Insulin Induced Lipohypertrophy and Glycemic Control among Children and Adolescents with Diabetes in Tikur Anbesa Specialized Hospital, Addis Ababa, Ethiopia

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This is to certify that the thesis prepared by Afewerki Gebremeskel, entitled: "*Insulin Induced Lipohypertrophy and Glycemic Control among Children and Adolescents with Diabetes in Tikur Anbesa Specialized Hospital"* and submitted in partial fulfillment of the requirements for the degree of Master of Pharmacy in Pharmacy Practice complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

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Abstract

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Lipohypertrophy (LH) is one of the clinical complications of insulin injection which affects insulin absorption and leads to poor glycemic control. Its occurrence was mainly associated with the use of non-human origins of insulin and repeated traumatization of injection sites. Aim of this study was to assess insulin induced LH and glycemic control among children and adolescent patients from April to July 2017 in Tikur Anbesa Specialized Hospital, Addis Ababa, Ethiopia. This cross sectional study was done on 176 diabetic children and adolescents who inject insulin for a minimum of one year. First, the anthropometric and clinical features of the patients were recorded in questionnaire and then observation and palpation techniques were used in assessing LH. Out of the total 176 participants, 103 (58.5%) had insulin induced LH, of them 3 (2.9%) had lipoatrophy. Factors such as age, weight, height and insulin syringe reuse had significant influence in development of insulin induced LH, considering *p*-value <0.05 as significant level. LH in turn was associated with the use of higher dose of insulin and non-optimal glycemic control. Overall, some insulin injection malpractices have been found among participants of this study. As a result injection site uncleaning was significantly associated with the occurrence of non-optimal glycemic control. Findings of this study revealed that inspite of using recombinant human insulin, the magnitude of the LH still remained high. Therefore, a regular examination of the diabetic patients for this complication is necessary, especially in the individuals who have a defective glycemic control.

Key words: *Diabetes mellitus, Insulin, Lipohypertrophy, Lipodystrophy, Glycemic control, Tikur Anbesa Specialized Hospital, Ethiopia*

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Abbreviations and Acronyms

ADA	American Diabetic Association
AMD-OSDI	AMD: Association of Clinical Diabetologists; OSDI: Italian Diabetes Healthcare Professionals
AOR	Adjusted Odds Ratio
BMI	Body Mass Index
CI	Confidence Interval
COR	Crude Odds Ratio
DM	Diabetes Mellitus
EDA	Ethiopian Diabetic Association
FIT	Forum for Injection Technique
HbA1C	Glycated Hemoglobin
HIV	Human Immunodeficiency Virus
IDF	International Diabetic Association
ISPAD	International Society for Pediatric and Adolescent Diabetes
IU	International Unit
LA	Lipoatrophy
LFAC	Life for a Child
LH	Lipohypertrophy
mmol/l	Milimole per liter
NPH	Neutral Protamine Hagedorn

OR	Odds Ratio
SBGM	Self-Blood Glucose Monitoring
SC	Subcutaneous
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
TASH	Tikur Anbesa Specialized Hospital
WHO	World Health Organization

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1 Introduction

1.1 Background

Diabetes mellitus (DM) includes group of common metabolic disorders, having common characteristics with hyperglycemia phenotype and is divided in to type 1 and type 2(Longo et al., 2012). Type 1 diabetes is chiefly characterized by the inability of the pancreas to produce insulin resulting from the autoimmune destruction of the beta cells(Oikawa and Shimada, 2015); therefore insulin therapy is life-saving and lifelong. A person with type 1 diabetes needs to follow a structured self-management plan, including insulin use and blood glucose monitoring, physical activity, and a healthy diet. In many countries, especially in low-income families, access to self-care tools, including self-management education, as well as to insulin, is limited. This leads to severe disability and early death in children with diabetes (IDF, 2017). Patients who are able to access insulin therapy, two or more daily insulin injections are mandatory, with dose adjustments based on blood glucose levels and this make it difficult to follow lifelong(Hayek et al., 2016).

As a routine practice diabetes management involves patients injecting themselves with the newer insulin such as rapid-acting and basal analogues, as well as, of innovative therapeutic regimes(Hayek et al., 2016). In spite of technological progresses, and a general improvement in the quality of diabetic care, an association of clinical diabetologists in Italy reported that only 22.2% T1DM and 43.8% T2DM patients reached HbA1c levels below 7% and the factors related to insulin administration, storage and handling might contribute to such low magnitude of optimal glycemic control (Gentile et al., 2016). Therefore, patients must learn the correct injection technique to avoid intramuscular injections and appropriately deliver the insulin into the subcutaneous tissues, as well as to prevent common clinical complications such as skin complications(Hayek et al., 2016).

Skin complication such as Lipoatrophy (LA) or local fat loss, is clinically characterized by visible cutaneous depression and palpable atrophy of subcutaneous fat tissue at the injection site. It may result from a local immune reaction against impurities of the insulin preparations and due to the use of purified human insulin preparations this condition has dramatically decreased since the 1950s(De Villiers, 2007, Kordonouri et al., 2014). However Lipohypertrophy (LH) which

remains to be the most common cutaneous complication and may result from the local trophic action of insulin(De Villiers, 2007). LH is characterized by a tumor-like swelling of fatty tissue around subcutaneous insulin injection sites(Fujikura et al., 2005). Histologically the hypertrophic adipocytes are twice as large as those from normal subcutaneous areas and contained numerous small lipid droplets. Electron microscopic analysis also revealed a minor population of small adipocytes, suggesting active differentiation or proliferation(Omar et al., 2011).

LH occurs because patients inject the same site day after day. It frequently occurs on both sides of the umbilicus or in the mid-thigh areas as these are convenient places to inject, and where the patient's hands reach most naturally. Eventually the area becomes hyposensitive. Once the patient feels pain when injecting elsewhere, but not in the lipohypertrophic area, he or she tends to continue injecting in the same site even if aware of the need to rotate sites(De Villiers, 2007). The injection of insulin into a site of LH may lead to erratic absorption of the insulin, with the potential for poor glycaemic control and unpredictable hypoglycaemia (MT Cunningham and MJMcKenna, 2013, Omar et al., 2011).

1.2 Statement of the Problem

Diabetes mellitus is a huge and growing global health problem which affects every race, age and sex of human beings. According to international diabetes federation report, 424.9 million adults were living with diabetes mellitus worldwide in 2017 and expected to be 628.6 million by 2045 (IDF, 2017). Type 1 diabetes is one of the most common endocrine and metabolic conditions in childhood. The number of children developing this form of diabetes every year is increasing rapidly, especially among the youngest children. In a growing number of countries, type 2 diabetes is also being diagnosed in children. Worldwide it is estimated that there are about 1,106,500 children and adolescents living with type 1 diabetes and 132,600 children under 20 years are estimated to develop type 1 diabetes annually. There are strong indications of geographic differences in trends but the overall annual increase is estimated to be around 3-5% (IDF,2017). Data to estimate the number of children with type 1 diabetes remain very scarce in Africa; however it is reported to be 50,200 in 2017 and this was derived from studies in Ethiopia, Nigeria, Rwanda, United Republic of Tanzania and Zambia(IDF, 2017). In Ethiopia community based studies are non-existent at the national level and hospitals may give figures of those who

come for treatment and follow up. As a result, the national estimate is based on neighboring countries with similar socio-economic situations and accordingly, 2%-3% of the population is estimated to live with diabetes in Ethiopia(EDA, 2016). Unpublished data which was found from Ethiopian diabetes association revealed that there are about 8000 diabetic children in Ethiopia by 2016. This high incidence of diabetes results in huge economic burden as a result it was estimated to be 727 billion USD in 2017 and is expected to be 776 billion by 2045 worldwide. Much of the expenditure is related to insulin and it's devices to administer(IDF,2017).

Modern therapy involves greater and earlier use of intensive insulin regimens in order to achieve better control of blood glucose levels and reduce the long-term risks associated with the condition(WHO, 2016). However recently reports revealed that an alarming increase rate of diabetic patients having poor glycemic control inspite of their routine insulin use(Gentile et al., 2016). As a result this condition might attribute for the incidence of clinical complications which affects quality of life and survival of diabetic patients. An obvious explanation for the condition is lacking; however previous study generated a hypothesis that associated poor glycemic control with insulin administration, storage, handling and skin complications such as LH among DMT1 and DMT2(Gentile et al., 2016). LH has been a recognized complication of insulin therapy for many years, yet researches showed that its prevalence in insulin-injecting patients with diabetes remains high. For instance, in Spain 64.4% (Blanco et al., 2013), Pretoria 52% (De Villiers, 2007), Alexandria 54.9% (Omar et al., 2011), in Ethiopia 31% LH of 100 insulin injectors(Seyum and Abdulkadir, 1996). The problem for the patients is that, injection of insulin into a site of LH, although painless, may lead to erratic absorption of the insulin, with the potential for poor glycaemic control and unpredictable hypoglycaemia(Hambridge, 2007).

Therefore proper injection technique is essential for optimal functioning of insulin and other injected medications in diabetes. However, healthcare professionals rarely instruct patients adequately on the proper techniques. Rarely do such professionals explain the importance of using a needle length appropriate for the patients' subcutaneous tissue depth, or train them to rotate properly, change needles between injections or monitor their injection site for the presence of lipodystrophy (Connic et al., 2010).

So far several factors have been reported to be associated with the development of LH and poor glycemic control, such as: insulin use duration, gender, body mass index (BMI), injection site,

recurrent tissue trauma from failure to rotate injection sites, and the frequency of needle reuse(Hauner et al., 1995, Blanco et al., 2013, Ibarra and Gallego, 1998).

Although LH and LA of injection sites was a major problem with the old insulin, the problem improved somewhat with the advent of the monocomponent bovine and porcine insulin and the current pure human insulin, such that LA in particular is now very rare. However it now manifests more subtly, with thickening of the skin rather than the formation lumps and pitting(De Villiers, 2007). Therefore this study will emphasize on insulin induced LH as it is related with insulin injection technique and insulin regimens unlike that of LA which is mostly related to the source of insulin. Currently diabetic center of TASH only avail recombinant human insulin of NPH, lente, regular and mixtared 70/30 insulin.

Despite LH is still continuing to be high, very limited information and researches are available on LH particularly in our country Ethiopia. Therefore this study was done to determine the magnitude of LH and non-optimal glycemic control; identify factors associated with these conditions and try to assess the effect of LH on glycemic control.

We hope that findings of this study might contribute to the body of knowledge of insulin-induced LH and glycemic control, and factors associated to them in Ethiopia. On top of that it will provide recommendations and directions towards solving these problems to patients, the hospital administrative as well as to the national health administrations. Although assessment of insulin induced LH is considered to be routine activity, it is not a common practice in diabetic center of TASH; this study might remind the health providers to perform this activity at regular visits of insulin injecting patients. Health policy makers and program planners will also find it crucial to evaluate the quality of existing services. Since limited information is available about insulin-induced LH and glycemic control in Ethiopia, researchers could find essential and basic information from this study.

1.3 Literature Review

The incidence of type 1 diabetes among children is increasing in many countries, particularly in children under the age of 15 years(IDF,2015). Concerning its management, insulin therapy is mandatory to achieve better control of blood glucose levels and reduce the long-term risks

associated with the condition(WHO, 2016). However, some adverse clinical complications of insulin therapy have been associated with poor glycemic control. LH has been a recognized complication of insulin therapy for many years and its incidence was associated with impurities of the old insulin (Hauner et al., 1995).

1.3.1 Prevalence of LH in Patients Injecting Insulin

Despite the emergence of new recombinant human insulin, LH remains to be high. A multicenter study involving 430 insulin injecting out-patients in Spain showed prevalence of LH in 64.4% patients(Blanco et al., 2013). Another large study was conducted in European insulin-injecting type 1 or 2 diabetes patients those use insulin for at least 6 months via an insulin pen or syringe. It was done in 22 sites in seven countries, 1002 patients. Thirty percent of patients reported having LH. Concurrent nurse evaluation found the prevalence to be 27%(Strauss et al., 2002). Similarly a large study was also done in National Center for Diabetes, Endocrinology, and Genetics (NCDEG, Amman, Jordan) between October 2011 and January 2012. This study involved a total of 1090 patients with T2DM aged 20 to 89 years, who attended the diabetes clinics. This study revealed that prevalence of LH was 37.3% (27.4% grade 1, 9.7% grade 2, and 0.2% grade 3)(Al Ajlouni et al., 2015).

