to 200 mg/dl | 54 | 44.3% |
| | > 200 mg/dl | 67 | 54.9% |

## Results

### Sociodemographic and clinical characteristics

Of a total of 233 patients who attended the ACSH Clinic for Pediatric Endocrinology during the three-month study period, 122 participants met the eligibility criteria. Male patients made up 63 (51.6%) of the study participants, corresponding to an M: F ratio of 1.07:1. The median age of patients enrolled in the study was 13 years, with the age distribution led by adolescents at 65 (53.3%) and children at 57 (46.7%). The most common educational status of patients was primary school, accounting for 77 (63.1%) of them. About 80% of patients reside in urban areas. The mean duration of insulin injection was 4.06 (±2.56 SD) years. All participants were injected with Neutral Protamine Hagedorn (NPH) insulin and regular insulin. Sixty-five (53.3%) of the participants were responsible for the injection, while 57 (46.7%) received the injection from others. The thigh and arm were equally the most commonly preferred injection sites (48, 39.3% each). Eighty-eight (71.9%) patients inject at 90°, while 34 (27.1%) inject at 45°. Fifty-six (45.9%) patients rotate injection sites every injection (Table 1).

Regarding the educational status of the caregivers, more than half (63, 52.5%) of the injection providers attended primary school, and about a third attended secondary school (Fig. 2).

All participants reused their needles, with 51 (41.8%) reusing the needle 6–10 times, 40 (32.8%) 3–5 times, 21 (17.2%) > 10 times, and 10 (8.2%) 2 times. Almost all participants (117, 95.9%) used an 8-mm needle, the syringe available in the clinic (Fig. 3).

### Prevalence of lipodystrophy

In this study, lipodystrophy was observed in 60 participants (49.2%, 95% CI: 40.4–58.1%). The thigh was the most common site of lipohypertrophy (20, 33.3%), followed by the arm (18, 30%) and multiple sites (13, 21.7%), while the abdomen was the least common site (9, 15%). The ratio between male and female participants with lipodystrophy was equal (1:1). Of the subjects with lipohypertrophy, 32 (53.3%) were teenagers, and 28 (46.7%) were young children. Grade II lipohypertrophy was seen in 81.7% of cases with lipodystrophy. Grade I affected 16.7%, while only 1 participant had lipoatrophy (1.6%) (Fig. 4).

### Predictors of lipodystrophy

In multivariable binary logistic regression analysis, insulin injection duration (AOR = 3.7, 95% CI, 1.5 to 9.0, and $p = 0.005$) and frequency of injection site rotation (AOR = 9.0, 95% CI, 2.2 to 37.0, $p = 0.002$) persisted significantly associated with lipodystrophy, while insulin dose and frequency of needle reuse became less important. The odds of lipodystrophy were 3.7 times higher

