Insulin Injection Practice and Injection Complications – Results from Bangladesh Insulin Injection Technique Survey

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Introduction: Diabetes mellitus is highly prevalent in Bangladesh and insulin is often needed for diabetes control. We lack sufficient data on the insulin injection technique and injection-related complications. **Methods**: Bangladesh Insulin Injection Technique Survey (BIITS) was conducted in 2018 in 18 centres throughout Bangladesh involving 847 patients taking insulin for at least 6 months. All of the study subjects were interviewed by using a structured questionnaire focusing on key insulin injection parameters. **Results**: The mean duration of insulin use by the study subjects was 3.84 (±4.05) years and the mean daily dose of insulin was 41 (±25) units. A total of 71.6% participants performed ≤2 injections/day and premixed insulins were the most commonly used insulins. Mean glycated haemoglobin (HbA1c) was 9.5% (±2%). The proportion of syringe users and pen-device users was 68.1% and 31.9%, respectively. Most of the participants injected in the abdomen and rotated the injection site(s). The majority lifted skinfold correctly and inserted the needle at a 90-degree angle, but their dwell times after injections were not adequate. A total of 9.2% of the subjects had injection-site lipohypertrophy (LH) and among them, 38.5% injected into the lesion. Patients with LH had higher HbA1c. Higher duration of insulin use (≥5 years), reusing needles for more often (>10 times), and injecting at angles other than 90 degrees were independent predictors of LH. The incidences of hypoglycaemia (36.7%) and hyperglycaemia (67.4%) were very high, and subjects with LH had higher chances of both hypoglycaemia and hyperglycaemia. Though most (92.1%) of the patients received education about insulin injection initially, it was not repeated in the recent follow-up and was found ineffective. **Conclusion**: A huge gap between the insulin administration guidelines and current practice was observed in this study. Complications of insulin injections were also common. Health care providers should pay more attention to insulin education and re-evaluate injection practices from time to time.

Diabetes mellitus (DM) is a major global health problem. The national prevalence of diabetes in Bangladesh is 6.9% which is increasing at an alarming rate.[1] Though the prevalence of type 1 diabetes mellitus (T1DM) is low in this area, the prevalence of gestational diabetes and young-onset T2DM is very high.[1] Insulin is an indispensable component of diabetes management.[2] Although the proportion of insulin users was 42.49% among patients with diabetes in a single-centre study, unfortunately, reliable statistics on insulin use are lacking in Bangladesh.[3] The insulin injection technique plays an important role in glycaemic control, and poor injection technique is one of the important, modifiable reasons for inadequate glycaemic control.[4] Insulin storage is also important as it may affect the potency of insulin, influencing its efficacy.[5] Faulty injection technique is associated with injection-site complications including lipohypertrophy (LH).[6] Moreover, improper handling of needles and other sharps used in insulin injection may increase the risk of accidental injury and transmission of blood-borne infections in the patients and their close contacts.[7] Many guidelines have been published for ideal insulin injection practice.[2,8] But unfortunately, there is a large gap between the guideline recommendations and actual practice of insulin use throughout the world.[9–13] Data from Bangladesh are scarce in this aspect. Therefore, we conducted this nationwide survey, the Bangladesh Insulin Injection Technique Survey (BIITS), to assess the current practice of insulin injection and complications of the injection in this area.

Methods
This cross-sectional survey was conducted in 18 centres delivering specialised diabetes care throughout Bangladesh from January to December 2018. Among the centres, six were endocrine out-patient departments (OPDs) of government hospitals, six were endocrine OPDs of non-government hospitals, and the remaining six were private chambers of the endocrinologists. All the centres participated voluntarily and without financial incentive.

Patients with diabetes (all subtypes) using insulin for at least 6 months by either syringe or pen were included in the sample. All the consented subjects underwent a survey using an investigator-administered questionnaire focusing on the key insulin injection parameters. The questionnaire was based on the Injection Technique Questionnaire (ITQ) used in the Worldwide Injection Technique Questionnaire Study, with a little modification for the convenience and better understanding in our settings.[10] Relevant socio-demographic data were also collected in face-to-face interviews with the help of a pre-tested data collection sheet. The investigators checked the insulin device used by the patient and examined their insulin injection site(s). The study subjects were asked to perform a dummy insulin injection in front of the investigator concerned. The most recent glycated haemoglobin (HbA1c) results (within the previous 3 months of data collection) were collected from their treatment records.

Besides the demographic information of the subjects, the key insulin injection parameters, including the current injection practice, observed anomalies at injection sites, injection safety, injection technique education, and blood glucose anomalies, were recorded in the data collection sheet.

The study was conducted according to Good Clinical Practice and the Helsinki accords. Patient identity was kept confidential at all times. Subjects were neither placed at any health risk by the study nor treatment decisions were made based on it. In addition, no financial compensation was offered for participation. Ethics committee approval, although not required for such a survey, was nevertheless obtained whenever specifically requested by a centre. Informed consent was obtained from all subjects for being included in the study.