A cross sectional study was done on 220 diabetics referring to Imam Educational Hospital of Sari Township in 2007- 2008 who had been under treatment with recombinant human insulin at least three months before. From the total 220 diabetics under study, 35 (15.9%) had insulin induced lipodystrophy, of them 32 (14.5%) had LH and 3 (1.4%) with LA(Hajheydari et al., 2011). Another study with similar design was conducted on 174 patients with T1DM (aged 13–18 years) treated with multiple daily insulin injections for a minimum duration of 1 year. A substantial percentage of patients approximately 47% showed grade 1 LH, followed by 33.7% with grade 2 and 19.3% with grade 3 LH. A higher frequency of LH was observed in the thigh region (n = 28, 33.7%) than in the arm, which was second highest (n = 23, 27.7%)(Hayek et al., 2016). Additional study with similar design on the frequency of insulin-induced LH at injection sites was assessed in 223 type 1 and 56 type 2 diabetic patients. 64 (28.7%) of the subjects with type 1 diabetes, but only 2 (3.6%) of those with type 2 diabetes presented clinical evidence of LH(Hauner et al., 1995). In consideration of the period of development of LH, a research was

done among 215 diabetics who had been using insulin for at least 2 years. This study established LH in 48.8% of the individuals(Vardar and Kızılcı, 2007).

A total of 119 Patients were evaluated and examined for the presence of LH at routine follow-up clinic visits at the Diabetes Clinic for children at El-Chatby University Children's Hospital, Alexandria. LH occurred in 54.9% of patients, Grade 1 LH occurred in 42.5% and grade 2 in 12.4%(Omar et al., 2011a). Another prospective study involving 55 people with diabetes was done in four outpatient clinics in St Michael's Hospital, Dublin. The population consisted of 41 people with type 1 diabetes and 14 people with type 2 diabetes. LH was identified in 28 of 55 study participants (51%)(MT Cunningham and MJMcKenna, 2013).

A study include twenty-three patients between the ages of 6.5 and 18.5 years revealed that LH had a prevalence rate of 52% in the population. Counting only those patients who had been examined on several occasions, the prevalence rate for LH was 80%. It was mild in 6 patients, moderate in 3 and severe in 2 (De Villiers, 2007).

1.3.2 Factors Associated with the Development of LH

Knowledge regarding the different factors that may influence development of insulin induced LH is expanding. Many factors, including Sociodemographic, anthropometric, clinical, patient related factors have been reported in literatures.

On the study done by Blanco et al, there was a strong relationship between the presence of LH and non-rotation of sites, with correct rotation technique having the strongest protective value against LH. Of the patients who correctly rotated sites, only 5% had LH while of the patients with LH 98% either did not rotate sites or rotate incorrectly. LH was also related to needle reuse, with risk increasing significantly when needles were used> 5 times. Total insulin doses for patients with and without LH averaged 56 and 41 IU/day, respectively (Blanco et al., 2013). Similar factors were also revealed by the study done in European insulin-injecting type 1 or 2 diabetes patients. In this study independent risk factors for LH were found to be failure by the patients to check injection sites regularly, failure to rotate sites and longer duration of DM and needle reuse. Needle reuse, even more than once, increased the risk of LH by 31%(Strauss et al.,

2002). Data given by this study were in line with data revealed by Vardar et al(Vardar and Kızılcı, 2007).

The study done by Hajheydari et al revealed that factors such as age, sex, level of education, body mass index (BMI), type of diabetes, period of using insulin and injection site had significant influence in development of insulin induced lipodystrophy(Hajheydari et al., 2011). Another study found that LH was significantly associated with the duration of diabetes, needle length, duration of insulin therapy, lack of systematic rotation of insulin injection sites(Al Ajlouni et al., 2015). In addition to the above factors, abdominal injection site was revealed to be a factor by a study done by Hauner et al(Hauner et al., 1995).

On the study conducted by Cunningham et al, factors which significantly associated with LH were injection area movement at each time, injecting four or more times per day, long duration of insulin therapy. There were no significant differences in age, needle length, total insulin dose and whether the needle was changed at time of each injection(MT Cunningham and MJMcKenna, 2013). Like the above studies, duration of diabetes and body mass index was also found to have significant association with development of LH on the study done by Omar et al. However LH also was related significantly to the dose of insulin units per kg of body weight in this study(Omar et al., 2011).

Additional finding was found on the study done by Hayek et al. The independent risk factors for LH were found to be as follows: higher BMI, a higher rate of needle reuse and failed to alternate the injection site but additionally a higher number of injection sites was also associated with development of LH(Hayek et al., 2016).

1.3.3 Effects of LH on Glycemic Control

A case report done by Chowdhury et al showed that, a diabetes specialist nurse noted a patient having fluctuating blood sugar concentrations, ranging from 2.0 mmol/l to 18.9 mmol/l, and unpredictable hypoglycemic episodes occurring three or four times a week, with good awareness. The nurse reviewed patient's injection technique and noted significant LH at the sites of her abdominal injections. Patient was advised to avoid these sites for future injections and to reduce her insulin dose by 10%. Over the next six months her glycaemic control improved, with home

tests showing blood sugar concentrations ranging from 3.4 mmol/l to 9.8 mmol/l before meals and 6.7 mmol/l to 12.3 mmol/l after meals. The frequency of occurrences of hypoglycaemia reduced to less than once a month. Her glycated haemoglobin fell to 6.8% from 9.1% within three months, despite the reduction in insulin dose. Another patient with similar scenario was also reported by the above author. A woman with HgbA1C of 9.5% was seen by a diabetes specialist nurse. The nurse reviewed her injection technique and injection sites and noted that she had severe LH. She was advised to avoid injecting into these sites, to rotate injection sites, and to reduce her insulin dose by 10%. Within three months her glycated haemoglobin fell to 6.7%, her blood sugar concentrations improved to between 4.5 mmol/l and 10 mmol/l, despite her lower dosage of insulin, and she had no further episodes of hypoglycaemia(Chowdhury and Escudier, 2003).

Another case study by Wallymahmed et al., 2004 showed worsening of diabetic control. Glycated haemoglobin (HbA1c) increased from 10.6% to 16.5%) despite increased insulin dose over the past 12 months in a 46 years old man who is diabetic type 1 patient and showed a typical case of LH.

Study done by Blanco et al., 2013 showed that, 39.1% of patients with LH had unexplained hypoglycemia and 49.1% had glycemic variability compared with only 5.9% and 6.5%, respectively, in those without LH.

Generally LH was significantly associated with poor glycemic control in several studies (Hayek et al., 2016, Al Ajlouni et al., 2015). However, a study revealed that, the mean HbA1c levels of patients with grade 1 and grade 2 LH did not differ from diabetics without LH (Omar et al., 2011).

1.3.4 Insulin Injection Practices

Insulin injection practices have a significant effect on the performance of the agent injected, as well as on overall diabetes management(Connic et al., 2010). However, there is usually a great emphasis placed on the type of insulin the patient is taking and an even greater emphasis on the amount than injection techniques. Thus, there is a need to teach the patient and then periodically review the practical aspects of insulin injections (Dolinar, 2009).

A study done by Connic et al., 2010 revealed that Overall, 3.6% of patients use the 12.7-mm needle, 1.8% use the 12-mm needle, 1.6% use the 10-mm needle, 48.6% use the 8-mm needle, 15.8% use the 6-mm needle, and 21.6% use the 5-mm needle; 7% of patients do not know what length of needle they use. Twenty-one percent of patients admitted injecting into the same site for an entire day, or even a few days, a practice associated with LH. Approximately 50% of patients have or have had symptoms suggestive of LH. Abdominal LH seems to be more frequent in those using the two smaller injection size areas, and less frequent in those using larger areas. Nearly 3% of patients reported always injecting into lipohypertrophic lesions and 26% inject into them sometimes. Of the 65% of patients using cloudy insulin (e.g. NPH), 35% do not remix it before use.

Another prospective study with pre and post insulin injection education was done among patient whose age is 18 and above in Malaysia. This study showed that, in response to insulin storage, majority (83.3%) kept the insulin in use under room temperature. Most of the respondents (95.6%) injected insulin at the abdomen, with very small percentage (4.4%) injected at the thigh. None of the participants injected insulin at the buttock or deltoid areas. About half of the patients (50.9%) turned the pen up and down and/or roll the pen for 10 times. The percentage of participants who performed this step correctly increased to 91.2% after the intervention. All participants managed to fit the new pen needle. Performing air-shot (priming) by dialling 2 to 4 units of insulin before the injection were executed by 28.1% of the participants. The number of participants who performed these steps appropriately after education technique increased to 76.3%. The steps of counting to 10 prior to removing needle from skin or also known as ‘dwell time’ was observed in more than half (62.3%) of the participants even during pre-education stage. The numbers of participants who performed this step after re-education of technique increased to (93.9%)(Ahmad et al., 2016).

In a study which was done worldwide about injection practices, one of the parameters checked was whether the patient lifted a skin fold and if so, was it lifted correctly and was it released appropriately. 63.7% of patients lifted a skin fold and 75.0% did it correctly. However, less than half released the fold appropriately. About half of patients worldwide use their needle more than once. Pen users tend to reuse more than syringe users. Most reuse is less than 5 times, but up to 30% of reusers use the needle 6 times or more. 10.2% of them roll or tip cloudy insulin up to 20

cycles to reconstitute it before injecting. 88.6% patients reported that they store unopened insulin in the refrigerator. After opening it, 43.0% continued to store it in the fridge. Of these only 56.3% let it warm up to room temperature before injecting it. The 43.7% who injected it cold were at higher risk of having painful injections(Worldwide injectable technique study, 2015).

2 Objectives

2.1 General Objective

To assess insulin-induced LH and glycemic control among children and adolescents with diabetes from April to July 2017 in Tikur Anbesa Specialized Hospital, Addis Ababa, Ethiopia.

2.2 Specific Objectives

To determine prevalence of insulin-induced LH

To determine proportions of glycemic control

To identify factors associated with insulin-induced LH

To assess glycemic control in relation with insulin injection practices

To assess the effect of insulin-induced LH on glycemic control

3 Methods and Materials

3.1 Study Setting

The study was conducted in TASH, Addis Ababa, Ethiopia. TASH is located in Lideta Sub-City, Addis Ababa, Ethiopia and established in 1972. Affiliated with Addis Ababa University College of Health Sciences, TASH serves as a training center for undergraduate and postgraduate medical students, dentists, nurses, midwives, pharmacists, medical laboratory technologists and radiology technologists. It is the largest referral hospital in Ethiopia, with 800 beds. It is also an institution where specialized clinical services that are not available in other public or private institutions are rendered to the whole nation.

TASH has 3,300 health professionals dedicated to providing health care services. The various departments, faculty members and residents under specialty training in the School of Medicine provide patient care in the hospital. The hospital also has 1178 technical, 1109 support and 230 contract staff. In addition, almost all regional and federal hospitals in Addis Ababa use TASH as referral unit and training sites.

TASH serves about 500,000 patients per year in its outpatient department and about 50,000 in the inpatient and 40,000 in the emergency departments. The major services provided by the hospital are: internal medicine, emergency medicine, surgery, gynecology and obstetrics, pediatrics, **diabetic center**, oncology/chemo-radiology, radiology, psychiatry and dermatology. The pharmacy services in the TASH are organized for outpatient, emergency and inpatients.

Diabetic center in TASH was established in 1994. It is the largest diabetic center which offers services to all outpatient diabetic patients in Ethiopia. It involves two adult endocrinologists, a pediatric endocrinologist, 2 pharmacists, 8 nurses and many medical and pediatric residents. Its services are based on schedules for adults, children and pregnant women. The schedule for children is every Wednesday and they deliver service for about 70-80 patients who are diabetic and Down's syndrome patients. On average about 25 diabetic patients get service on this day from this center.

3.2 Study Design and Period

A facility based cross-sectional study was conducted on insulin-injecting children and adolescent diabetic patients. This study was conducted from April to July 2017 G.C in the outpatient diabetic center of TASH.

3.3 Population

3.3.1 Source Population

All insulin-injecting children and adolescents diabetic patients who have follow-up in TASH diabetes center were the source population of this study.

3.3.2 Study Population

All insulin-injecting children and adolescent diabetic patients who have follow-up in TASH diabetes center at the time of data collection period, fulfilling the inclusion criteria and willing to participate were the study participants.

3.4 Eligibility Criteria

3.4.1 Inclusion Criteria

All insulin-injecting children and adolescent diabetic patients who have followed up for a minimum of 1 year, with the insulin either self-administered or injected by a caregiver. Participants who were included in this study are children and adolescents less than 18 years old.

3.4.2 Exclusion Criteria

Patients excluded from the study were those whose insulin treatment was only transient including decompensated patients with acute hyperglycemia who do not ordinarily use insulin and hospitalized patients, HIV patients, Cushing's syndrome patients and those with incomplete data charts.

3.5 Study Variables

3.5.1 Dependent Variables

Insulin-induced LH and glycemic control were outcome variables of this study.