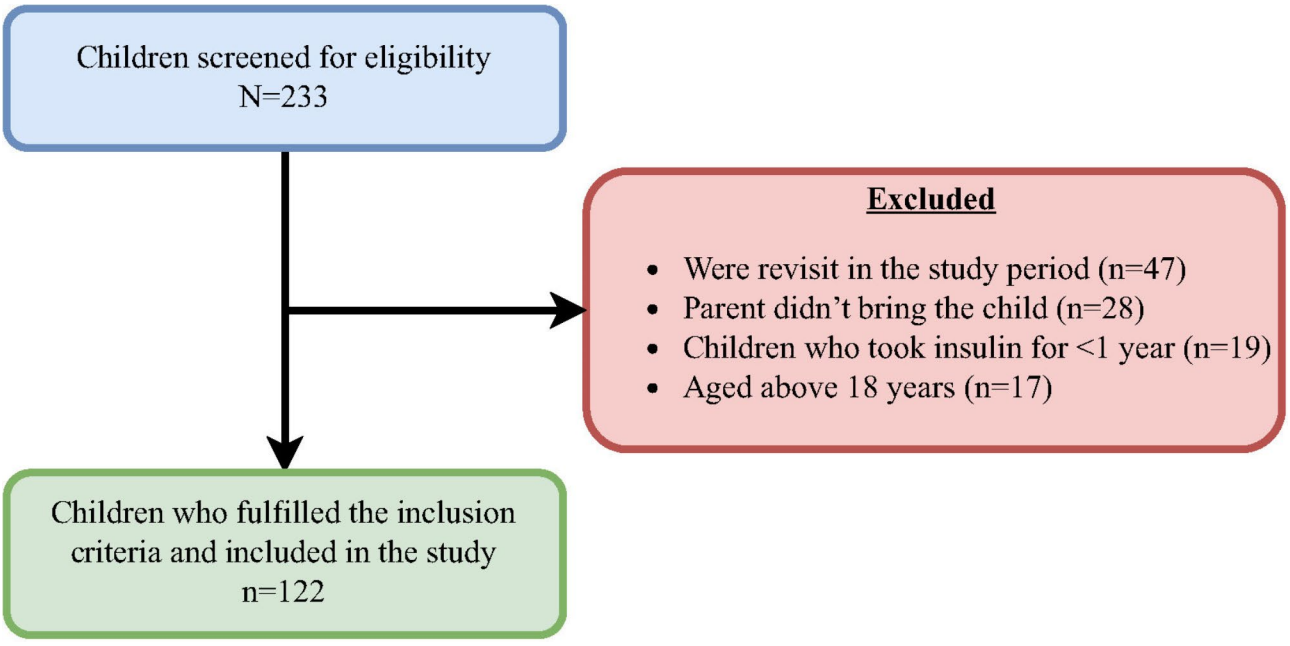


**Fig. 1** Sampling procedure in children and adolescents with T1DM, at ACSH

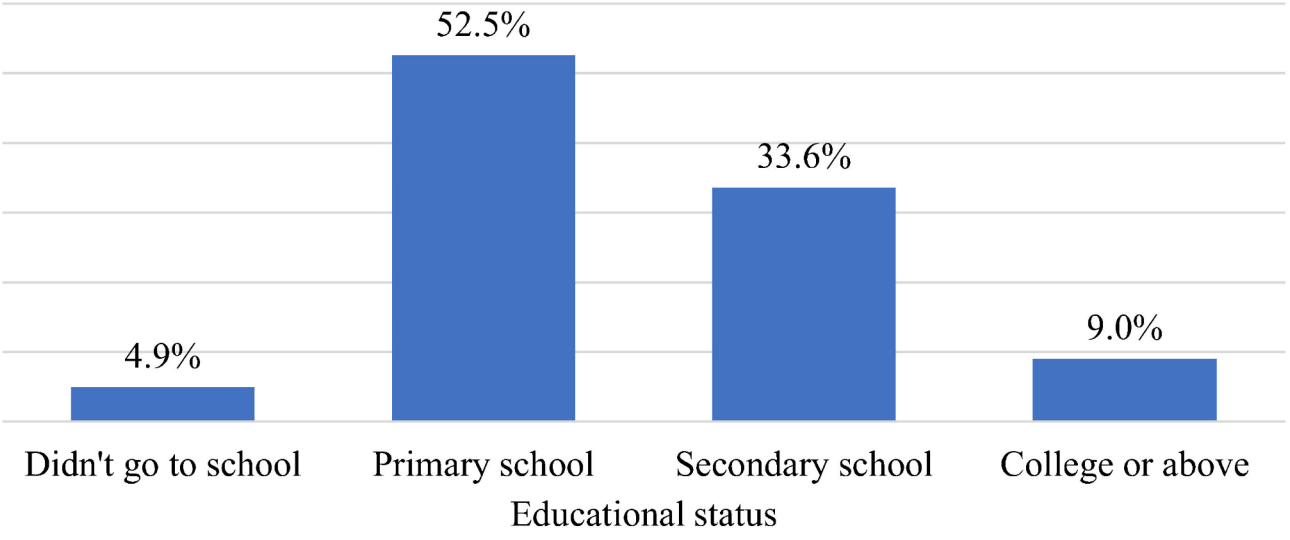


**Fig. 2** Educational status of insulin injection providers in T1DM children and adolescents at ACSH

in patients with a duration of insulin injection of 6 years or more compared to patients with a duration of insulin injection of 5 years or less. Compared to those who rotate the injection site for every injection, the likelihood of lipodystrophy was nine-fold higher in those who changed the injection site after a week (Table 2).