Statistical analysis
Descriptive statistics were performed using IBM SPSS Statistics for Windows, version 23.0 software. The continuous variables with normal distribution and without a normal distribution were expressed as mean ± standard deviation and median, respectively. The categorical variables were presented as the percentage (number). Student's t-test and Chi-square test were performed for comparing the variables between different groups as appropriate. Multiple logistic regression analysis was performed to find out the important predictors of LH, hypoglycaemia, and hyperglycaemia. P values ≤0.05 were considered as statistically significant.

Results
General characteristics, insulin use, and glycaemic control
The study investigated a total of 847 insulin injectors. The mean duration of diabetes was 9.79 (±6.98) years and the mean duration of insulin use was 3.84 (±4.05) years. The mean insulin dose was 41 (±25) units, and 73.3% injected <50 units insulin per day. Though the majority (68.2%) were self-injectors, a large proportion of the study subjects were dependent on family members (30.6%) and paramedics (1.2%) for insulin injections. More than 70.0% of participants received one or two injections per day. Human premixed insulin was the most commonly used insulin (46.4%). The mean HbA1c was 9.5% (±2.0); the majority of participants (94.1%) had uncontrolled diabetes (HbA1c ≥7%) (*Table 1*).

Insulin injection device use and reuse practice by the study population
Syringes were used by 68.1% of the study subjects, whereas 31.9% used pen devices. Needles with 8 mm length were most commonly used (40.5%), followed by 6 mm (31.8%), 5 mm (14.4%), 4 mm (8.3%), and 12 mm (5.1%). Most (98.8%) of the syringe users reused the syringes, the frequency of reusing pen needles was 98.5% among the pen users. A total of 40.7% of the syringe users and 38.9% of the pen users reused the needles >10 times. The reasons for reusing needles were to save money (49.3%), for convenience (39.7%), not knowing how many times needles can be used (21.9%), to prevent excess waste (14.7%), and unavailability of another syringe/pen needle (3.0%).

Handling insulin before and during injection
Most of the study subjects (82.3%) stored their insulin vials and pen devices in the non-freezing part of the refrigerator before starting their use while 15.6% kept in room temperature, and 1.7% kept insulins in the earthen pit with water seal. In between the injections, the frequency for the syringe users and pen users refrigerating the used insulins were 74.5% (430/577) and 72.6% (196/270), respectively. Of the of 626 patients keeping insulins in the refrigerator in between the injections, 429 of them (68.5%) wait until the insulin reaches room temperature before injecting. Though 37.3% never checked the expiry date of the insulins, only 4.5% (24/531) of those who checked the expiry date ever injected the date-expired insulins. Only 1.3% of the subjects injected through clothing. Though 78.3% (443/566) of the cloudy insulin users suspended those before injecting, only a few (0.2%, 1/443) tipped or rolled the insulin vials or pen devices for the recommended 20 times or more.

Insulin injection site(s) and rotation patterns
The frequency of single-site and multiple-site (≥2) users for insulin injections were 35.1% and 64.9%, respectively. The abdomen was the most frequent site of injection in both single-site (70.7%) and multiple-site (59.8%) users, followed by arm (16.8% and 27.3% in single- and multiple-site users, respectively); thighs were less commonly used (12.1%

Table 1: Population demographic and baseline characteristics

Characteristic	N=847
Age, mean years ± SD	49.89 ± 13.13
Male	369 (43.6)
Female	478 (56.4)
Diabetes subtype	
T1DM	14 (1.7)
T2DM	794 (93.7)
GDM	31 (3.7)
Other*	8 (0.9)
Years with diabetes, mean ± SD	9.79 ± 6.98
Years on insulin, mean ± SD	3.84 ± 4.05
Responsible for injecting	
Self	578 (68.2)
Family member	259 (30.6)
Paramedic	10 (1.2)
Total daily dose of insulin, mean units ± SD	41 ± 25
<50 units	621 (73.3)
50–99 units	185 (21.8)
≥100 units	41 (4.8)
Type of insulin used	
Human premixed	393 (46.4)
Human regular only	82 (9.7)
NPH only	2 (0.2)
NPH + human regular	96 (11.3)
Basal analogue only	55 (6.5)
Bolus analogue only	14 (1.7)
Basal-bolus analogue	47 (5.5)
Premixed analogue	76 (9.0)
Basal analogue + human regular	76 (9.0)
Analogue co-formulation	6 (0.7)
Frequency of injections (per day)	
1	66 (7.8)
2	540 (63.8)
3	121 (14.3)
4	113 (13.3)
≥5	7 (0.8)
HbA1c %, mean ± SD (n=758)	9.5 ± 2.0
<7%	45/758 (5.9)
≥7%	713/758 (94.1)

Data are presented as n (%) unless otherwise stated.
GDM = gestational diabetes mellitus; NPH = Neutral protamine Hagedorn; SD = standard deviation; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus.
*Specific types of diabetes due to other causes.

of single-site users and 12.5% of multiple-site users) and buttocks were seldom used for injections. Most of the study subjects (84.5%) practiced some form of rotation pattern of injection sites.

