Contents lists available at ScienceDirect



Journal of Clinical & Translational Endocrinology

journal homepage: www.elsevier.com/locate/jcte



Original research

Ultrasound-guided measurement of skin and subcutaneous tissue thickness in children with diabetes and recommendations for giving insulin injections



Soo Ting Joyce Lim^a, Yuen Ching Angela Hui^a, Pei Kwee Lim^a, Chin Choo Evelyn Lim^b, Yen Yen Chia^b, Rashida Farhad Vasanwala^{c,*}

^a Division of Nursing, Speciality Care Service, KK Women's and Children's Hospital, Singapore

^b Division of Nursing, KK Women's and Children's Hospital, Singapore

^c Department of Paediatrics, Endocrinology Service, KK Women's and Children's Hospital, Singapore

ABSTRACT

Aim: To measure skin thickness (ST) and skin + subcutaneous layer thickness (SCT) by ultrasound and estimate the risk of intramuscular injection (IM) with different needle lengths across injection sites according to age group.

Method: Children recruited between 1 and 18 years with type 1 and 2 diabetes on insulin injections and divided into three age groups: 1–6 years, 7–12 years and 13–18 years. A portable ultrasound was used to measure ST and SCT at four injection sites on the abdomen, arm, thigh and buttock.

Results: Total 153 children enrolled for the study. The mean (SD) measurement of ST & SCT at four sites on abdomen, arm, thigh & buttocks were as follows; $4.33 \text{ mm} (\pm 2.22)$, $5.55 \text{ mm} (\pm 2.26)$, $5.83 \text{ mm} (\pm 3.12)$, $6.48 \text{ mm} (\pm 3.47)$ in 1–6 years old; $7.11 \text{ mm} (\pm 3.68)$, $7.79 \text{ mm} (\pm 4.54)$, $7.17 \text{ mm} (\pm 3.62)$, $8.51 \text{ mm} (\pm 3.65)$ in 7–12 years old; $8.94 \text{ mm} (\pm 4.50)$, $8.42 \text{ mm} (\pm 5.00)$, $8.61 \text{ mm} (\pm 4.76)$, $9.76 \text{ mm} (\pm 4.38)$ in 13–18 years old. Young children, 1–6 years have the highest risk of IM injection with all needle lengths, i.e. 4, 5, 6, 8 & 12.7 mm, while older children 7–12 & 13–18 years have a lower risk with shorter needles (4, 5 and 6 mm) as compared to longer needles (8 and 12.7 mm).

Conclusions: Children with diabetes on insulin therapy should be advised on the appropriate needle length accordingly to their age and BMI.

Introduction

Multiple-dose insulin injections are the mainstay of diabetes management in children and are given subcutaneously at four recommended sites with the prescribed technique. In recent years, the effectiveness of insulin therapy has improved tremendously with the availability of different needle lengths. Since injections are to be administered three to four times daily, the three most important points of the correct site, needle length and technique [1] are emphasised from the start to ensure delivery of insulin into the subcutaneous (SC) tissue and optimise insulin absorption. SC is the correct site for insulin administration as blood flow through this fat layer is slow and predictable in contrast to muscle wherein it is fast and ever-changing. If the injection becomes intramuscular, the absorption of insulin is rapid and can cause hypoglycaemia. Therefore, to avoid fluctuations in blood glucose, it is essential that injections are given consistently in the SC tissue.

Repeated injections at the same site over time can also lead to skin injuries such as hypertrophy, lipoatrophy and subcutaneous nodularity, thereby altering skin thickness [1]. Therefore, patients are advised to rotate and rest the sites as needed on a day-to-day basis. The technique to be used for insulin injections are part of standard diabetes education, and needle length depends on patient's age [2]. But the most objective recommendation should be based on total skin and subcutaneous layer thickness (SCT) measurement across age groups [3–6]. Even among the different age groups ST and SCT will vary according to body mass index (BMI) which differs across ethnicity and gender. In children studies comparing this variability is lacking. However the adult study has shown that factors which influence ST at the abdomen and upper arms were gender and BMI whereas SCT at abdomen was gender and BMI, and SCT at upper arms was gender, BMI and age [5]. The studies done using ultrasonography to measure ST and SCT in children with type 1 diabetes showed that there is a progressive increase in thickness with age and also it varies at different sites (arm, thigh, abdomen and

* Corresponding author.

E-mail address: rashida.farhad@singhealth.com.sg (R.F. Vasanwala).

https://doi.org/10.1016/j.jcte.2018.04.004

Received 6 February 2018; Received in revised form 20 April 2018; Accepted 24 April 2018

2214-6237/ © 2018 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/BY-NC-ND/4.0/).