3.5.2 Independent Variables

Sociodemographic, anthropometric parameters, duration on insulin therapy, needle length, number of daily injections, washing hands before injection, insulin regimen, rotation of injection site, individuals giving the injection were documented to be independent variables.

3.6 Sample Size and Sampling Techniques

Participants were included to this study based on their availability during their routine outpatient clinic visit within the study period. Averages of 25 diabetic children were seen every Wednesday on their appointment day and this study was estimated to be conducted for a total of three months period. Hence this study calculated to have a total of 300 study populations; however 176 participants actually were found to have complete data charts over four months period. Participants were selected using consecutive sampling technique and those patients who have fulfilled the inclusion criteria were immediately included in the study. Study personnel were not having knowledge of the LH status of patients at study entry, when an assessment of their injection technique as well as examination of their injection sites was made later.

3.7 Data Collection Tools and Techniques

A questionnaire was developed using a relevant literature search and incorporating the recent Forum for Injection Technique (FIT) and AMD-OSDI consensus for insulin injection technique. FIT was conceived in the UK and now has Boards in Ireland, Canada, Switzerland, India and South Africa. FIT is an autonomous organization comprising specialist diabetes nurses and its mission is to support people with diabetes using injectable therapies by educating and supporting healthcare workers(Forum for Injection Technique, 2012, MT Cunningham and MJMcKenna, 2013). The questionnaire included issues regarding (A) Socio-demographic characteristics such as age, sex, duration of DM, educational level, and duration of insulin treatment; (B)

Anthropometric measurements such as height, weight, BMI, (C) Clinical characteristics such as types of insulin, number of insulin injections per day, dose of insulin per day, sites of insulin injection, and needle size; (D) Laboratory measurements including glycosylated hemoglobin (HgbA1c). Information on the participants' most recent insulin dose and HgbA1c values to assess blood glucose control were retrieved from their medical records or their own record book for the research. The HgbA1c test is the most reliable form of diabetes diagnostic assessment, providing a good indication of glycemic control over several months. HgbA1c value <7.5% was normally accepted as an optimal level of control in children less than 19 years. (Hayek et al., 2016, ADA, 2017, ISPAD, 2017).

Observation and palpation techniques were used in assessing LH in these diabetics, as some lesions can be more easily felt than seen. Normal skin can be pinched together easily whereas LH cannot (Blanco et al., 2013). LH was assessed as "present" or "not present". The presence of a noticeable or palpable lump at the injection site indicated that LH is present. Then LH was graded as following: grade 1 = visible hypertrophy of fat tissue but palpably normal consistency; grade 2 = massive thickening of fat tissue with firm consistency; and grade 3 = Lipoatrophy (Hayek et al., 2016).

Insulin injection practices have been assessed using a likert scale measurement tool which was formulated by reviewing guidelines and literatures. This tool assessed how common participants performed each practice on their daily life. However the tool's internal consistency was not acceptable enough with Cronbachs' $\alpha = 0.356$. Nevertheless our study has applied this data collection tool since no option was available to perform this activity. Data regarding patients' insulin injection practices were directly solicited from patients or their care givers. The questionnaire was translated from English language to Amharic language for the sake of interview with participants.

Five experienced diabetes nurses who are involved in patient follow ups were recruited to extract data and perform physical examination. One of them was extracting all the necessary data based on the questionnaire and other one was performing the visual inspection and palpation of injection sites to detect LH. This type of data collection technique was intentionally applied to reduce bias that would happen if a single data collector was involved in both activities. A

supervisor and principal investigator were supervising the data collection process at every data collection day.

3.8 Data Quality Control Issues

Quality of the data was assured by a properly designed data collection format. The data collection formats was pretested in 5 % of the study participants and necessary modifications were done accordingly prior to the actual data collection commenced. A day training was given to data collectors and supervisor about objective of the study, data collection format, on how to extract information from patient files and registers, and ethical consideration. The data collection process was supervising by a supervisor at every data collection day.

3.9 Data Processing and Analysis, Interpretation and Presentation

The collected data was checked for completeness, missed values and then manually cleaned up on such indications. The data was entered using Epi data version 3.1 and analysed using SPSS version 20 statistical package. Frequency distributions, percentages, measure of central tendencies, dispersion were used to show descriptive statistics. For analytical purpose chi-square, T-test and bivariate logistic regression with 95% confidence level (C.I) were calculated. Multivariate logistic regression was used for the adjustment of potential confounders. P values ≤ 0.05 was considered as statistically significant. The result was presented by tables, graphs and as a statement.

3.10 Ethical Considerations

Ethical clearance was obtained from Ethics Review Board of School of Pharmacy. Permission was obtained from department of pediatrics of TASH to conduct this study. Participants and their parents were informed for their written consent prior to involving them in the study by explaining the objectives of the study, how to collect the data and it's benefits. Information regarding data that was found by performing physical examination was told clearly to patients and their parents. There was not any personal identifier in the data collection format. Data was collected by trained diabetes nurses who works at the diabetic center and no other data collectors were involved for the purpose of data collection only to guarantee privacy of the study participants. Data was compiled and analyzed by principal investigator to further guarantee

privacy of the study participants. The collected data was not accessed by any third party apart from those who directly connected with the study to maintain confidenciality. The collected information was presented in an aggregate form that is not possible in identifying a particular participant. Respondents' information was kept locked until the end of the study. Respondents were informed the right to refuse or terminate at any point of the interview and physical examination. After getting their consent they were duly signed on the consent form to assure their willingness.

3.11 Operational Definitions

LH was assessed as "present" or "not present". The presence of a noticeable or palpable lump at the injection site indicated that LH is present and if there is not noticeable or palpable lump at the injection site indicated that LH is not present.

LH was then graded as following: grade 1 = visible hypertrophy of fat tissue but palpably normal consistency; grade 2 = massive thickening of fat tissue with firm consistency; and grade 3 (LA) = visible cutaneous depression and palpable atrophy of subcutaneous fat tissue at the injection site (Figure 1) (Gentile et al, 2016).

Glycemic control was defined as optimal glycemic control and non-optimal glycemic control.

- Optimal glycemic control is when the recent HbA1c levels is less than or equal to 7.5%, whereas non-optimal glycemic control is >7.5% in children less than 19 years old according to American Diabetic Association and International Society of Pediatric and Adolescent Diabetes.

Hypoglycemia was defined as the occurrence of one or more symptoms of hypoglycemia (such as palpitation, tiredness, sweating, strong hunger, dizziness and tremor) and a confirmed blood glucose meter reading of less than or equal to 70 mg/dl.

'Frequent unexplained hypoglycemia' was defined as having a hypoglycemic episode of one or more times a week in the absence of a definable precipitating event, such as a change in medication, diet or activity.

Skin manipulation is rubbing of insulin injecting sites before or/and after injection.

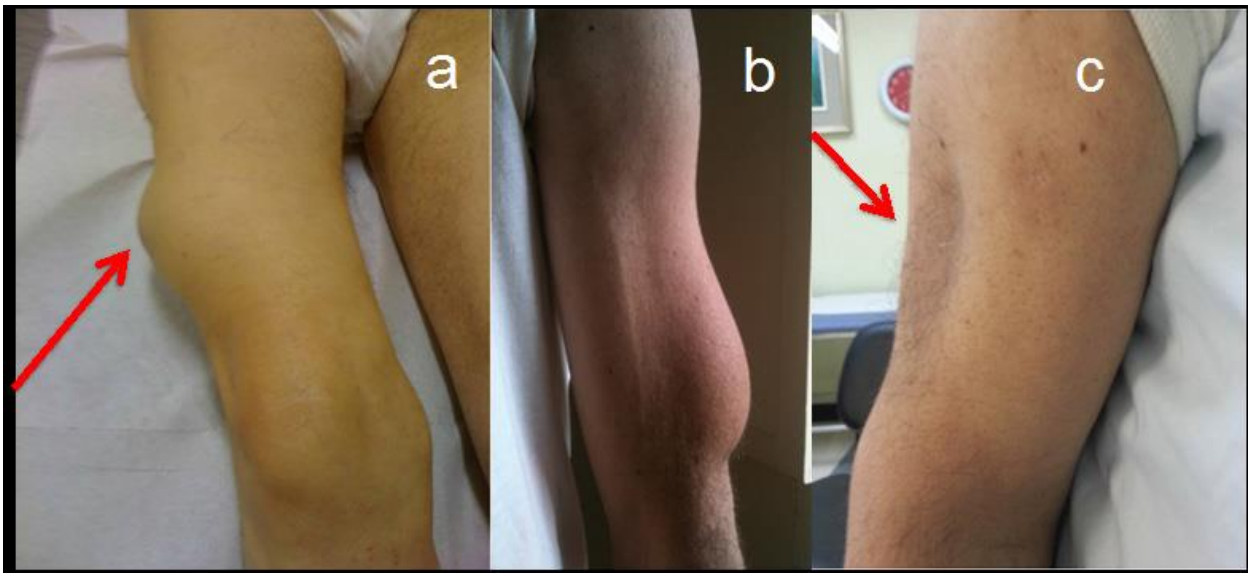

Figure 1: LH lesion of the right thigh as shown by the arrow (panel a) and left arm (panel b); LA lesion of the left arm as shown by the arrow (panel c) (Gentile et al., 2016).

4 Results

4.1 Socio-demographic Characteristics

Of the total 176 patients participated in this study, male to female ratio was almost equal (1:1.05). The mean (SD) age of participants was 11.36 (± 3.96) years and ranges from 2-18 years. Children (100, 56.8%) and adolescents shared almost similar proportion of the total population. Insulin injectors with primary level of education constituted the highest percentage (85, 48.3%) among the total participants. Almost similar proportions of parents (99, 56.3%) and patients themselves were in charge of injecting insulin daily (Table 1).

Table 1: Socio-demographic characteristics of patients with type 1 diabetes attending the diabetes clinic of Tikur Anbesa Specialized Hospital, Ethiopia, 2017.

Variable	Frequency	Percent
Sex		
Male	86	48.9
Female	90	51.1
Age (years)		
Children (1–12)	100	56.8
Adolescent (13–18)	76	43.2
Educational level of insulin injectors		
No schooling	2	1.1
Primary	85	48.3
Secondary	57	32.4
Higher	32	18.2
Person in charge of insulin injecting		
Parents	99	56.3
Patients	77	43.8

4.2 Clinical and Anthropometric Characteristics

Of the total participants, (130, 73.9%) of them was having a healthy weight whereas only few (10, 5.7%) participants were obese based on percentile adjusted BMI. Substantial percentage (111, 63.1%) of the participants was on insulin treatment for less than five years. Almost all patients were on combination treatment using intermediate acting insulin and regular insulin (173, 98.3%) and frequency of injection was two times per day in all patients. Higher frequency (105, 59.7%) of the patients was observed on insulin dose of greater than 0.7 units/kg. Insulin syringe needle size of each patient was 8 mm. Most (140, 83%) of the patients were having non-optimal glycemic control with HgbA1C of greater than 7.5% and about (56, 31.8%) of participants faced frequent unexplained hypoglycemia (Table 2).

Table 2: Clinical and anthropometric characteristic of patients with type 1 diabetes attending the diabetes clinic of Tikur Anbesa Specialized Hospital, Ethiopia, 2017.

Variable	Frequency	Percent
Percentile adjusted BMI		
Underweight	28	15.9
Healthy weight	130	73.9
Overweight	8	4.3
Obese	10	5.7
Insulin use duration (years)		
1–5	111	63.1
6–10	52	29.5
11–15	9	5.1
16–18	4	2.3
Insulin type		
Intermediate acting insulin	3	1.7
Intermediate acting insulin & regular	173	98.3
Daily insulin dose/kg		
≤ 0.7 U/kg	71	40.3
> 0.7 U/kg	105	59.7
HgbA1C %		
<7.5 %	36	17
≥7.5 %	140	83
Frequent unexplained hypoglycemia		
Yes	56	31.8
No	120	68.2

Abbreviations: DM=diabetes mellitus, HgbA1C%= glycated hemoglobin A1C, BMI=Body Mass Index

4.3 Insulin Injection Practices

Prior to insulin injection, about (95, 50.4%) of the patients were found to wash their hands always before injection but about half (84, 47.7%) of them never clean injection sites before injection. About (117, 66.5%) of patients always inspect their insulin vials for any appearance change. Substantial number (145, 82.4%) of the participants reported that, they always eliminate bubbles from the insulin syringes before injection. Almost half (42%) of the patients were found to manipulate their skin always before and after injection whereas half (40.3%) of them never manipulate their skin. Almost all the participants (164, 93%) have reported that they always lift skin fold of injection site while administering insulin subcutaneously. Majority (158, 89.8%) of them let the needle to be inserted long enough. Almost all (159, 90.3%) participants always inspect injection sites visually and using palpation for the presence of any abnormality (Figure 2).