HbA1c testing was conducted for 70 patients, and poor glycemic control (HbA1c≥7%) was found in 43 (61.4%) of them. Patients with lipodystrophy were more likely to have poor glycemic control (75%) than those without lipodystrophy (47.1%) ($p=0.016$).

## Discussion

Currently, there is a paucity of data available on the prevalence and associated factors of lipodystrophy among children and adolescents who live in developing countries like Ethiopia. Our study reports on 122 consecutive pediatric Type 1 diabetic patients on follow-up in the largest teaching hospital in the Tigray region, Ethiopia. Nearly half of the type 1 diabetic patients had lipodystrophy. Long duration of insulin injection and improper rotation of the injection site are associated with an increased risk of lipohypertrophy. In addition, patients

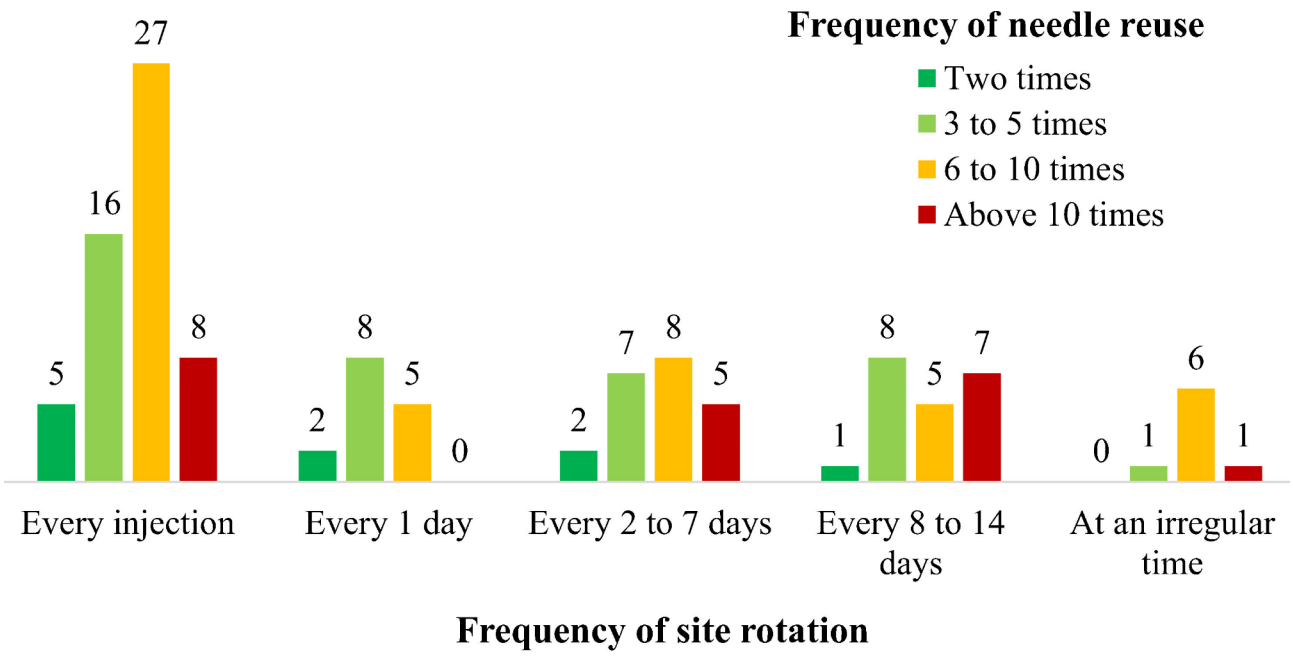