Table 1

Baseline characteristics of patients.¹

	Boys + Girls	;			Boys only				Girls only			
	1–6 years (n = 12) n (%)	7–12 years (n = 55) n (%)	13–17 years (n = 86) n (%)	p ²	1–6 years (n = 11) n (%)	7–12 years (n = 24) n (%)	13–17 years (n = 34) n (%)	p ²	1–6 years (n = 1) n (%)	7–12 years (n = 31) n (%)	13–17 years (n = 52) n (%)	p ²
Gender (n, %) Boys Girls	11 (91.7) 1 (8.3)	24 (43.6) 31 (56.4)	34 (39.5) 52 (60.5)	0.003*	-	-	-	-	-	-	-	-
Ethnicity (n,%) Chinese Malay/ Indian/ Others	9 (75.0) 3 (25.0)	34 (61.8) 21 (38.2)	54 (62.8) 32 (37.2)	0.68	8 (72.7) 3 (27.3)	18 (75.0) 6 (25.0)	23 (67.6) 11 (32.4)	0.82	1 (100) 0 (0)	16 (51.6) 15 (48.4)	31 (59.6) 21 (40.4)	0.53
BMI-for-age percentile (n, %) 3rd-25th 25th-75th 75th-90th 90th-97th	0 (0) 9 (75.0) 3 (25.0) 0 (0)	10 (18.2) 32 (58.2) 7 (12.7) 6 (10.9)	14 (16.3) 45 (52.3) 14 (16.3) 13 (15.1)	0.40	0 (0) 8 (72.7) 3 (27.3) 0 (0)	2 (8.3) 17 (70.8) 1 (4.2) 4 (16.7)	9 (26.5) 21 (61.8) 3 (8.8) 1 (2.9)	0.030*	0 (0) 1 (100) 0 (0) 0 (0)	8 (25.8) 15 (48.4) 6 (19.4) 2 (6.5)	5 (9.6) 24 (46.2) 11 (21.2) 12 (23.1)	0.26
Type of diabetes (n, %) Type 1	12 (100)	53 (96.4)	72 (83.7)	0.027*	11 (100)	23 (95.8)	31 (91.2)	0.51	1 (100)	30 (96.8)	41 (78.8)	0.072
HbA1c level (n,	0 (0)	2 (3.6)	14 (16.3)	0.78	0(0)	1 (4.2)	3 (8.8)	0.61	0 (0)	1 (3.2)	11 (21.2)	0.23
≤7.5% 7.6–9.0% ≥9.1%	2 (16.7) 6 (50.0) 4 (33.3)	14 (25.5) 19 (34.5) 22 (40.0)	18 (20.9) 29 (33.7) 39 (45.3)		1 (9.1) 6 (54.5) 4 (36.4)	6 (25.0) 7 (29.2) 11 (45.8)	8 (23.5) 14 (41.2) 12 (35.3)		1 () 0 () 0 ()	8 (25.8) 12 (38.7) 11 (35.5)	10 (19.2) 15 (28.8) 27 (51.9)	

¹ Values are expressed as n (%).

² Chi-square test conducted to compare different age groups; p < 0.05 taken to be statistically significant.

* p < 0.05.

buttocks) [1]. Additionally, the rate of intramuscular injection with the shortest needle (4mm) was found to be five times more in the 1–6 years old age group (20.2%) compared to 7–13 years (4.6%) and 14–17 years (2.4%) with a non-pinch skin-fold [6]. Lean children with a thin layer of subcutaneous tissue may also need to pinch a skin fold when using 4 or 5 mm needles for injection over arms or thighs [1,5]. In adults, a pinch-up skin fold is not required for 4 or 5 mm needle but may be necessary when using 6, 8, or 12.7 mm needle to ensure adequate delivery of insulin in the SC [7]. These findings highlight the importance of both appropriate injection technique and consideration on needle length across different age groups. Recommendations for insulin injection must include measurements of the ST and SCT to make an evidence-based recommendation for needle length.

The data for Asian children are lacking and it remains uncertain whether previous findings could be generalised to our local population with diabetes since ST and SCT thickness could differ by race and ethnicity. Therefore, this study aims to establish recommendation of appropriate needle length for insulin injection among children with diabetes across different age groups in Singapore.

Materials and methods

Patient recruitment

Children between 1 and 18 years with diabetes on insulin injections recruited between 1st August 2013 and 30th June 2014 at KK Children's & Women's Hospital. They were divided into three groups according to their age: 1–6 years, 7–12 years and 13–18 years. Children excluded include those with secondary diabetes, duration of diabetes less than one year and hypertrophy/lipoatrophy/nodularity at insulin injection sites. Singhealth Centralized Institutional Review Board (CIRB)

approved the study.