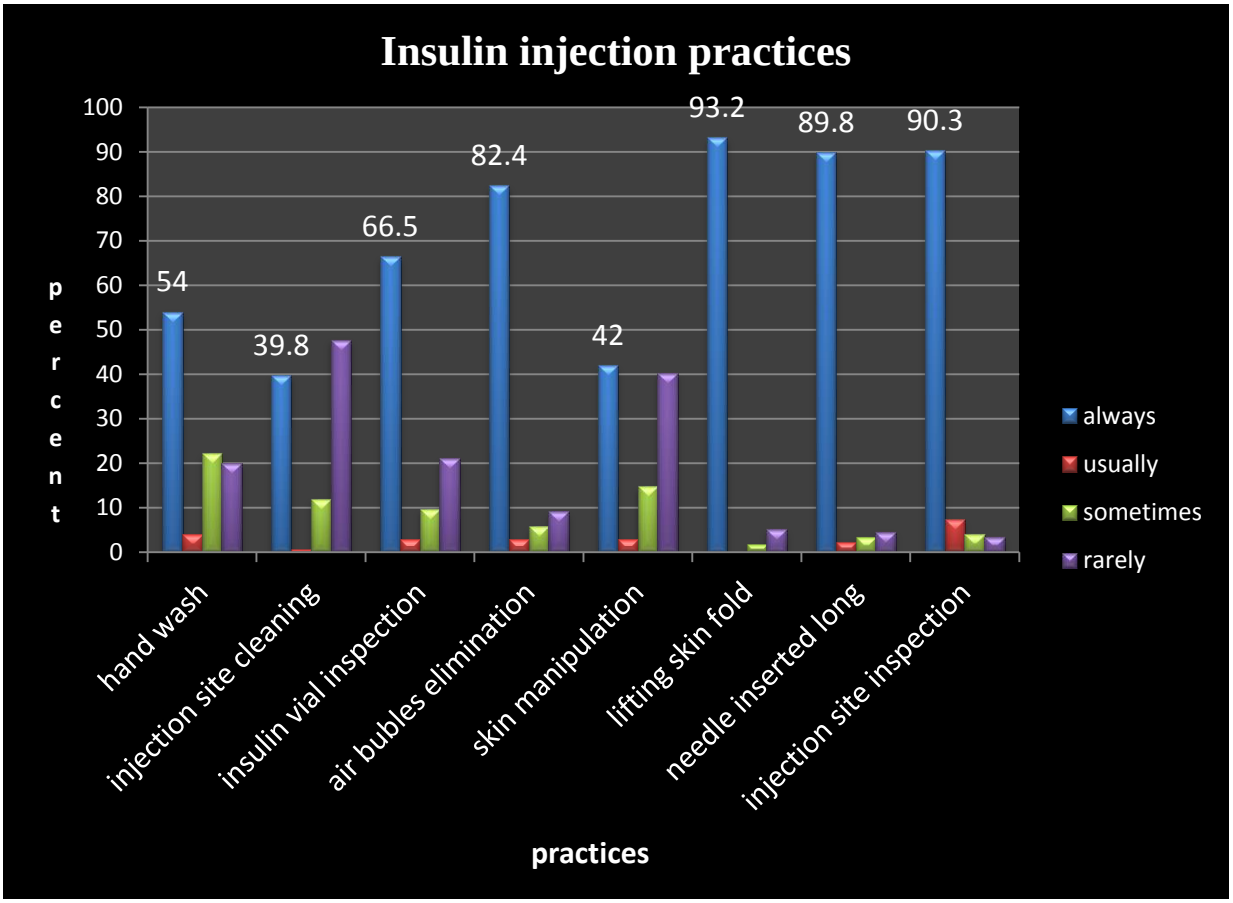

Figure 2: Insulin injection practices of study participants attending the diabetes clinic of Tikur Anbesa Specialized Hospital, Ethiopia, 2017.

Insulin storage condition was assessed for opened insulin already on use and unopened insulin. As a result patients who stores opened and unopened insulin in refrigerator were (95, 54%) and (146, 83%) respectively (Figure 3). It is noted that, cloudy insulin requires re-suspension prior to administration and in this study (67, 38.1%) of the participants were rolling or tilting cloudy insulin for less than 5 times but around 30 (17.0%) patients never roll or tilt insulin during their injection time. Only few (33, 15.3%) of the participants were changing insulin syringe at every injection time during their routine injection practice. Majorities (115, 65.3%) of the patients move or rotate to a different injecting area at every injection. Likewise, about half (73, 45.1%) of the participants have reported that, they measure by two finger apart from the previous injection point while injecting within the same injecting site. whereas almost similar number (64, 36.4%) of participants didn't measure at all. Patients who inserted insulin syringe perpendicular to the skin constituted a higher percentage (119, 67.6%) of the participants (Table 3). Around half (78, 44.3%) of the participants have reported that, they inject on more than one injection site. whereas the rest reported to inject frequently in one injection site and arms (50, 28.4%) constituted the highest number, thighs (28, 15.9%) and abdomen (20, 11.4%) (Figure 4).

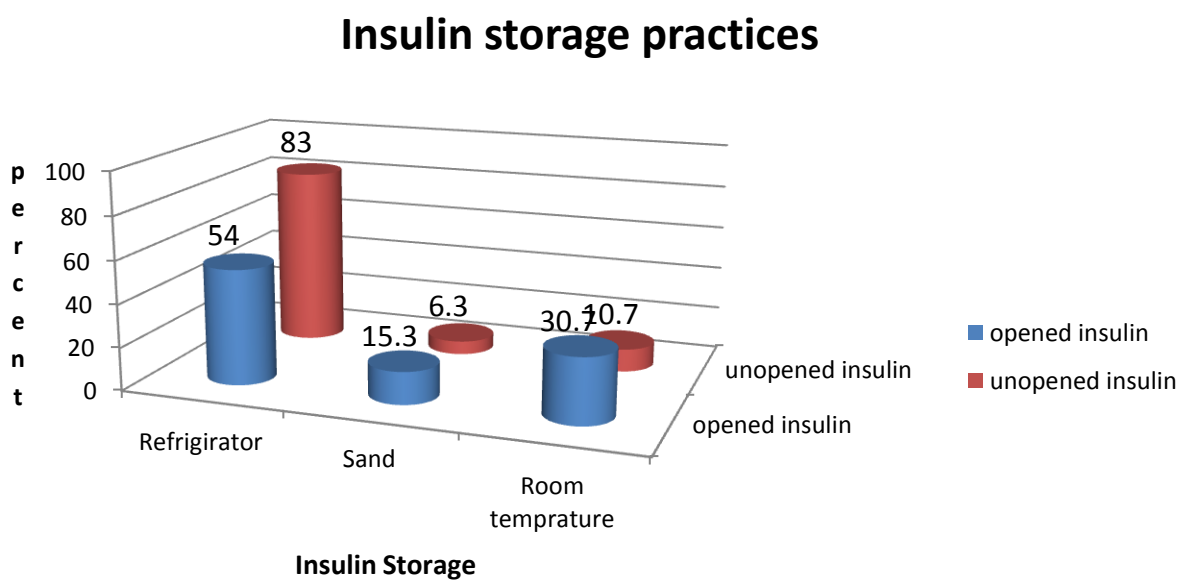

Figure 3: Insulin storage practices among study participants attending the diabetes clinic of Tikur Anbesa Specialized Hospital, Ethiopia, 2017.

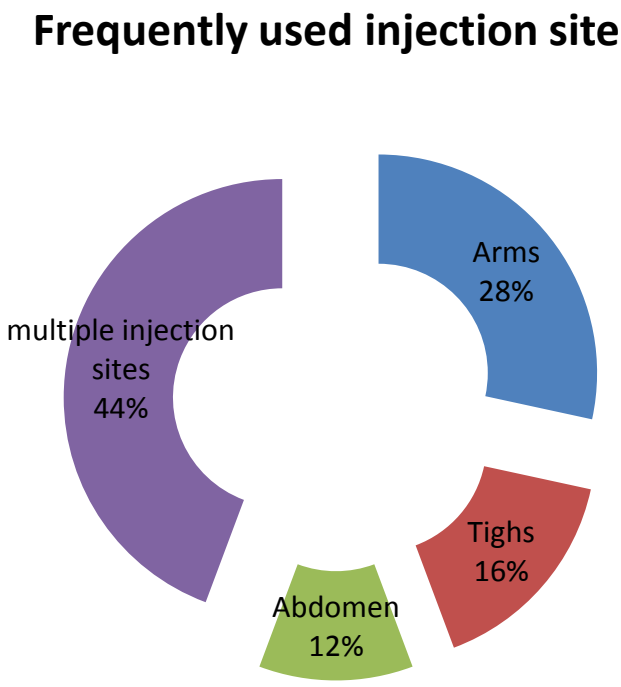

Figure 4: Frequently used insulin injection site among study participants attending the diabetes clinic of Tikur Anbesa Specialized Hospital, Ethiopia, 2017

Table 3: Insulin injection practices among study participants attending the diabetes clinic of Tikur Anbesa Specialized Hospital, Ethiopia, 2017.

Variable	Frequency (Percent)
Insulin syringe change	
At every injection	33 (18.8)
Every 2–3 injections	88 (50)
Every 4–5 injections	55 (31.3)
Injection site change	
At every injection	115 (65.3)
Every week	54 (30.7)
Occasionally when I remembered	7 (4.0)
Space measurement at one site	
1 finger	30 (17.0)
2 fingers	73 (45.1)
3 fingers	9 (5.1)
No measurement	64 (36.4)
Syringe insertion angle	
Straight	119 (67.6)
Diagonal	49 (27.8)
Both proportionately	8 (4.5)
Rolling of cloudy insulin	
No	30 (17.0)
< 5 times	67 (38.1)
6–10 times	50 (28.4)
11–15 times	18 (10.2)
16–20 times	11 (6.3)

4.4 Insulin Induced LH

The prevalence of insulin induced LH was (103, 58.5%) (Figure 5) and grade 2 LH which is characterized by massive thickening of fat tissue with firm consistency was the commonest type of LH which accounted (67, 65%) of patients but LA was a rare (3, 2.9%) condition. Arms constituted the highest (64, 62.7%) number of injection sites at which LH was developed followed by LH at more than one site (15, 14.7%). Among the few patients who were having LH on more than one injection site, patients who were having LH at their arms and abdomen constituted the highest proportion (8, 53.3%) (Figure 6).

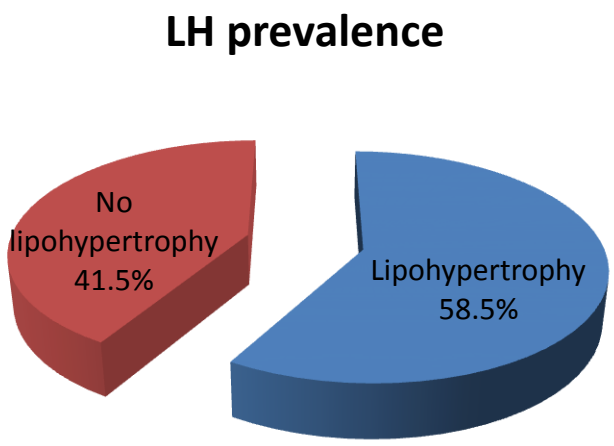

Figure 5: prevalence of insulin induced LH among patients with type 1 diabetes attending the diabetes clinic of Tikur Anbesa Specialized Hospital, Ethiopia, 2017.