**Fig. 3** Frequency of site rotation and needle reuse in T1DM children and adolescents at ACSH

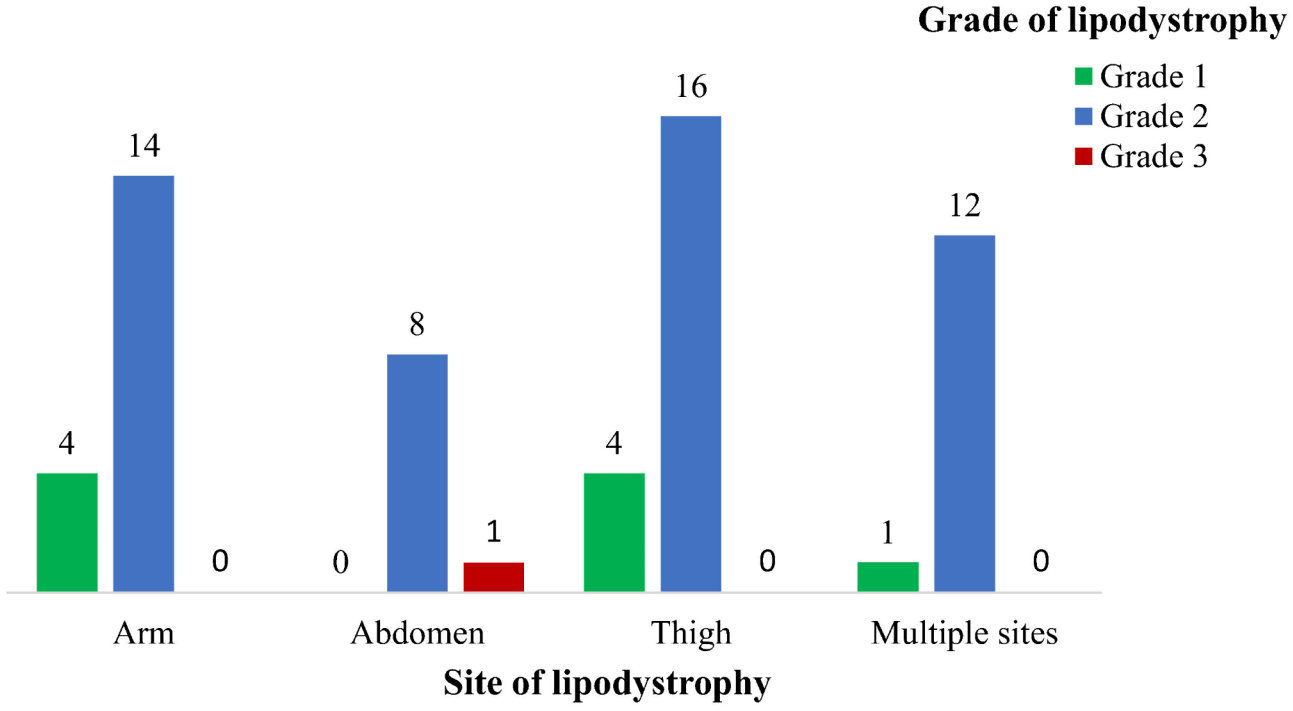


**Fig. 4** lipodystrophy grade and sites in children and adolescents with T1DM at ACSH

with lipodystrophy were more likely to have poor glycemic control than those without lipodystrophy.

The prevalence of lipodystrophy in this study was 49.2% (95% CI: 40.4–58.1%) and comparable to the studies in Saudi Arabia (47.7%), Ireland (51%), and South Africa (52%) [8–10]. This can be explained by the fact that most of the participants in these studies were in the pediatric age group and used physical examination to detect lipodystrophy.

Lower prevalence rates were reported in a systematic review and meta-analysis of 26 studies performed by Deng N and colleagues, who reported a prevalence of 38% [11]. The lower rate was also reported in another study from Jordan (37.3%) and Riyadh (39.7%) [12, 13].