Data collection

Questionnaires were administered to patients more than age 13 years old and to the parents of patients less than age 13 years old to obtain participants' demographics and medical history. The weight (kg) was measured using the digital weighing machine (Avalanche Mechatronic, Singapore) and height (cm) using (Wall mounted Stadiometer) and BMI (kg/m2) calculated from these measurements. A capillary one millimetre's blood sample was collected and tested for glycated haemoglobin (HbA1c) using clinical chemistry analyser (Bio-Rad Abbott Architect c8000, Unites States). Two trained Diabetes Nurse Educators did a measurement of ST and SCT in millimetres using portable M-Turbo® ultrasound system (Sonosite, United States) with 5-15 MHz transducer probe on four injection sites - arm, thigh, abdomen and buttocks on right or left side of the body. Standard procedures were adopted which include a selection of good sites, non-pinch (non-compressed) skin fold and transducer probe positioned perpendicularly to the marked area to obtain a clear and focused image to measure ST & SCT. The site of measurement was standardized using landmarks in order to reduce intersubject variability. The measurement site was mid-length directly inferior to the acromion process for the arms, greater trochanter for the thigh, 2 cm away from the umbilicus at the lateral abdomen and upper outer quadrant for the buttocks. No measurements were made over sites of lipohypertrophy. All measurements were calculated from an average of two readings obtained by each operator. Training for measurements was validated on two operators with inter-rater variability below 5%. The percentage of IM injection with different needle lengths (4 mm, 5 mm, 6 mm, 8 mm and 12.7 mm) across three age groups at four different injection sites was

Measurement of ST and SCT.¹ Table 2

	Boys + Girls				Boys only				Girls only				= p ⁴ (boys	vs girls)	
	1-6 years (n = 12)	7-12 years (n = 55)	13–17 years (n = 86)	p^2	1-6 years (n = 11)	7-12 years (n = 24)	13–17 years (n = 34)	p^2	1-6 years (n = 1)	7–12 years (n = 31)	13–17 years (n = 52)	p^3	1–6 years	7–12 years	13-17 years
Skin thickne	388 (ST) 1 E7 + 0 21 [§]	1 01 ± 0 10 [§]	0 EE + 0 60# †	* 0000	1 50 + 0 218	1 70 + 0.77	ג #ט בע	* 00 0	1 20	2 02 + 0 E0	3 EQ + 0 63	* 00.0	0.00	*270.0	0 50
Arm	1.33 ± 0.23^{8}	$1.59 + 0.40^{8}$	$2.33 \pm 0.36\%$	< 0.001 *	$1.32 + 0.24^{8}$	$1.51 + 0.28^{8}$	$2.30 \pm 0.30 $	< 0.001	1.40	1.65 + 0.47	1.91 + 0.39	0.008	0.76	0.19	0.22
Thigh	1.54 ± 0.19^{8}	1.68 ± 0.46^{8}	$1.96 \pm 0.38^{\# \dagger}$	< 0.001*	1.54 ± 0.20^{8}	$1.60 \pm 0.27^{\$}$	$1.87 \pm 0.34^{\# \dagger}$	0.001*	1.60	1.74 ± 0.56	2.02 ± 0.39	0.008*	0.77	0.29	0.063
Buttocks	$1.65 \pm 0.29^{\$}$	$1.99 \pm 0.50^{\$}$	$2.69 \pm 0.55 $ ^{# †}	$< 0.001^{*}$	$1.60 \pm 0.24^{\$}$	$1.87 \pm 0.37^{\$}$	$2.68 \pm 0.48^{\# \dagger}$	$< 0.001^{*}$	2.20	2.08 ± 0.57	2.70 ± 0.60	$< 0.001^{*}$	0.038*	0.12	0.84
Total skin a	nd subcutaneous	thickness (SCT)													
Abdomen	4.33 ± 2.22^{8}	$7.11 \pm 3.68^{\$}$	$8.94 \pm 4.50^{\#}$	$< 0.001^{*}$	$4.10 \pm 2.18^{\$}$	6.59 ± 3.11	$7.03 \pm 3.48^{*}$	0.033	6.80	7.52 ± 4.07	10.19 ± 4.60	$< 0.001^{*}$	0.26	0.36	0.001^{*}
Arm	5.55 ± 2.26	7.79 ± 4.54	8.42 ± 5.00	0.13	5.18 ± 1.96	7.38 ± 4.23	6.01 ± 2.74	0.13	9.60	8.10 ± 4.81	9.99 ± 5.52	0.117	0.056	0.57	$< 0.001^{*}$
Thigh	5.83 ± 3.12	7.17 ± 3.62	8.61 ± 4.76	0.037*	5.02 ± 1.39	6.79 ± 3.08	6.01 ± 3.58	0.30	14.80	7.47 ± 4.02	10.31 ± 4.69	0.006	$< 0.001^{*}$	0.50	$< 0.001^{*}$
Buttocks	$6.48 \pm 3.47^{\$}$	8.51 ± 3.65	9.76 ± 4.38 *	0.017*	5.73 ± 2.38	8.00 ± 3.23	7.50 ± 3.18	0.13	14.80	8.90 ± 3.95	11.23 ± 4.46	0.018^{*}	0.005*	0.37	$< 0.001^{*}$
ST, skin thic	kness; SCT, tot.	al skin and sul	bcutaneous thickness.												

¹ Values are expressed as mean \pm S.D. (in mm).

 2 Based on one-way ANOVA; p < 0.05 was considered to be statistically significant.

³ Based on independent t-test to compare ST or ST + SC of 7–12 years old and 13–17 years old girls; p < 0.05 was considered to be statistically significant.

⁴ Based on independent *t*-test to compare ST or ST + SC of boys and girls from each age group; p < 0.05 was considered to be statistically significant.