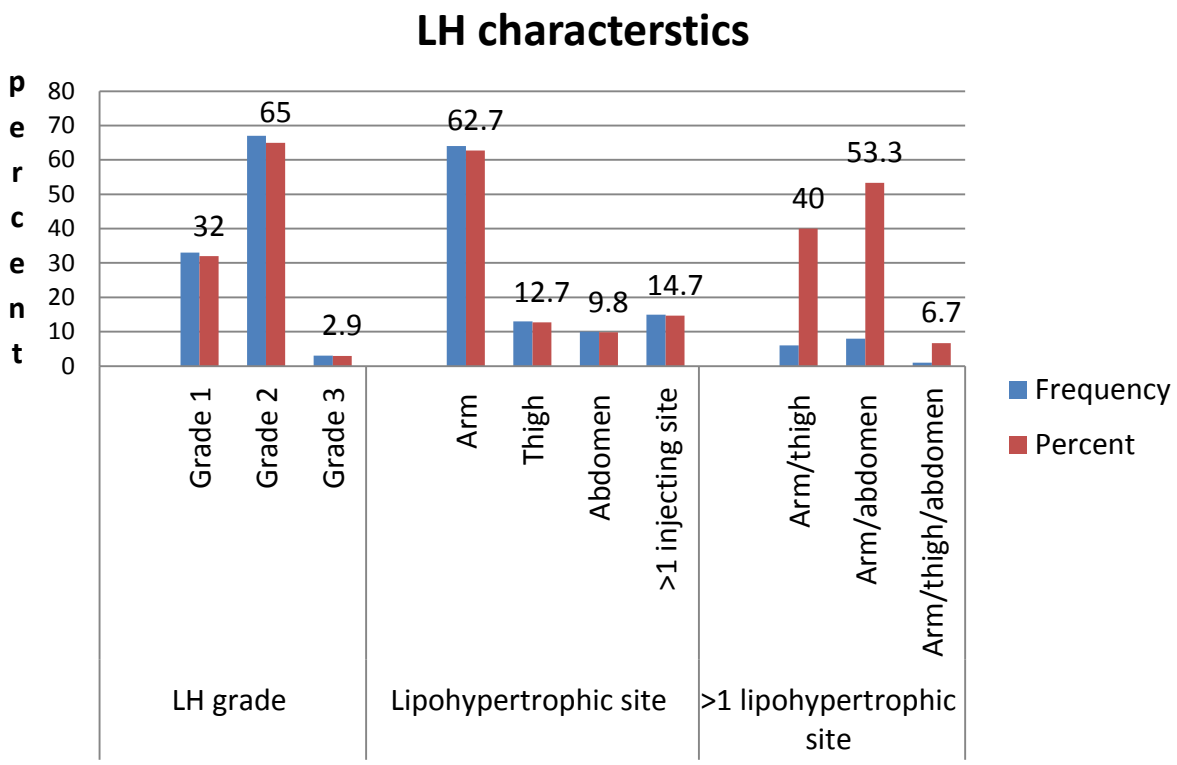

Figure 6: Characteristics of insulin induced LH among patients with type 1 diabetes attending the diabetes clinic of Tikur Anbesa Specialized Hospital, Ethiopia, 2017.

4.5 Predictors of Insulin Induced LH and Glycemic Control

4.5.1 Determinants of Insulin Induced LH

Findings from univariate binary logistic regression analysis on the association between Sociodemographic, anthropometric and clinical variables with insulin induced LH showed that, age group were having statistically significant difference (*P*-0.046) to predict the development of insulin induced LH. Hence children had 2 times higher [COR=1.86, 95% CI (1.01-3.415)] possibility of developing insulin induced LH compared to adolescents (Table 4). LH was also significantly associated with patients' weight (two-tailed *P*<0.010) and height (two-tailed *P*<0.010) but not with their percentile adjusted BMI (*P*-0.799). Hence weight difference was statistically significant between patients with insulin induced LH (M=34.08kg, SD=12.81) and without insulin induced LH (M=39.78, SD=15.16); *t*(138.24)=2.619, *P*<0.010 (two-tailed). The practical meaningfulness of the difference in weight means (mean difference=5.70, CI: 1.397 to

10.009) between the two groups was medium (Cohen's *d*=0.406). Similarly height difference between patients with insulin induced LH (M=137.17 Cm, SD=18.1) and without insulin induced LH (M=145.10 Cm, SD=21.9) was statistically significant *t*(174)=2.619, *P*<0.010 (two-tailed). The practical meaningfulness of the difference in height means (mean difference=7.921, CI: 1.952 to 13.890) was still medium (Cohen's *d*=0.394) (Table 5). Sex, percentile adjusted BMI, person in charge of injecting insulin were factors which had not statistically significant association with insulin induced LH.

Table 4: Insulin induced LH by Socio-demographic and anthropometric variables among type 1 diabetic patients attending the diabetes clinic of Tikur Anbesa Specialized Hospital, Ethiopia, 2017.

Variable	LH		COR, 95% CI	AOR, 95% CI
	No (n, %)	Yes (n, %)		
Age (years)				
Children (1-12)	35(35	65(65)	1.86(1.01-3.41)*	3.60(1.57-8.26)*
Adolescents (13-18)	38(50)	38(50)	1	1
Sex				
Male	33(38.4)	53(61.6)	1.28(0.70-2.34)	1.17(0.56-2.47)
Female	40(44.4)	50(55.6)	1	1
Educational level of insulin injectors				
No schooling	1(50)	1(50)	1.00(0.06-17.41)	0.85(0.04-19.0)
Primary	32(37.6)	53(62.4)	1.65(0.73-3.76)	0.83(0.29-2.36)
Secondary	24(42.1)	33(57.9)	1.37(0.57-3.28)	1.05(0.35-3.13)
Higher	16(50)	16(50)	1	1
Insulin injector				
Patient	37(48.1)	40(51.9)	0.62(0.34-1.13)	0.69(0.30-1.59)
Parent	36(36.4)	63(63.6)	1	1
Percentile adjusted BMI				
Underweight	14(50)	14(50)	0.67(0.15-2.88)	0.33(0.05-2.02)
Healthy weight	52(40)	78(60)	1.00(0.27-3.71)	0.52(0.11-2.48)
Overweight	3(37.5)	5(62.5)	1.11(0.164-7.50)	0.42(0.04-4.05)
Obese	4(40)	6(60)	1	1

*Statistically Significant: $P \leq 0.05$

Abbreviations: BMI= Body Mass Index, COR: Crude Odds Ratio, AOR: Adjusted Odds Ratio

Table 5: Insulin induced LH by anthropometric continuous variables among type 1 diabetic patients attending the diabetes clinic of Tikur Anbesa Specialized Hospital, Ethiopia, 2017.

Variable	Mean ± SD	*t*	df	*p*-value (two-tailed)	Mean difference [95% CI]
Height (Cm)					
LH	137.17±18.13	2.619	174	0.010*	7.92[1.95-13.89]
No LH	145.10±21.88				
Weight (Kg)					
LH	34.08±12.81	2.619	138.24	0.010*	5.70[1.39-10.01]
No LH	39.78±15.16				
BMI (Kg/m^2)					
LH	17.49±3.60	1.538	174	0.126	1.05[-0.29-2.39]
No LH	18.53±5.45				

*Statistically Significant: $P \leq 0.025$

Abbreviations: BMI= Body Mass Index, SD: Standard Deviation

LH was also determined by clinical characteristics of patients such as the dose of insulin (*P*=0.019). LH was observed 2 folds higher in patients who were on insulin daily dose of > 0.7 U/Kg than patients taking ≤ 0.7 U/Kg. Factors such as duration since insulin was started, type of insulin, frequency per day of insulin and frequent unexplained hypoglycemia were not having statistically significant association with the development of insulin induced LH (Table 6).

Table 6: Insulin induced LH by clinical characteristics among type 1 diabetic patients attending the diabetes clinic of Tikur Anbesa Specialized Hospital, Ethiopia, 2017.

Variable	LH		COR, 95% CI	AOR, 95% CI
	No (n, %)	Yes (n, %)		
Insulin use time (yrs)				
1–5	46(41.4)	65(58.6)	4.24(0.43-42.0)	12.6(0.34-466.3)
6–10	22(42.3)	30(57.7)	4.09(0.39-42.0)	3.49(0.27-45.2)
11–15	2(22.2)	7(77.8)	10.5(0.67-165.1)	10.4(0.47-233.0)
15–18	3(75)	1(25)	1	1
Daily Insulin dose/kg				
≤ 0.7 U/Kg	37(52.1)	34(47.9)	1	1
> 0.7 U/Kg	36(34.3)	69(65.7)	2.09(1.13-3.86)*	3.70(1.64-8.33)*
Frequent unexplained hypoglycemia				
Yes	27(48.2)	29(51.8)	1	1
No	46(38.3)	74(61.7)	1.49(0.79-2.84)	1.31(0.57-2.94)

*Statistically Significant: $P \leq 0.05$

Abbreviations: HgbA1C%= hemoglobin A1C, COR: Crude Odds Ratio, AOR: Adjusted Odds Ratio

Based on patients' insulin injection practices, univariate binary logistic regression analysis revealed that insulin needle reuse (*P*-0.005) and injection site rotation (*P*-0.018) was having statistically significant association with the development of insulin induced LH. Patients who changed their insulin syringe at every injection [COR=0.26, 95% CI (0.10-0.65)] and every 2-3 injections [COR=0.34, 95% CI (0.16-0.72)] were 4 and 3 times less likely to develop insulin induced LH respectively compared with patients who used single insulin syringe for 4-5 injections. Even though injection site rotation was significantly associated with development of insulin induced LH in chi-square analysis, it was not having between group differences on bivariate logistic regression analysis (Table 7).

After controlling different demographic, clinical, anthropometric and insulin injection practice factors through the use of multivariate logistic regression analysis, this study showed that age, weight, Height and insulin syringe reuse were independent factors that influenced the

development of insulin induced LH. LH in turn was an independent factor for the use of higher insulin daily dose. Injection site rotation was not independently significant and likely its influence on LH is depended to the other factors (Table 4, 5, 6, 7).

Table 7: Insulin induced LH by insulin injection practices among type 1 diabetic patients attending the diabetes clinic of Tikur Anbesa Specialized Hospital, Ethiopia, 2017.

Variable	LH		COR, 95% CI	AOR, 95% CI
	No (n, %)	Yes (n, %)		
Insulin syringe reuse				
Every injection	18(54.4)	15(45.5)	0.26(0.10-0.65)*	0.29(0.10-0.79)*
Every 2-3 injections	42(47.7)	46(52.3)	0.34(0.16-0.71)*	0.35(0.15-0.78)*
Every 4-5 injections	13(23.6)	42(76.4)	1	1
Injection site rotation				
Every injection	40(34.8)	75(65.2)	0.75(0.14-4.04)	0.76(0.13-4.39)
Every week	31(57.4)	23(42.6)	0.29(0.05-1.67)	0.38(0.06-2.30)
when I remember	2(28.6)	5(71.4)	1	1
Space measurement to inject in the same site				
1 finger	12(40)	18(60)	0.96(0.39-2.33)	1.14(0.43-3.03)
2 fingers	34(46.6)	39(53.4)	0.73(0.37-1.45)	1.27(0.59-2.75)
3 fingers	2(22.2)	7(77.8)	2.24(0.43-11.68)	2.24(0.41-14.36)
No measurement	25(39.1)	39(60.9)	1	1
Injection site frequently used				
Arm	18(36)	32(64)	1.48(0.69-3.00)	1.59(0.72-3.57)
Thigh	9(32.1)	19(67.9)	1.72(0.69-4.27)	1.46(0.55-3.86)
Abdomen	11(55)	9(45)	0.67(0.25-1.79)	0.55(0.19-1.55)
Proportionally rotate	35(44.9)	43(55.1)	1	1

*Statistically Significant: $P \leq 0.05$, COR: Crude Odds Ratio, AOR: Adjusted Odds Ratio

4.5.2 Glycemic control in Relation with Insulin Injection Practices

Generally there was a non-optimal glycemic control (83%) among participants of this study (Figure 7). Based on chi-square analysis, non-optimal glycemic control was significantly associated only with injection site uncleaning before injection (*P*-0.041) and non-optimal glycemic control was found to occur 2 times less likely inpatients who always clean injection sites before injection compared with patients who didn't always clean their injection site (Table 8).

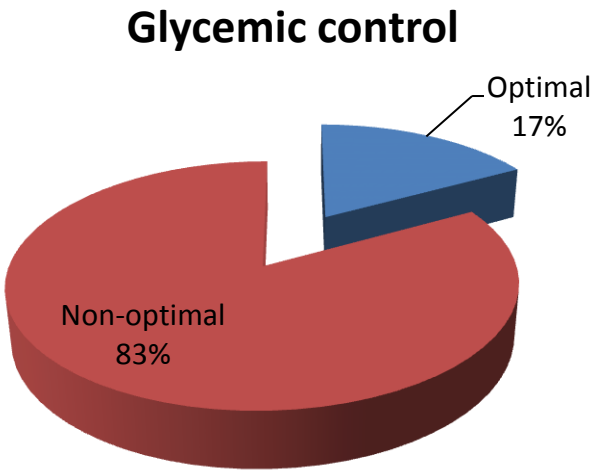

Figure 7: Glycemic control among patients with type 1 diabetes attending the diabetes clinic of Tikur Anbesa Specialized Hospital, Ethiopia, 2017.

Table 8: Glycemic control by insulin utilization practices among type 1 diabetic patients attending the diabetes clinic of Tikur Anbesa Specialized Hospital, Ethiopia, 2017.