**Table 2** Binary logistic regression analysis of factors associated with lipodystrophy in children and adolescents with T1DM at endocrinology follow-up clinic of ACSH, Mekelle, 2020

| | | Lipodystrophy, *n* (%) | | | | | |
|---|---|---|---|---|---|---|---|
| **Characteristics** | | **Absent** | **Present** | **COR [95% CI]** | ***p*-value** | **AOR [95% CI]** | ***p*-value** |
| Injection provider | | | | | | | |
| | Myself | 33 (27.0) | 32 (26.2) | 1.0 [0.5, 2.0] | 0.991 | | |
| | Care giver | 29 (23.8) | 28 (23.0) | 1 | | | |
| Duration of insulin injection | | | | | | | |
| | 1–5 years | 50 (41.0) | 33 (27.0) | 1 | | 1 | |
| | ≥ 6 years | 12 (9.8) | 27 (22.1) | 3.4 [1.5, 7.7] | 0.003 | 3.7 [1.5, 9.0] | 0.005 |
| Dose of insulin (Unit/kg/day) | | | | | | | |
| | < 0.7 | 36 (29.5) | 22 (18.0) | 1 | | 1 | |
| | ≤ 0.7 | 26 (21.3) | 38 (31.1) | 2.4 [1.2, 5.0] | 0.019 | 2.1 [0.9, 4.7] | 0.087 |
| Frequency of site rotation | | | | | | | |
| | Every injection | 33 (27.0) | 23 (18.9) | 1 | | 1 | |
| | Every 1 to 7 days | 21 (17.2) | 16 (13.1) | 1.1 [0.5, 2.5] | 0.835 | 1.2 [0.5, 3.0] | 0.723 |
| | ≥ 8 days | 3 (2.5) | 18 (14.8) | 8.6 [2.3, 32.7] | 0.002 | 9.0 [2.2, 37.0] | 0.002 |
| | At irregular time | 5 (4.1) | 3 (2.5) | 0.9 [0.2, 4.0] | 0.848 | 0.6 [0.1, 3.2] | 0.588 |
| Distance between injection sites | | | | | | | |
| | 1 to 3 fingers | 33 (27) | 27 (22.1) | 1 | | | |
| | Did not measure | 29 (23.8) | 33 (27.0) | 1.4 [0.7, 2.8] | 0.364 | | |
| Frequency of needle reuse | | | | | | | |
| | 2 to 5 times | 31 (25.4) | 19(15.61) | 1 | | 1 | |
| | ≥ 6 times | 31 (25.4) | 41 (33.6) | 2.2 [1.0, 4.5] | 0.041 | 2.3 [1.0, 5.5] | 0.057 |
| Technique of injection | | | | | | | |
| | 45 ° | 15 (12.3) | 19 (15.6) | 1.5 [0.7, 3.2] | 0.358 | | |
| | 90 ° | 47 (38.5) | 41 (33.6) | 1 | | | |

These studies were conducted in more developed countries, and adults were more involved. The counseling process in these setups may be better than ours, which may impact the development of lipodystrophy.

Grade II lipohypertrophy was the most common form, at 81.7% in this study, consistent with studies in Ethiopia and Spain [14, 15]. Other studies have shown that lipohypertrophy Grade I is the most common site [8, 12]. This difference may be due to the difference in diagnosis by visual inspection of grade I, which can be difficult, especially in children. Lipoatrophy remained rare in this study (only 1 patient), as in other studies [15].

The duration of insulin injection was significantly associated with the development of lipodystrophy, consistent with studies conducted in Dublin (p-value=<0.001) and Alexandria (AOR=1.16; 95% CI, 1.05–1.32; *P*=0.004) [9, 14]. However, there was no significant association in studies in Addis Ababa (AOR=0.71, CI, 0.34–1.49), and Chandigarh, India (p-value=0.381) [7, 8, 12, 16].

Injection site rotation was also significantly associated with lipodystrophy in this study, which is similar to that of Addis Ababa (AOR=0.41, CI, 0.21–0.81), Alexandria ($p$=0.001) and India ($p$<0.0005) [12, 16, 17]. In contrast to other studies [8–10, 12, 14, 18, 19], the importance of BMI for the development of lipodystrophy could not be demonstrated in this study, which could be due to the different body habitus of the participants. There were no obese patients in this study.

Most of the participants with lipodystrophy continue to inject the LH site (63.3%). Most of them indicated that this happened as part of their site rotation (68.4%), and some were unaware of the impact of the injection there (18.4%). The possible reason could be a poor counseling process.

Most participants in this study used 8-mm needles, and all participants reused their needles. Those who reused their needles more than 5 times were 1.5 times more likely to develop lipodystrophy than those who reused them less than or equal to 5 times.