* Bonferroni post hoc test significantly different from 1 to 6 years old; p < 0.05 was considered to be statistically significant.

 $^{\circ}$ Bonferroni post hoc test significantly different from 7 to 12 years old; p < 0.05 was considered to be statistically significant.

 8 Bonferroni post hoc test significantly different from 13 to 17 years old; p < 0.05 was considered to be statistically significant.

 * p < 0.05.



Fig. 1. Scatterplot of total skin and subcutaneous thickness (SCT) at (a) abdomen, (b) arm, (c) thigh, and (d) buttocks against age (stratified into different age groups). Age group 1: 1–6 years old; Age group 2: 7–12 years old; Age group 3: 13–17 years old.



Fig. 2. Bar chart of mean total skin and subcutaneous thickness (SCT) at various body sites of children from different age groups.

analysed based on measurements of ST and SCT. We considered participants to have experienced intramuscular injection when needle length exceeded SCT measurement with the assumption of a non-pinch skin fold technique.

Statistical analysis

Differences across age groups were compared using Fisher's exact test for categorical variables and one-way analysis of variance (ANOVA) for continuous variables. P < 0.05 was considered as statistically significant. All statistical analyses were performed using Statistical Package for the Social Sciences, Version 19.0 (IBM New York).

Results

Baseline characteristics of patients

A total of 153 children were enrolled in this study. They comprised 12 (8%) 1–6 years old, 55 (36%) 7–12 years old and 86 (56%) 13–18 years old children. Table 1 shows the comparison of participants' characteristics across age groups. In the three age groups majority of children had type 1 diabetes (p = 0.027) and in the older age group 7–12 years and 13–18 years there were more female (p = 0.003) while there were more boys in the younger age group 1–6 years. There were no significant differences in ethnicity (p = 0.68) and HbA1C (p = 0.78) among the three groups. Among the boy's majority of them have BMI in the 25th to 75th percentile across all age groups (p = 0.03).



Fig. 3. Scatterplot of total skin and subcutaneous thickness (SCT) at (a) abdomen, (b) arm, (c) thigh, and (d) buttocks against body mass index (BMI).



Fig. 4. Bar chart of mean total skin and subcutaneous thickness (SCT) at various body sites of children from different body mass index (BMI)-for-age percentile groups (with reference to CDC Growth Chart 2000).

Measurement of skin and subcutaneous thickness (ST & SCT)

Table 2 shows the measurements of ST and SCT at abdomen, arm, thigh and buttocks across the age groups. ST measurements over four sites across the three age group vary significantly and are higher in 13–18 years compared to 1–6 and 7–12 years (p < 0.001). Overall ST at all sites does not differ between boys and girls except that the ST at abdomen in the age group of 7–12 years is more in girls as compared to boys (p = 0.047). While SCT also varies at different sites across the age groups, in girls is it higher in 13–18 years at all sites as compared to the boys ($p \leq 0.001$). Fig. 1 scatter plot and Fig. 2 bar chart shows SCT measurement across age groups at different sites and Fig. 3 & Fig. 4 shows SCT measurement in relation to BMI percentile.

Percentage of intramuscular (IM) injection using different needle lengths

Table 3 shows the estimated percentage of IM injection risk with varying needle lengths across three age groups at the four different injection sites based on measurements of ST and SCT assuming a nonpinch injection technique and Table 4 shows IM risk across BMI percentile. In 1–6 years there is a high risk of IM injection with all needle lengths over four sites. Interestingly the risk of IM injection with 4 mm needle was highest at abdomen for 1–6 years (66.7%) & 7–12 year (21.8%) as compared to other sites, but for 13–17 year it was more at arm (11.6%) and thigh (9.3%) vs abdomen (7%). The risk of IM injection proportionately increases with the length of the needle in all age groups at four sites. The 8 mm and 12.7 mm needle carries a high risk of

Table 3

Percentage of intramuscular (IM) injection in children from different age groups due to different needle length.¹