Variable	*P*-value
Wash hands before injecting	0.632
Injection site cleansing before injecting	0.041*
Inspect insulin vial for any appearance change before injecting	0.091
Eliminate air bubbles in the syringe before injecting	0.881
Injection site visual inspection and palpation	0.998
Injection site frequently used	0.240
Rolling/tilting of cloudy insulin	0.939
Storage of opened insulin	0.734
Storage of unopened insulin	0.289

*Statistically Significant: $P \leq 0.05$

4.5.3 Effects of LH on Glycemic Control

The presence of insulin induced LH was significantly (*P*-0.009) associated with the occurrence of non-optimal glycemic control. Patients who were having insulin induced LH [COR=2.943, 95% CI (1.303-6.649)] were 3 fold more likely to have non-optimal glycemic control than patients without insulin induced LH. However, severity of LH (*P*-0.107) and site of LH (*P*-0.555) were not significantly associated with the occurrence of non-optimal glycemic control (Table 9).

Table 9: Effects of LH on glycemic control of type 1 diabetic patients attending the diabetes clinic of Tikur Anbesa Specialized Hospital, Ethiopia, 2017.

Variable	Glycemic control		COR, 95% CI	*P*-value
	Optimal (n, %)	Non-optimal (n, %)		
LH				0.009*
yes	11(10.7)	92(89.3)	2.943(1.303-6.649)*	
No	19(26)	54(74)	1	
LH grade				0.107
Grade 1	1(3.0)	32(97)	5.614(0.687-45.878)	
Grade 2	10(14.9)	57(85.1)	1	
LH site				0.555
Arm	5(7.8)	59(92.2)	2.95(0.62-14.04)	
Thigh	2(15.4)	11(84.6)	1.375(0.192-9.834)	
Abdomen	1(10)	9(90)	2.250(0.200-25.369)	
More than 1 site	3(20)	12(80)	1	

*Statistically Significant: $P \leq 0.05$, COR: Crude Odds Ratio

5 Discussion

LH as a local complication of insulin therapy is well recognized, it is the most common clinical complication of insulin therapy. Despite improvements in insulin purity and the introduction of recombinant human insulin its prevalence has remained high. The importance of this complication is not only cosmetic, but it also may impact on insulin absorption, and therefore affects glycaemic control(Roper and Bilous, 1998).

In the present study all of the study subjects were type 1 diabetic patient and were using recombinant human insulin. Among them 58.5% patients presented clinical evidence of LH and this figure was comparable with most of the studies done so far. Study from Spain reported LH prevalence of 64.4%(Blanco et al., 2013), from Dublin 51%(MT Cunningham and MJMcKenna, 2013), Pretoria 52%(De Villiers, 2007) and Alexandria 54.9%(Omar et al., 2011b). However the prevalence was relatively higher than results found from Saudi Arabia 47%(Hayek et al., 2016) and Germany 47.8%(Kordonouri et al., 2002). The reason behind this difference was that, in the study done in Saudi Arabia study participants were only adolescents and according to our study LH was found to be higher in children than adolescents. Thus it might be related to the study participants' age difference between the studies. The difference from the study done in Germany was the duration of insulin use at which participants were able to be involved in the studies. Our study recruited participants who were on insulin treatment for a minimum of 1 year whereas the study from Germany didn't set any time restriction on their participant recruitment. In most previous studies, time restriction of insulin use at least for three months was applied because these studies considered development of LH is related with time since insulin is started. Therefore the study done in Germany might have underestimated the magnitude of insulin induced LH. This study's LH prevalence was also significantly higher than reports from Safri Township which is 15.9%(Hajheydari et al., 2011) and a study from 22 centers of 7 European countries which is 30%(Strauss et al., 2002). Similarly this gap was explained by the participants' duration of insulin use required for recruitment. Safri Township's and European's studies were recruiting participants if they were on insulin treatment for at least 3 and 6 months respectively. Therefore recruitment of participants while they are on their earlier insulin treatment period might have underestimated the total magnitude of LH in these studies.

In this study grade 2 LH which is characterized by massive thickening of fat tissue with firm consistency was found in 65% of patients. This finding was not in line with previous studies which reported as grade 1 was the commonest type of LH (Omar et al., 2011, Hayek et al., 2016). Like the previous studies (Hajheydari et al., 2011 , Blanco et al., 2013) LA was still continuing to be a rare (2.9%) condition in this study too. This could be due to the introduction of high purity human recombinant insulin. LH was seen to develop mostly in the arms. This was related to the high number of patients who reported as injections were mostly in their arms and administered by their parents. This result was also true with other studies (Hajheydari et al., 2011 , Omar et al., 2011).

Generally in this study the development of insulin induced LH was independently influenced by age, weight, Height, daily dose of insulin and insulin syringe reuse. However factors such as percentile adjusted BMI, time since insulin started, injection site rotation and injection site frequently used did not contribute to the occurrence of this clinical complication.

Children were found to develop injection site LH almost 4 times higher than adolescents and this was also similarly reported by other studies(Hauner et al., 1995, Hajheydari et al., 2011). It might be due to the fact that skin thickness increases as age increase (Frid et al., 2010) therefore LH might be easily visualized and felt in children with less skin thickness than adolescents. Another plausible reason might be that, the minimum age at which injection was started in this study was 9 years and mostly parents were taking the responsibility of injection at this class of age. Our data also showed that parents were highly involved in causing LH therefore it might not be directly related with the children physiology but their parents were involved in causing most of the LH in this class of age.

On logistic regression analysis percentile adjusted BMI of patients was not having statistically significant association with development of LH, whereas weight and height of patients were having statistically significant association with development of LH on independent samples T-test analysis. Hence LH was reported in lower amount as weight and height of participants were increasing. This finding was in line with the data given by Hauner et al and Omar et al (Hauner et al., 1995, Omar et al., 2011). This might be explained by the reason that, in thinner and shorter patients the areas of LH are more easily seen and felt than in obese and taller patients. This is due to the fact that LH in such patients is deposited in small areas that enable data collectors to detect

it easily. However the mean weight and height differences between those with LH and without LH were not having good clinical significance (Cohen's d=0.4). This finding actually requires further investigations. Unlike our data, many studies reported the role of BMI as an effective factor in the development of the LH (Hajheydari et al., 2011 , Hayek et al., 2016, Omar et al., 2011, Vardar and Kızılcı, 2007). The main reason to this gap could be the different classification of BMI (natural, overweight and obese) used by Vardar and Kizilci and (BMI ≤25, >25) used by Al Hayek and Robert whereas in our study, percentile adjusted BMI was categorized in 4 classes as underweight, healthy weight, overweight and obese.

In the present study patients with LH were observed to use a significantly higher dose of insulin units per kg of their body weight compared to those without LH. This could be due to defective absorption of insulin by the abnormal injection sites. The same finding was also revealed by study conducted by Omar et al(Omar et al., 2011). Even though patients with LH were on relatively higher daily doses of insulin than those without LH, they were still found 3 folds more likely to have non-optimal control of blood sugar compared to patients without LH. Similarly other relevant studies (Hajheydari et al., 2011 , Hayek et al., 2016, Kordonouri et al., 2002) have also showed similar findings. This finding could be attributed to the altered insulin absorption in the lipohypertrophic areas. It is vital to note that blood glucose control in the diabetes is the main aim of preventing systemic complications, therefore patients should mandatorily stop injecting in to the abnormal injecting site for months to years till the lipohypertrophic areas recovers to normal(Frid et al., 2010). One recent study (Blanco et al., 2013) has revealed that frequent unexplained hypoglycemia was another adverse metabolic outcome of LH and in that study patients with LH were facing frequent unexplained hypoglycemia six times more commonly compared to those without LH but this was not reproduced by our study. The former study suggested that the reason for the occurrence of frequent unexplained hypoglycemia in patients with LH might be due to injection of similar insulin dose that was being injected to lipohypertrophic site in normal areas. Yet again patients should avoid injecting in to abnormal injection sites till recovery so that plasma concentration of insulin will be kept uniform.

Participants of this study were using insulin syringes of different types, called Shanchuan, Dispovan and BD syringe but no one was using insulin pen. All the insulin syringes were 8 mm in length and this was in contrary with the recommendation from Frid et al(Frid et al., 2010),

Gentile S et al(Gentile et al., 2016) and FIT (forum for injection technique) of UK(Hicks et al., 2011) and Canada(Berard et al., 2015). The above four guidelines recommend the use of insulin syringe which is not longer than 6 mm in children and adolescents. These guidelines stated that syringe length longer than 6 mm may result in intramuscular injection which leads to fast absorption and hypoglycemic events as well as painful injections.

In addition to the use of non-recommended length of insulin syringe, participants were observed to reuse syringes for more than one time. This leads to the development of LH 3.5 and 3 times more likely in patients who used one syringe for 4 to 5 and 2 to 3 injections compared to patients who used only for one injection respectively. This finding was also supported by other studies(Hayek et al., 2016, Strauss et al., 2002). This could be due to deformation of the needle on repeated use so that it can either raise injection morbidity or, more likely, render the patient susceptible to LH by inducing bleeding or infection at the injection site. Despite injection site rotation was the one and the main factor which was associated with the development of LH in many previous studies(Blanco et al., 2013, Hauner et al., 1995, Hayek et al., 2016, MT Cunningham and MJMcKenna, 2013, Strauss et al., 2002), in the present study it was not an independent factor that influence development of LH. The former studies put plausible reason for the formation of LH on patients who rotate injections less frequently. They suggested that, it is due to the repeated traumatization of the injection sites that leads to the hypertrophic lipid cells to replace the mid-dermal collagen(Hayek et al., 2016). It is quite natural that, patients feel comfortable while injecting at the lipohypertrophic areas but the consequence to glycemic control is bad. Therefore patients should be reminded the importance of injection site rotation. Recent guidelines recommend that patients should divide each injection site into quadrant (or halves when using thighs or buttocks) then using one quadrant per week and moving always clockwise. Injections within any quadrant or half should be spaced at least 1-2 cm from each other in order to avoid repeat tissue trauma (Berard et al., 2015, Frid et al., 2010, Gentile et al., 2016, Hicks et al., 2011).

In the present study insulin injection practices have been assessed in relation with glycemic control. The only factor which was significantly associated with the occurrence of non-optimal glycemic control was injection site uncleaning before injection. In order to put directions and

solutions, this study has discussed patients' insulin injection practices in comparison to recent well evidenced insulin injection guidelines.

Patients should always wash their hands with soap and water before injection (Berard et al., 2015, Frid et al., 2010, Hicks et al., 2011) but this practice was observed to be performed by only half of the patients in this study. Similarly injection sites should be always cleaned using either soap with water or antiseptics such as alcohol. Disinfection of the injection site is generally not required; however, alcohol swabs may be mandated for use prior to injections administered in a hospital or long term care setting, or wherever nosocomial infection are more prevalent. If alcohol is used to clean the site, the skin must dry completely before the injection is administered to reduce pain during injection (Berard et al., 2015, Frid et al., 2010, Hicks et al., 2011). Finding of this study was in line with what the guidelines recommend in regards to cleaning injection sites. Patients who were always cleaning injection sites before injection were 2 times less likely to have non-optimal glycemic control compared to patients who didn't always clean their injection site.

Two third of the study participants have reported that they inspect insulin vials for any appearance change and eliminate air bubbles in the syringe before injection. This finding was higher than the data given by Ahmad et al which showed about 28.1% of patients reported to air-shot by dialing 2-4 units of insulin(Ahmad et al., 2016). If air bubbles are seen in the syringe, it should always be avoided by holding the syringe with the needle pointed upwards, tap the barrel to bring them to the top, and then remove the bubbles by pushing the plunger to expel the air (Berard et al., 2015, Frid et al., 2010, Hicks et al., 2011). This practice will enable patients to take the correct dose of insulin so that they make their disease well controlled.

In this study no one of the patients was using insulin syringe < 8mm. Therefore if needle length is ≥ 8mm, children and adolescents should inject by lifting a proper skin fold with the thumb and index finger (possibly with the addition of the middle finger) and letting the needle to be inserted at 45^0 (diagonally) and completely. Lifting skin fold, angled and complete insertion of the needle will prevent intramuscular injection as well as reduce painful sensation (Frid et al., 2010). Our data showed that, despite most patients were lifting a skin fold; only few of them have reported that they were inserting the needle at 45^0 and this was in contrary with the recommendation.

Generally injection skin manipulation before or after insulin administration is not recommended. This is due to the reason that it will facilitate insulin absorption and results in hypoglycemic events (Frid et al., 2010). About half of the study participants were doing this action against the recommended practice. Injection sites should be inspected by health care providers at every visit, especially if LH is already present and patients should always inspect their own sites to detect LH (Berard et al., 2015, Frid et al., 2010, Hicks et al., 2011). This was done by almost all of the study participants of this study.

When using cloudy insulin (i.e. NPH and premixed insulin), the vial, cartridge or pen device should first be gently rolled 10 times, then tipped (not shaken) 10 times; finally, it should be inspected to ensure the suspension has a consistently milky white appearance (Berard et al., 2015, Frid et al., 2010, Hicks et al., 2011). In contrary to this recommendation, very few patients have reported that they re-constitute cloudy insulin by rolling up to 20 cycles. This data was in line with a study that was done worldwide about injection practices(Worldwide injectable technique study, 2015). Unlike this study, a higher percentage of participants who remix NPH insulin up to 20 cycles prior to use were seen in another study(Connic et al., 2010).