In this study, all of the participants rotated injection sites, but the frequency of rotation was more than a week in 21 patients, 18 of whom had lipodystrophy and were nine times more likely to develop lipodystrophy than those to rotate each injection. A similar association was observed in Ethiopia, Saudi Arabia, and Spain [12, 18, 20].

The other remarkable finding of this study is that poor glycemic control was significantly higher in patients with lipodystrophy. Lipodystrophy impairs insulin absorption due to the formation of fatty lumps following repeated insulin injection at the same site. The overall prevalence of poor glycemic control among the patients who had HbA1c tests was 61.4% [95% CI, 49.8–72.2%], and this

finding is comparable to the study conducted in Gondar (66%), and lower than Addis Ababa (83%) [18, 21].

### Limitations of the study

There was a relatively small sample size, and the study was done in a single center. It would have been better to be multicenter with a larger sample size to generalize the result. HgA1c was not determined in all patients, which makes for a smaller sample to determine the poor glycemic control effect of lipohypertrophy. The diagnosis of LH was done by physical examination, which is less sensitive than ultrasound.

## Conclusion

The prevalence of lipodystrophy was comparable to other studies. Factors such as the long duration of insulin injection and failure to rotate the injection site properly are associated with an increased risk of lipodystrophy. Patients with lipodystrophy were more likely to have poor glycemic control defined by higher HgA1c than those without lipodystrophy. Proper education of patients and their parents must include correct injection techniques, rotating injection sites, and changing injection sites intermittently to lessen the risk of developing lipodystrophy. Health professionals should provide health education to patients and their guardians regarding proper injection techniques and the importance of site rotation. In addition, health professionals should give clear instructions on avoiding prolonged use of specific sites, monitor patients' injection habits, and screen for signs of lipodystrophy during each visit. Health bureaus should promote lipodystrophy awareness through community-based health education campaigns, prepare leaflets, and develop guidelines for healthcare providers.

### Abbreviations

| | |
|---|---|
| ACSH | Ayder Comprehensive Specialized Hospital |
| BMI | body mass index |
| DKA | diabetic ketoacidosis |
| DM | diabetes mellitus |
| HbA1c | glycated hemoglobin |
| LH | lipodystrophy |
| NPH insulin | Neutral Protamine Hagedorn insulin |
| SC | Subcutaneous |
| SPSS | Statistical Package for Social Scientists |
| T1DM | Type 1 diabetes |
| T2DM | Type 2 diabetes |

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12887-024-05018-0.

Supplementary Material 1

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NA.

### Author contributions

Conception or design of the work: Data collection: Tsehaye AlemsegedData analysis and interpretation: Tsehaye Alemseged, Abraha Gebreegziabher Hailu, Fikaden Berhe HadguDrafting the article: Tsehaye Alemseged, Abdikarin Ahmed Mohamed, Mohammed Mustefa MohammedaminCritical revision of the article: Tsehaye Alemseged, Abdikarin Ahmed Mohamed, Abraha Gebreegziabher Hailu, Fikaden Berhe Hadgu, Mohammed Mustefa MohammedaminFinal approval of the version to be published: Tsehaye Alemseged, Abdikarin Ahmed Mohamed, Abraha Gebreegziabher Hailu, Fikaden Berhe Hadgu, Mohammed Mustefa Mohammedamin.

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### Data availability

The original contributions presented in the study are comprised in the article; further inquiries can be contacted by the corresponding author.

## Declarations

### Consent for publication

NA.

### Competing interests

The authors declare no competing interests.

### Ethics statement

Ethical clearance was obtained from the Institutional Review Board (IRB) of the College of Health Sciences of Mekelle University with IRB number ERC 1720/2020. Permission from Ayder Comprehensive Specialized Hospital clinical director offices and a support letter from the chief clinical director were obtained before the commencement of the study. All procedures performed in this study were conducted in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments.

### Informed consent

Consent was obtained from all caregivers of children involved in the study after they were informed about the objective and purpose of the study. They were also informed about their right to refuse to participate in the study at any time.

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