	Site	Boys + Girls			Boys only			Girls only		
		1–6 years (n = 12) n (%)	7–12 years (n = 55) n (%)	13–17 years (n = 86) n (%)	1–6 years (n = 11) n (%)	7–12 years (n = 24) n (%)	13–17 years (n = 34) n (%)	1–6 years (n = 1) n (%)	7–12 years (n = 31) n (%)	13–17 years (n = 52) n (%)
Needle length	Abdomen									
4 mm		8 (66.7)	12 (21.8)	6 (7.0)	8 (72.7)	6 (25.0)	3 (8.8)	0 (0.0)	6 (19.4)	3 (5.8)
5 mm		9 (75.0)	21 (38.2)	16 (18.6)	9 (81.8)	11 (45.8)	10 (29.4)*	0 (0.0)	10 (32.3)	6 (11.5)*
6 mm		10 (83.3)	27 (49.1)	30 (34.9)	10 (90.9)	12 (50.0)	17 (50.0)*	0 (0.0)	15 (48.4)	13 (25.0)*
8 mm		11 (91.7)	36 (65.5)	49 (57.0)	10 (90.9)	15 (62.5)	25 (73.5)*	1 (100)	21 (67.7)	24 (46.2)*
12.7 mm		12 (100)	52 (94.5)	68 (79.1)	11 (100)	24 (100)	32 (97.0)**	1 (100)	28 (90.3)	36 (69.2)**
Needle length	Arm									
4 mm		4 (33.3)	7 (12.7)	10 (11.6)	4 (36.4)	3 (12.5)	6 (17.6)	0 (0.0)	4 (12.9)	4 (7.7)
5 mm		8 (66.7)	16 (29.1)	24 (27.9)	8 (72.7)	8 (33.3)	16 (47.1)**	0 (0.0)	8 (25.8)	8 (15.4)**
6 mm		8 (66.7)	25 (45.5)	39 (45.3)	8 (72.7)	11 (45.8)	22 (64.7)**	0 (0.0)	14 (45.2)	17 (32.7)**
8 mm		9 (75.0)	41 (74.5)	55 (64.0)	9 (81.8)	20 (83.3)	27 (79.4)*	0 (0.0)	21 (67.7)	28 (53.8)*
12.7 mm		12 (100)	46 (83.6)	68 (79.1)	11 (100)	21 (87.5)	33 (97.1)**	1 (100)	25 (80.6)	35 (67.3)**
Needle length	Thigh									
4 mm		3 (25.0)	5 (9.1)	8 (9.3)	3 (27.3)	1 (4.2)	7 (20.6)**	0 (0.0)	4 (12.9)	1 (1.9)**
5 mm		7 (58.3)	19 (34.5)	26 (30.2)	7 (63.6)	9 (37.5)	21 (61.8)***	0 (0.0)	10 (32.3)	5 (9.6)***
6 mm		8 (66.7)	28 (50.9)	34 (39.5)	8 (72.7)	13 (54.2)	25 (73.5)***	0 (0.0)	15 (48.4)	9 (17.3)***
8 mm		11 (91.7)	43 (78.2)	51 (59.3)	11 (100)	19 (79.2)	30 (88.2)***	0 (0.0)	24 (77.4)	21 (40.4)***
12.7 mm		11 (91.7)	50 (90.9)	72 (83.7)	11 (100)	23 (95.8)	32 (94.1)*	0 (0.0)	27 (87.1)	40 (76.9)*
Needle length	Buttocks									
4 mm		5 (41.7)	1 (1.8)	0 (0.0)	5 (45.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.2)	0 (0.0)
5 mm		6 (50.0)	9 (16.4)	6 (7.0)	6 (54.5)	4 (16.7)	6 (17.6)**	0 (0.0)	5 (16.1)	0 (0.0)**
6 mm		7 (58.3)	18 (32.7)	15 (17.4)	7 (63.6)	8 (33.3)	12 (35.3)***	0 (0.0)	10 (32.3)	3 (5.8)***
8 mm		9 (75.0)	28 (50.9)	42 (48.8)	9 (81.8)	13 (54.2)	24 (70.6)**	0 (0.0)	15 (48.4)	18 (34.6)**
12.7 mm		11 (91.7)	50 (90.9)	63 (73.3)	11 (100)	22 (91.7)	32 (94.1)***	0 (0.0)	28 (90.3)	31 (59.6)***

¹ Values are expressed as n (%)

 * Chi-square test or fisher's exact test comparing boys and girls, p < 0.05

** Chi-square test or fisher's exact test comparing boys and girls, $p\,<\,0.01$

*** Chi-square test or fisher's exact test comparing boys and girls, p < 0.001

IM injections of more than 50% in 7–12 years and 75–100% in 1–6year-old age group. In the 13–18 years old even with thicker SCT, IM risk is still prevalent on all sites, with 8 mm it is about 50%, and with 12.7 mm it is more than 70%. Interesting to note that boys in the age group of 13–18 years have a higher risk of IM injection as compared to girls at all sites with 5, 6, 8 & 12.7 mm needle. With regards to BMI,boys with BMI between 25th–75th percentile are at higher risk of IM injection with 4,5,6,12.7 mm needle at the abdomen,with 5 & 8 mm needle at the arm, with 5,6,8,12.7 mm needle at thigh and 5,6,8,12.7 mm at buttock. Fig. 5 shows the risk of IM injection in different age groups at four sites with four needle length and Fig. 6 shows the rick against the BMI percentile.

Discussion

The ST and SCT measurements are important factors in determining the needle length for insulin injection and its subsequent absorption. Our study reported a progressive increase of ST and SCT across all age groups with age, body mass index (BMI) and sites of injection (buttocks > thigh > arm > abdomen). Our findings were consistent with other pediatric studies which showed a similar correlation between ST and SCT with age, BMI and sites of injection (3–6, 8).