Unopened insulin vials and cartridges should be stored at refrigeration temperature (2 to 8 degrees C). Once in use, insulin should be stored at room temperature because it will be stable for a maximum of 1 month with in expiry date. Insulin administered at room temperature may reduce irritation, burning or painful injections, and facilitates the re-suspension of cloudy insulin (Berard et al., 2015, Frid et al., 2010, Hicks et al., 2011). In the present study, most patients have reported that they store unopened insulin in refrigerator and similarly about half of them reported as they store opened insulin in the same manner. The latter is in contrary with recommendations. This finding was comparable with the data given by a study done worldwide (Worldwide injectable technique study, 2015) whereas the later finding was lower than a finding from Ahmad et al(Ahmad et al., 2016). However these two studies were having different age of study participants.

6 Limitation of the Study

This study was having cross sectional design and conducted in single center. It would have better population coverage if it was done multi-centrally. Detection and characterization of LH in the diabetics was done only by observation and palpation techniques. However it would have been better if it was supported by ultrasonography imaging since observation and palpation techniques might be affected by skin thickness and total areas of the injection sites. Finding of this study cannot be generalized to all children and adolescents with type I DM due to smaller sample size used in this study. A validated data collection tool for evaluating patients' insulin injection practices was not present; hence this study has applied a data collection tool which was formulated by authors.

7 Conclusions

Despite patients were using the new recombinant human insulin, LH is still continuing to be high. The main factors that influenced the development of LH were younger age, lighter weight, shorter height and insulin syringe reuse. LH in turn has affected patients' insulin daily dose and HgA1C to be higher. This study has also revealed that very high number of the patients was having non-optimal glycemic control. Overall, some insulin injection malpractices have been found among participants of this study. As a result injection site uncleaning before injection was significantly associated with the occurrence of non-optimal glycemic control.

8 Recommendations

- Injection sites should be inspected by health care providers at every visit for all patients.
- Patients should use one insulin syringe for only single injection.
- Patients should avoid injection into lipohypertrophic areas to reduce wastage of insulin and to achieve better glycemic control.
- Generally it is vital note that, health care providers should educate all patients about the correct insulin injection techniques and practices such as hands and injection sites washing, avoiding syringe air bubbles, needle insertion, insulin vial and injection site inspection, insulin storage and re-suspension of cloudy insulin.
- Further studies are strongly recommended to formulate and validate a data collection tool to evaluate insulin injection practices.
- Generally further studies are strongly recommended in this area especially with longitudinal study designs.

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10 Annex I: Participant Information Sheet and Questionnaire

Participant information sheet and consent form (English version)

Dear respondent my name is _____. I am here to collect data for a study entitled **"Insulin induced lipohypertrophy and glycemic control among children and adolescents with diabetes in Tikur Anbesa Specialized Hospital".** The research investigator is Afewerki G/meskel, a Masters student in pharmacy practice at Addis Ababa University, School of Pharmacy. The purpose of this study is to assess Insulin induced LH and glycemic control among children and adolescent patients in Tikur Anbesa Specialized Hospital. The results obtained from this study are useful to develop better strategies to improve patient care and will enable health care providers to implement other care beyond metabolic control to solve problems for the future. To achieve the study objective, your honest and genuine participation by responding to the question prepared is very important and highly appreciated.

You will not receive any payment or other personal benefit for participation in this study. But study findings will be used to better improve patient care in the study setting. There is also no cost to you for participation but it will take 10-15 minutes of your time.

Your selection to participate in this study is randomly because you come to hospital in the predetermined time for the study and there is no specific issue targeting you as participants. You do not have any harm because of participating in this study. Your participation in this study is completely voluntary. You have the right to be in the study or to withdraw in any time; there is no influence that insists you to participate, unless you voluntarily confirmed to participate. Your refusal to participate will in no way affect your service at the hospital.

We would like to assure you that privacy will strictly be maintained throughout. Your personal information will be maintained through the use of unique identifiers, and through restricting access to the data set to the principal investigator and those working directly with him. The data collected from each participant will be entered into a computer where it will be maintained in password control. Hard copies of completed instruments will be kept in a locked file and will be available only for research study staff. If you have any questions or would like to receive further information about the study; please contact the following responsible bodies:

Persons to contact:

Afewerki G/meskel

Mob: +251-914-032885

E-mail: afegeb431@gmail.com

Or my advisor: Dr. Teshome Nedi

E-mail: teshome.nedi@aau.edu.et

Consent: I have read the document stated above or it has been read to me by the data collector as I can understand all conditions stated above. Therefore, I:

1. Agree _____on participation of the study

And I confirmed it by signature _____

Name of the interviewer: _____Sign. _____ Date of interview_____

Name of the supervisor: _____ Sign. _____ Date_____

Thank you for your time.

Semi-structured data collection format prepared for the study

"Insulin induced lipohypertrophy and glycemic control among children and adolescent patients in Tikur Anbesa Specialized Hospital" (English version)

Part I. Demographic and anthropometric data of study participants		
SN	**Questions**	**Response category**
0	ID number	
1	Sex	1. Male 2. Female
2	Age (years)	
3	Educational level of the person in charge of administering insulin mostly	1. No schooling 2. Primary 3. Secondary 4. Higher education
4	Height in meters	
5	Weight in kg	
6	Body mass index (BMI) m/kg	
Part II. Questions related to clinical data of study participants		
1	Duration of diabetes mellitus	1. 1-5 years 2. 6-10 years 3. 11-15 years 4. 16 -18 years
2	Three (3) most recent HgbA1c within two years	
3	Average of 3 most recent HgbA1c	1. <7.5% 2. ≥7.5%
4	Did patient has frequent unexplained hypoglycemia	1. Yes 2. No

Part III. Questions related insulin and its devices used for administration		
1	How long have you been injecting insulin?	1. 1‑5 years 2. 6‑10 years 3. 11‑15 years 4. 16 -18 years
2	Types of insulin used in this year	1. NPH 2. lente 3. Regular 4. Glargine 5. Mixed of NPH and regular
3	How many times a day do you inject?	1. Twice daily 2. Three times daily 3. Four times a day or more
4	How much insulin do you inject daily recently?	
5	How much insulin do you inject on average recently?	1. Daily ≤ 0.7/kg 2. Daily > 0.7/kg
6	What type of syringe do you use mostly?	1. Shanchuan 2. Dispovan 3. BD syringe
7	What size needle do you use?	1. 4 mm 2. 5 mm 3. 6 mm 4. 8 mm 5. Greater than 8 mm

Part IV. Questions related to study participants' insulin injecting practices by likert scale (thick in the best answer)				
Questions	**Always**	**Usually**	**Sometimes**	**Never**
1. How common you wash your hands before injecting?				
2. How common you swab the injection sites before injecting?				
3. How common you inspect insulin vial for any appearance change before injecting?				
4. How common you eliminate air bubbles in the syringe before injecting?				
5. How common you manipulate the skin before and after injection?				
6. How common you pinch the skin while injecting?				
7. How common you let needle to be inserted long enough?				
8. How frequent you visually inspect and palpate injection site?				
9. How frequently you measure and record your blood sugar?				
10. How common you arrange the dose of insulin out of health providers' recommendation?				
11. How common you follow the exercise programs recommended by health providers?				

Part V. Questions related to study participants' insulin injection Practices		
1	How often do you change the insulin syringe?	1. At every injection 2. Every 2-3 injections 3. Every 4-5 injections 4. When the insulin I have is finished
2	How frequent do you move to a different area when you inject?	1. I move to a different site at every injection 2. I move to a different site every week 3. I move around sites occasionally, when I remember 4. No, I only use one site
3	How much space do you measure to inject within the same area apart from the previous injection site?	1. One finger apart 2. Two fingers apart 3. Three fingers apart 4. No measurement at all
4	Who do the insulin injections give?	1. Patient himself/herself 2. Parents
5	How do you insert needles in to the skin mostly?	1. Straight 2. Diagonally 3. Both
6	How many times do you roll the cloudy insulin?	1. I don't roll at all 2. < 5 times 3. 5-10times 4. 11-15 times 5. 16-20 times

7	Where do you store opened insulin?	1. Refrigerator 2. Sand 3. Room temperature
8	Where do you store unopened insulin?	1. Refrigerator 2. Sand 3. Room temperature
9	Which injection site do you frequently use?	1. Arm 2. Thigh 3. Abdomen 4. Proportionally rotate to all

Part VI. Questions related to LH of study participants based on physical examination		
1	Lipohypertrophy status by visual and palpation exams	1. Presence of swelled or depressed skin at injection site 2. No abnormality
2	Type of lipohypertrophy	1. Swelled skin which has smooth consistency 2. Swelled skin which has firm consistency 3. Depressed skin
3	Site of lipohypertrophy developed	1. Arm 2. Thigh 3. Abdomen 4. More than 1 site

Thank you for your time and cooperation!!

የስኳር በሽታ ኣገልግሎት ተጠቃሚዎች በጥናቱ ለመሳተፍ ፈቃደኝነታቸዉን የሚገልፁበት ቅጽ

ኣዲስ ኣበባ ዩኒቨርሲቲ

ፊርማሲ ትምህርት ቤት

ፊርማሲፕራክቲስ ድሕረ ምረቃ ፕሮግራም

እኔ _____የተባልኩኝ፣ ኢንሱሊን የሚያስከትለው የስብ ክምችት እና የስኳር መጠን ቁጥጥር በሚል ርእስ ኣፈወርቂ ገ/መስቀል በተባለ የኣዲስ ኣበባ ዩኒቨርስቲ ፋርማሲ ትምህርት ቤት የፋርማሲ ፕራክቲስ ድሕረ ምረቃ ተማሪ ለሚከናወን ጥናት መረጃ ሰብሳቢ ነኝ፡፡ የዚህ ቅፅ ዋና ዓላማ ለናንተ ለተሳታፊዎች ስለ ምርምሩ ምንነት መብራርያ መስጠት ነው፡፡

የምርምሩ ዋና ዓላማ ኢንሱሊን ለሚያስከትለው የስብ ክምችት እና የስኳር መጠን ቁጥጥር መገምገም ነው፡፡ የምርምሩ ውጤት የጤና ባለሞያዎች ለስኳር በሽተኖች እየሰጡት ያለው ኣገልግሎት በበለጠ እንዲሻሻልና የበሽተኞች ተጠቃሚነት ለማሳደግ ይሆናል፡፡ ይሄ እንዲሳካ ደሞ የእናንተ በፍላጎት እና ፈቃደኝነት ላይ የተመሰረተ ቀና ተሳትፎ ወሳኝ ነው፡፡

መጠይቁ ከጊዜዎ ከ 10 – 15 ደቂቃ የሚወስድ ሲሆን በዚህ ጥናት ውስጥ የርስዎ ተሳታፉነት ሙለ በሙለ በርስዎ ፈቃደኝነት ላይ የተመሰረተ ነዉ፤ በዚህ ጥናት ውስጥ መሳተፍዎም ሆነ ላለመሳተፍ መወሰንዎ በሆስፒታሉ ውስጥ በሚያገኙነት ኣገልግሎት ላይ ምንም ኣይነት ተጽእኖ የማይኖረው ሲሆን ቃለመጠይቁን በማንኛውም ሰኣት ማቋረጥ ወይም ጥያቄዎችን ኣለመመለስ ይችላሉ፡፡ በጥናቱ ውስጥ ለተነሱት ጥያቄዎች የሚሰጡት መልሶች ሙለ በሙለ በምስጢር የሚጠበቁ ሲሆን የርስዎም ስም በማንኛዉም መልኩ በጥናቱ ውስጥ ኣይገለጽም፤ እንዱሁም የሚሰጡት ምላሽ ከርስዎ ማንነት ጋር በማንኛውም መልኩ ኣይያያዝም፡፡
ምርምሩን በተመለከተ ተጨማሪ ጥያቄ ወይም መረጃ ከፈለጉ በሚቀጥለው ኣደራሻ ለዋናው ተመራማሪ/ኣማካሪው መጠየቅ ይቻላል፡፡
ኣፈወርቂ ገ/መስቀል (ሞባይል፡ 0914032885፣ ኢመይል፡ afegeb431@gmail.com)
ኣማካሪ፡ ዶ/ር ተሾመ ነዲ (ኢመይል፡teshome.nedi@aau.edu.et)