Children with diabetes can experience day-to-day variation in insulin absorption rate where accidental intramuscular insulin injection is one of the factors [4], commonly causing hypoglycemia which is an acute complication reported in many studies [3,4,9]. Hypoglycaemia can be a significant factor causing morbidity and mortality in patients with diabetes [10,11]. Subcutaneous layer is the ideal site for insulin administration as blood flow through this fat layer is slow and predictable. The blood flow to the muscle is faster and ever-changing, depending on the state of muscle activity and therefore the risk of hypoglycaemia is high with IM injection [6]. In children, it is crucial to avoid hypoglycaemia and erratic fluctuations in blood glucose as it has an immediate effect on their function and concentration. Therefore, the clinical question in caring for children with daily insulin injection is how to avoid hypoglycemia which depends on balancing food, insulin doses and avoiding intramuscular injections during insulin administration. The objective is to deliver insulin safely into the subcutaneous layer without any leakage or discomfort and avoid IM injection by selecting needle of appropriate length, and this will impact on insulin absorption and ultimately glycaemia control. In addition to the choice of needle length, a pinch-up skin fold may be helpful to avoid intramuscular injection.

Skin thickness in children is less than in adults and increases with age. Ultrasonography is rapidly evolving with high-frequency transducers readily available for measurement of ST and SCT [8]. Many studies on skin and subcutaneous thickness measurements were done by either computed tomography (CT) or ultrasonography to project visualisation of insulin into the subcutaneous layer. A study using ultrasonography visualisation reported 86% intramuscular location of insulin deposits in children despite appropriate pinch-up skin fold technique when using longer needles (12.7 mm) [12]. A similar ultrasound study on children with diabetes of mean age 10.4 \pm 2.3 years with BMI 17.6 \pm 2.3 kg/ m² visualised the location of air injected using angled or pinch-up skin fold technique with 6 mm or 8 mm needle length and also demonstrated intramuscular delivery with increased incidence over thigh as compared with abdomen [9]. On the contrary, variations in pinch-up skinfold thickness and insulin absorption may partly explain the wellknown inter-individual variation in insulin absorption [13]. The pinchup skin fold only expands a modest degree in children and IM injections are still at risk when the needle is > 6 mm [3,9]. Even adult study reported that IM risk could vary across sites, and is greatest at thigh and increased with 8 mm and 12.7 mm needles [2]. Such findings have led some authorities to recommend the use of a 45-degree angle to avoid

							,					
Site	Boys + Girls				Boys only				Girls only			
	3rd–25th percentile (n = 24)	25th-75th percentile (n = 86)	75th-90th percentile (n = 24)	90th–97th percentile (n = 19)	3rd-25th percentile (n = 11)	25th-75th percentile (n = 46)	75th-90th percentile (n = 7)	90th -97 th percentile (n = 5)	3rd-25th percentile (n = 13)	25th-75th percentile (n = 40)	75th-90th percentile (n = 17)	90th -97 th percentile (n = 14)
	(147 – 11) n (%)	u (%)	(HZ – LI) n (%)	(%) u (%)	(11 – 11) (%) u	u (%)	u (%)	(%) u	(61 – 11) 1 (%)	(m – 40) n (%)	u (%)	(HI – II) n (%)
Needle length Abdomen												
4 mm	8 (33.3)	15 (17.4)	2 (8.3)	1 (5.3)	3 (27.3)	$12(26.1)^{*}$	2 (28.6)	0 (0.0)	5 (38.5)	3 (7.5)	0 (0.0)	1 (7.1)
5 mm	10 (41.7)	30 (34.9)	4 (16.7)	2(10.5)	4 (36.4)	23 (50.0)	3 (42.9)	0 (0.0)	6 (46.2)	7 (17.5)	1 (5.9)	2 (14.3)
6 mm	15 (62.5)	44 (51.2)	6 (25.0)	2 (10.5)	6 (54.5)	$29 (63.0)^{*}$	4 (57.1)*	0 (0.0)	9 (69.2)	$15(37.5)^{*}$	$2(11.8)^{*}$	2 (14.3)
8 mm	20 (83.3)	62 (72.1)	12 (50.0)	2 (10.5)	9 (81.8)	35 (76.1)	6 (85.7)	0 (0.0)	11 (84.6)	27 (67.5)	6 (35.3)	2 (14.3)
12.7 mm	22 (91.7)	81 (94.2)	20 (83.3)	9 (47.4)	10 (90.9)	$46(100)^{*}$	7 (100)	4 (80.0)	12 (92.3)	35 (87.5)*	13 (76.5)	5 (35.7)
Needle length Arm												
4 mm	3 (12.5)	16 (18.6)	2 (8.3)	0 (0.0)	1 (9.1)	11 (23.9)	1 (14.3)	0 (0.0)	2 (15.4)	5 (12.5)	1 (5.9)	0 (0.0)
5 mm	10 (41.7)	33 (38.4)	4 (16.7)	1(5.3)	6 (54.5)	24 (52.2)**	2 (28.6)	0 (0.0)	4 (30.8)	9 (22.5)**	2 (11.8)	1 (7.1)
6 mm	12 (50.0)	49 (57.0)	9 (37.5)	2(10.5)	8 (72.7)*	30 (65.2)	3 (42.9)	0 (0.0)	4 (30.8)*	19 (47.5)	6 (35.3)	2 (14.3)
8 mm	19 (79.2)	70 (81.4)	12 (50.0)	4 (21.1)	9 (81.8)	$41(89.1)^{*}$	5 (71.4)	1(20.0)	10 (76.9)	29 (72.5)*	7 (41.2)	3 (21.4)
12.7 mm	23 (95.8)	83 (96.5)	16 (66.7)	4 (21.1)	11 (100)	46 (100)	7 (100)	1 (20.0)	12 (92.3)	37 (92.5)	9 (52.9)	3 (21.4)
Needle length Thigh												
4 mm	7 (29.2)	7 (8.1)	2 (8.3)	0 (0.0)	4 (36.4)	5 (10.9)	2 (28.6)	0 (0.0)	3 (23.1)	2 (5.0)	0 (0.0)	0 (0.0)
5 mm	13 (54.2)	34 (39.5)	4 (16.7)	1 (5.3)	8 (72.7)	25 (54.3)	3 (42.9)	1(20.0)	5 (38.5)	9 (22.5)	1 (5.9)	0 (0.0)
6 mm	17 (70.8)	45 (52.3)	6 (25.0)	2(10.5)	10 (90.9)	32 (69.6)	3 (42.9)	1(20.0)	7 (53.8)	13 (32.5)	3 (17.6)	1 (7.1)
8 mm	20 (83.3)	72 (83.7)	11 (45.8)	2(10.5)	10 (90.9)	44 (95.7)**	5 (71.4)	1(20.0)	10 (76.9)	28 (70.0)	6 (35.3)	1 (7.1)
12.7 mm	22 (91.7)	81 (94.2)	19 (79.2)	11 (57.9)	10 (90.9)	$46(100)^{*}$	7 (100)	3 (60.0)	12 (92.3)	35 (87.5)	12 (70.6)	8 (57.1)
Needle length Buttocks												
4 mm	0 (0.0)	5 (5.8)	1 (4.2)	0 (0.0)	0 (0.0)	4 (8.7)	1 (14.3)	0 (0.0)	0 (0.0)	1 (2.5)	0 (0.0)	0 (0.0)
5 mm	5 (20.8)	15 (17.4)	1 (4.2)	0 (0.0)	2 (18.2)	$13(28.3)^{*}$	1 (14.3)	0 (0.0)	3 (23.1)	2 (5.0)*	0 (0.0)	0 (0.0)
6 mm	8 (33.3)	27 (31.4)	5 (20.8)	0 (0.0)	3 (27.3)	23 (50.0)***	1 (14.3)	0 (0.0)	5 (38.5)	4 (10.0)***	4 (23.5)	0 (0.0)
8 mm	18 (75.0)	51 (59.3)	9 (37.5)	1 (5.3)	9 (81.8)	33 (71.7)*	4 (57.1)	0 (0.0)	9 (69.2)	$18 (45.0)^{*}$	5 (29.4)	1 (7.1)
12.7 mm	21 (87.5)	82 (95.3)	16 (66.7)	5 (26.3)	10 (90.9)	$46(100)^{*}$	7 (100)	2 (40)	11 (84.6)	36 (90.0)	9 (52.9)	3 (21.4)

BMI, Body mass index.

² With reference to CDC Growth Charts 2000. ¹ Values are expressed as n (%).

 $^{\ast}\,$ Chi-square test or fisher's exact test comparing boys and girls, $p\,<\,0.05.$

** Chi-square test or fisher's exact test comparing boys and girls, p < 0.01. *** Chi-square test or fisher's exact test comparing boys and girls, p < 0.001.



Fig. 5. Bar chart of risk of intramuscular injection with different needle lenghts across the three age groups at (a) abdomen, (b) arm, (c) thigh, (d) buttocks.

IM injections [6], but this is limited to individual's capacity in visualising an angled approach when injecting insulin.

Our study evaluates the measurements of ST and SCT layer using a non-pinch skin fold. The minimum SCT thickness is at abdomen (4.33 mm) in 1-6 years old and maximum at buttocks (9.76 mm) in 13-18 years old group. Young children between 1 and 6 years old have the highest risk with 5 mm, 6 mm, 8 mm, and 12.7 mm needle from 58.3% to 100% at all four injection sites. The 4 mm needle has a lower risk of IM injection across all age groups, and 8 mm and 12.7 mm needle lengths are not recommended due to the high percentage of IM injection at all four sites across all three age groups. The most appropriate needle for insulin injection in 1-6 years old according to our study is 4 mm needle which corresponds to SCT layer measurement at the abdomen, arm, thigh, buttock (4.33, 5.55, 5.83, 6.48 mm) respectively. But even with 4 mm the risk of IM injection is high at abdomen (66.7%) & buttock (41.7%). When stratified against BMI the risk of IM injection in the 25th-75th BMI percentile is higher in boys versus girls. Sites over abdomen and thigh remain at risk of IM injection across all BMI despite the shortest needle used. Therefore, we recommend a pinch-up skin fold for SC insulin injection at abdomen and thigh sites regardless of BMI

percentile. Similar studies on the use of 4 mm needles were reported to be safer for all children in avoiding intramuscular delivery, more so when used in children aged 2–6 years old [6,8]. Another study analyzed the use of 4 & 5 mm needle for the abdomen and 4 mm for the arm to avoid the risk of intramuscular injection [5].