ከላይ በቀረበልኝ መረጃ መሰረት የምርምሩ ጠቃሚነት ስለገባኝ ምርምሩ ውስጥ ለመሳተፍ ፡-

ፍቃደኛ ነኝ---------- ፊርማ----------

የ መረጃው ሰብሳቢ ፊርማ---------- ቀን----------

የ ምርምሩ ኣስተባባሪ ፊርማ----------ቀን----------

ኢንሱሊን የሚያስከትለው የስብ ክምችት እና በደም ውስጥ የስኳር መጠን ቁጥጥር በተመለከተ የተዘጋጀ መጠይቅ (በአማርኛ የተዘጋጀ)

ክፍል ነ. ኣንተን/ኣንቺን በተመለከተ አጠቃላይ መጠይቅ		
ቁ	**ጥያቄ**	**መልስ**
0	መለያ ቁጥር	
1	ፆታ	1. ወንድ 2. ሴት
2	ዕድሜ (በዓመት)	
3	ኢንሱሊንን በብዛት የሚወጋው ሰው የትምህርት ደረጃ	1. ኣልተማረም 2. ኣንደኛ ደረጃ 3. ሁለተኛ ደረጃ 4. ከፍተኛ ደረጃ
4	ቁመት በሜትር	
5	ክብደት በኪሎግራም	
6	የውፍረት መጠን በ ሜ/ኪ.ግ	
ክፍል 2. የተሳታፊዎች የጤንነት ደረጃን በተመለከተ አጠቃላይ መጠይቅ		
1	ስኳር በሽታ ኣለብህ/ሽ ከተባልክ/ሽ ስንት ዓመት ሆነህ/ሽ?	1. ከ 1-5 ዓመት 2. ከ 6-10 ዓመት 3. ከ 11-15 ዓመት 4. ከ ነ6 - ነ8 ዓመት
2	በሁለት ዓመት ውስጥ የተመዘገቡት ሦስት ወቅታዊ HgbA1c ዘርዝር	
3	የሦስት ወቅታዊ HgbA1c ኣማካይ ውጤት	1. <7.5% 2. ≥7.5%
4	ምክንያቱ በየማይታወቅ ሁኔታ በተደጋጋሚ በደም ውስጥ የስኳር መጠን መቀነስ ያጋጥምሃል/ሻል?	1. ኣዎ 2. ኣያጋጥመኝም

ክፍል 3. ኢንሱሊንን እና ኢንሱሊንን ለመስጠት የምንጠቀምባቸው መሳሪያዎችን በተመለከተ አጠቃላይ መጠይቅ		
1	ኢንሱሊን ለስንት ዓመት ተወጋህ/ሽ?	1. ከ 1-5 ዓመት 2. ከ 6-10 ዓመት 3. ከ 11-15 ዓመት 4. ከ 16 -18 ዓመት
2	በዚህ ዓመት በብዛት የተጠቀምከው/ሽው የኢንሱሊነ ዓይነት?	1. NPH 2. lente 3. Regular 4. Glargine 5. Mixed of NPH and regular
3	በቀን ስንት ጊዜ ትወጋለህ/ትወጊያለሽ?	1. ሁለት ጊዜ 2. ሦስት ጊዜ 3. ላራት ጊዜና ከዛ በላይ
4	በአሁኑ ጊዜ የምትወጋው የኢንሱሊን መጠን?	
5	በአሁኑ ጊዜ የምትወጋው የኢንሱሊን መጠን በአማካይ?	ነ. በቀን ≤ 0.7 ዩኒት/ኪ.ግ 2. በቀን > 0.7ዩኒት/ኪ.ግ
6	በብዛት የምትጠቀመው የኢንሱሊን መርፌ ዓይነት?	1. Shanchuan 2. Dispovan 3. BD syringe
7	የምትጠቀምበት የኢንሱሊን መርፌ ርዝመት?	1. 4 ሚ.ሜ 2. 5 ሚ.ሜ 3. 6 ሚ.ሜ 4. 8 ሚ.ሜ 5. ከ 8 ሚ.ሜ በላይ

ክፍል 4. ኢንሱሊን ኣወሳሰድ በተመለከተ በላይከርት ስኬል የተዘጋጀ መጠይቅ (መልሱ ላይ ቲክ ያድርጉ)				
ጥያቄ	**ሁል ጊዜ**	**ኣብዛኛውን ጊዜ**	**ኣልፎ ኣልፎ**	**በጭራሽ**
1. ኢንሱሊን ከመውጋትህ/ትሽ በፊት እጆችህን/ችሽን መታጠብ ምን ያህል ታዘወትራለህ/ሽ?				
2. ኢንሱሊን ከመውጋትህ/ትሽ በፊት የምትወጋበትን/ጊበትን ቦታ መጥረግ ምን ያህል ታዘወትራለህ/ሽ?				
3. ኢንሱሊን ከመወጋትህ/ሽ በፊት የኢንሱሊን ብልቃጥ ላይ የመልክ ለውጥ መኖሩን ምን ያህል ታረጋግጣለህ/ሽ				
4. ኢንሱሊን ከመወጋትህ/ሽ በፊት በምትወጋበት/ጊበት መርፌ ውስጥ የሚገኘውን የኣየር ኣረፋ ምን ያህል ታስወግዳለህ/ሽ?				
5. ኢንሱሊን ከመውጋትህ/ትሽ በፊት እና ከተወጋህ/ሽ በሃላ ቆዳህን/ቆዳሽን ምን ያህል ታሸዋለህ/ታሺዋለሽ?				
6. ኢነሱሊን ስትወስድ/ጂ የሚወጋውን ቆዳ ቆንጥጠህ መያዝ ምን ያህል ታዘወትራለህ/ሽ?				
7. ኢነሱሊን ስትወጋ/ጊ መርፌው እስከመጨረሻ እነዲገባ ምን ያህል ታደርጋለህ/ታደርግያለሽ?				
8. ኢንሱሊን የምትወጋበትን/ጊበትን ቦታ በመመልከት እና በመዳሰስ ምን ያህል ትገመግመዋለህ/ሽ?				
9. በደም ውስጥ የሚገኘውን የስኳር መጠን መለካትና መመዝገብ ምን ያህል ታዘወትራለህ/ሽ?				
10. የጤና ባለሞያው ከሚሰጥህ/ሽ ትዕዛዝ ውጭ የምትወስደውን/ጂውን የኢንሱሊን መጠን ማቀያየር ምን ያህል ታዘወትራለህ/ሽ?				
11. የጤና ባለሞያው የሚሰጥህን/ሽን የኣካል እንቅስቃሴ ትዕዛዝ ምን ያህል ትሰራለህ/ሽ?				

ክፍል 5. ኢንሱሊን ላወሳሰድ በተመለከተ አጠቃላይ መጠይቅ		
1	የኢንሱሊን መርፌ በየስንት ጊዜ ትቀይራለህ/ትቀይሪያለሽ?	1. ሁል ጊዜ በምወጋበት ወቅት 2. ከ 2-3 ጊዜ ከወጋው በሃላ 3. ከ 4-5 ጊዜ ከወጋው በሃላ 4. የተሰጠኝ ኢንሱሊን ሲያልቅ
2	ኢንሱሊን በምትወጋበት/ጊበት ወቅት በየስንት ጊዜው ወደ ተለያየ መውጊያ ቦታ ትቀያይራለህ/ትቀያይሪያለሽ?	ሀ. ሁል ግዜ በምወጋበት ወቅት 2. በአንድ ሳምንት ልዩነት 3. ባማስታወስበት ጊዜ ብቻ 4. ላንድ ቦታ ብቻ ላይ ነው የምወጋው
3	ተመሳሳይ ቦታ ላይ ስትወጋ/ጊ ቀድሞ ከወጋህበት/ሽበት ቦታ ምን ያህል ለከተህ/ተሽ ትወጋለህ/ጊያለሽ?	ሀ. በአንድ ጣት ልዩነት 2. በሁለት ጣት ልዩነት 3. በሦስት ጣት ልዩነት 4. ምንም አልለካም
4	ኢንሱሊንን የሚሰጠው ሰው ማን ነው?	1. ታካሚው ራሱ/ራስዋ 2. ቤተሰብ
5	የኢንሱሊን መርፌ በአብዛኛው ጊዜ የምትወጋበት አቅጣጫ?	1. ቀጥ ኣድርጌ 2. በስያፍ/ በአግድመት 3. በሁለቱም
6	ያልጠራውን ኢንሱሊን ከመውጋትህ/ሽ በፊት ለምን ያህል ጊዜ ታንከባልለዋለህ/ሽ?	ሀ. ምንም አላንከባልለውም 2. ከ 5 ጊዜ በታች 3. ከ 5- ሀ0 ጊዜ 4. ከ ሀሀ- ሀ5 ጊዜ 5. ከ ሀ6- 20 ጊዜ
7	ላንዴ ተከፍቶ መጠቀም የጀመርከውን/ሽውን ኢንሱሊን የት ታስቀምጠዋለህ/ታስቀምጪዋለሽ?	1. ፍርጅ ውስጥ 2. ላሸዋ ውስጥ እቀብረዋለው 3. በላከባቢ የሙቀት መጠን ላይ ላስቀምጠዋለው
8	ከፍተህ/ሽ መጠቀም ያልጀመርከውን/ሽውን ኢንሱሊን የት ታስቀምጠዋለህ/ሽ?	1. ፍርጅ ውስጥ 2. ላሸዋ ውስጥ እቀብረዋለው 3. በላከባቢ የሙቀት መጠን ላይ

9	በብዛት የምትጠቀመው/ሚው የኢንሱሊን መውጊያ ቦታ የትኛው ነው?	ı. ጡንቻ ላይ 2. ታፋ ላይ 3. ሆድ ላይ 4. በተመጣጣኝ ሁሉም ላይ
ክፍል 6. ኢንሱሊን የሚያስከትለውን የስብ ክምችትን ለመፈተሽ ኢንሱሊን የሚወጋበት ቦታ ዳሰሳ		
1	የስብ ክምችት ሁኔታ በማየት እና በመዳሰስ?	1. ኢንሱሊን የሚወጋበት ቦታ ላይ ያበጠ ወይም የሰረጎደ ክፍል ኣለ 2. የለበትም/ባትም
2	የስብ ክምችት ምን ዓይነት ነው?	1. ያበጠው ክፍል ሲዳሰስ ገባ ወጣ ያለ ኣይደለም 2. ያበጠው ክፍል ሲዳሰስ ገባ ወጣ ያለ ነው 3. የሰረጎደ ክፍል ነው
3	የስብ ክምችት የታየበት ቦታ የት ነው?	ı. ጡንቻ ላይ 2. ታፋ ላይ 3. ሆድ ላይ 4. ከኣንድ ቦታ በላይ

ተሳታፊያችን ለጊዜህ/ሽ እና ለትብብርህ/ሽ እናመሰግናለን!!

11 Annex II: Recommended Insulin Injection Practices.

Injection practice		Recommended practice
Insulin storage	Opened	Unopened insulin vials and cartridges should be stored at refrigeration temperature (2 to 8 degrees C).[a]
	Unopened	Once in use, insulin should be stored at room temperature because it will be stable for a maximum of 1 month with in expiry date and minimizes pain during injection.[a]
Injection site cleaning		Injection sites should be always cleaned using either soap with water or antiseptics such as alcohol. Disinfection of the injection site is generally not required; however, alcohol swabs may be mandated for use prior to injections administered in a hospital or long term care setting, or wherever nosocomial infection are more prevalent.[a]
Injection skin manipulation		Injection skin manipulation before or after insulin administration is generally not recommended. It facilitates insulin absorption.[b]
Needle size		No medical reasoning to use insulin syringe needle longer than 6 mm in children and adolescents. Needles longer 6mm are related with intramuscular injection.[a]
Lifting skin fold		Children and adolescents who use syringe needle ≥ 8mm should inject by lifting a proper skin fold with the thumb and index finger (possibly with the addition of the middle finger).[a]
Needle insertion angle		Children and adolescents who use syringe needle ≥ 8mm should inject at 45^0 (diagonally).[a]
Needle insertion		Syringe needle should be inserted long enough.[a]
Re-suspension cloudy insulin		When using cloudy insulin (i.e. NPH and premixed insulin), the vial, cartridge or pen device should first be gently rolled 10 times, then tipped (not shaken) 10 times; finally, it should be inspected to ensure the suspension has a consistently milky white appearance.[a]
Injection site rotation		Patients should divide each injection site into quadrant (or halves when using thighs or buttocks) then using one quadrant per week and moving always clockwise. Injections within any quadrant or half should be spaced at least 1-2 cm from each other in order to avoid repeat tissue trauma.[a]
Needle reuse		A needle should be used for a single use. Needle reuse could result in deformation of the needle on repeated use so that it can either raise injection morbidity or, more likely, render the patient susceptible to LH by inducing bleeding or infection at the injection site.[a]

a-Berard et al., 2015; Frid et al., 2010; Hicks et al., 2011 b-Frid et al., 2010