Conclusion

Although skin thickness increases with age, the risk of intramuscular injection is still high. The shorter needle of 4 mm is considered safest for children of all age groups, followed by 5 mm and 6 mm needle. The 8 mm and 12.7 mm needle carries a high risk of intramuscular injections in all age groups, therefore, should generally not be used in Pediatrics. If there are concerns of an intramuscular injection in young children or in children with low BMI, ultrasonography is a useful and quick office tool to measure ST and SCT to recommend appropriate needle length.



Fig. 6. Bar chart of mean total skin and subcutaneous thickness (SCT) at (a) abdomen, (b) arm, (c) thigh, and (d) buttocks of children from different body mass index (BMI)-for-age percentile groups (with reference to CDC Growth Chart 2000).

Acknowledgements

Ms Lim S.T.J., Ms Hui Y.C. and Ms Lim P.K. collected the data. Ms Lim C.C.E. and Dr Chia Y.Y. provided support for data template. Ms Lim S.T.J. researched and analysed the data. Dr Rashida V. contributed to discussion and reviewed/edited the manuscript. Becton, Dickinson and Company (BD) provided Sonosite M-Turbo ultrasound machine.

Conflict of interest

Ms Lim STJ and all authors declare no conflict of interest.

References

- Frid A, Hirsch L, Gaspar R, Hicks D, Kreugel G, Liersch J, et al. New injection recommendations for patients with diabetes. Diab Metab 2010 Sep;36(Suppl 2):S3–18.
- [2] Hirsch L, Byron K, Gibney M. Intramuscular risk at insulin injection sites– a measurement of the distance from skin to muscle and rationale for shorter-length needles for subcutaneous insulin therapy. Diabetes Technol Ther 2014 Dec;16(12):867–73.

- [3] Polak M, Beregszaszi M, Belarbi N, Benali K, Hassan M, Czernichow P, et al. Subcutaneous or intramuscular injections of insulin in children. Are we injecting where we think we are? Diabetes Care 1996 Dec;19(12):1434–6.
- [4] Birkebaek NH, Johansen A, Solvig J. Cutis/subcutis thickness at insulin injection sites and localisation of simulated insulin boluses in children with type 1 diabetes mellitus: the need for individualisation of injection technique? Diab Med 1998 Nov;15(11):965–71.
- [5] Sim KH, Hwang MS, Kim SY, Lee HM, Chang JY, Lee MK. The appropriateness of the length of insulin needles based on the determination of skin and subcutaneous fat thickness in the abdomen and upper arm in patients with type 2 diabetes. Diab Metab J 2014 Apr;38(2):120–33.
- [6] Lo Presti D, Ingegnosi C, Strauss K. Skin and subcutaneous thickness at injecting sites in children with diabetes: ultrasound findings and recommendations for giving the injection. Pediatr Diab 2012 Nov;13(7):525–33.
- [7] Gibney MA, Arce CH, Byron KJ, Hirsch LJ. Skin and subcutaneous adipose layer thickness in adults with diabetes at sites used for insulin injections: implications for needle length recommendations. Curr Med Res Opin 2010 Jun;26(6):1519–30.
- [8] Akkus Oktay, Oguz Aytekin, Uzunlulu Mehmet, Kizilgul Muhammed. Evaluation of skin and subcutaneous adipose tissue thickness for optimal insulin injection. J Diabetes Metab 2012;3:8. http://dx.doi.org/10.4172/2155-6156.1000216. Volume 3 * Issue 8 * 1000216.
- [9] Hofman PL, Derraik JG, Pinto TE, Tregurtha S, Faherty A, Peart JM, et al. Defining the ideal injection techniques when using 5-mm needles in children and adults. Diabetes Care 2010 Sep;33(9):1940–4.
- [10] Hofman PL, Lawton SA, Peart JM, Holt JA, Jefferies CA, Robinson E, et al. An

angled insertion technique using 6-mm needles markedly reduces the risk of intramuscular injections in children and adolescents. Diab Med 2007 Dec;24(12):1400–5.

- [11] Clarke W, Jones T, Rewers A, Dunger D, Klingensmith GJ. Assessment and management of hypoglycemia in children and adolescents with diabetes. Pediatr Diab 2009 Sep;10(Suppl 12):134–45.
- [12] Strauss K, Gols HD, Letondeur C, Matyjaszczyk M, Frid A. The second injection technique event (SITE), May 2000, Barcelona, Spain. Pract Diab Int 2002;19(1):17–21.
- [13] Tubiana-Rufi N, Belarbi N, Du Pasquier-Fediaevsky L, Polak M, Kakou B, Leridon L, et al. Short needles (8 mm) reduce the risk of intramuscular injections in children with type 1 diabetes. Diabetes Care 1999 Oct;22(10):1621–5.