Insulin injection practice by the study population

One-third (33.8%) of the study subjects never cleaned the injection site before injection, whereas the frequencies of the subjects cleaning the injection sites always, often and sometimes were 43.2%, 3.3%, and 19.7%, respectively. Hexisol was the most commonly used (73.3%)

cleansing material followed by Savlon/Detol (13.9%), alcohol swab (6.8%) and water (6.1%). Of the alcohol swab or disinfectant users, 57.3% (302/527) waited until the evaporation of those before injection, and 42.7% did not. A total of 89.7% (760/847) injected into a skinfold and 86.3% (656/760) of them lifted the skin correctly (with one or two fingers plus the thumb); 9.2% (70/760) released the skinfold immediately after inserting the needle into the skin, 60.8% (462/760) after injecting the total dose of the insulin, and 30.0% (228/760) released after removing the needle at the completion of insulin injection. The angles of needle entry were 45 degrees in 27.7%, 90 degrees in 64.6%, and ≤30 degrees in 4.8% of the subjects; 2.8% injected intra-dermally.

The dwell times of the needles after injections were <5 seconds in 34.7% (294/847), 5–10 seconds in 44.3% (375/847), and >10 seconds in 7.7% (65/847); 13.3% (113/847) of the study subjects were not aware of the duration of needle dwell time after injections. The frequency of subjects with higher dwell times was higher among pen users than the syringe users (among the syringe users, dwell time was <5 seconds in 40.9%, 5–10 seconds in 38.3%, and >10 seconds in 5.2%; the frequencies were 21.5%, 57.0%, and 13.0%, respectively among the pen-users).

Skipping insulin injections – frequency and causes

More than half (55%, 466/847) of the study subjects gave their history of skipping insulin injections; among them, 7.5% (35/466) skipped several times a week, 66.1% (308/466) skipped several times a month, and 26.4% (123/466) skipped insulin injection several times a year. When asked why the participants were skipping injections, the answers provided were as follows: forgot (58.4%), was sick (24.2%), just didn't want to inject (23.8%), too low glucose (20.6%), didn't eat (8.2%), and other causes (4.7%).

Disposal practice of used sharps

The majority (69.3%) of the study subjects disposed of the used syringes/pen needles into the rubbish with the cap on, 12.4% into the rubbish without recapping, 7.8% into a home sharps container such as an empty bottle, 7.6% into a container specially made for used sharps, and 3.0% disposed the used sharps anywhere without recapping. Among those who disposed of the sharps into a container, 87.7% (114/130) put the containers into the rubbish.

Injection site complications

More than half (58.5%) of the study subjects experienced pain during injection, whereas the frequencies of bleeding/bruising, insulin leakage from the injection site, and dribbling of insulin from needle tip after injection were 35.5%, 38.8%, and 29.9%, respectively. A total of 9.2% of the subjects had injection-site LH and among them, 38.5% injected into the lesion (*Table 2*). Subjects with LH had higher HbA1c than those without (10.0 ± 2.2% versus 9.5 ± 2.0%, p<0.001). The factors associated with painful injections and insulin leakage after injecting are highlighted in *Table 3* and *Table 4*, respectively. The important predictors of the presence of LH in the study subjects are given in *Table 5*.

Accidental injuries and blood-borne infections

Accidental injury with diabetic sharps (needle or lancet) happened in 2.5% cases (the patient or others); 1.7% of the patients had a blood-borne infection(s).

Insulin injection education and self-monitoring of blood glucose practices

Most of the study subjects (92.1%) reported that they had received education about insulin injection; the education was given by the doctors (endocrinologists in 32.1% and other specialists or general physicians in

Table 2: Injection-site complications

Variables	No. of subjects (n/N)	Frequency (%)
Painful injections	473/847	55.8
Frequency of painful injections		
Always	9/473	1.9
Often*	40/473	8.5
Sometimes†	413/473	87.3
Almost never‡	11/473	2.3
Bleeding and/or bruising	301/847	35.5
Frequency of bleeding and/or bruising		
Always	3/301	1.0
Often*	10/301	3.3
Sometimes†	254/301	84.4
Almost never‡	34/301	11.3
Insulin leakage from skin after injection	329/847	38.8
Frequency of insulin leakage		
Always	2/329	0.6
Often*	9/329	2.7
Sometimes†	258/329	78.4
Almost Never‡	60/329	18.2
Dribble/leakage of insulin from the needle tip after injection	253/847	29.9
Frequency of insulin dribble/leakage		
Always	4/253	1.6
Often*	36/253	14.2
Sometimes†	185/253	73.1
Almost Never‡	28/253	11.1
Lipohypertrophy	78/847	9.2
Site of lipohypertrophy		
Abdomen	41/78	52.6
Arm	17/78	21.8
Thigh	18/78	23.1
Buttock	1/78	1.3
Other site(s)	1/78	1.3
Inject into the lipohypertrophy	30/78	38.5
Reason of injecting into the lipohypertrophy		
It is less painful	5/30	16.7
It is convenient	4/30	13.3
Just as a habit	13/30	43.3
Cannot explain	8/30	26.7

*'Often' refers to several times a week.
†'Sometimes' refers to several times a month.
‡'Almost never' refers to several times a year.[10]

36.8% of cases) in most of the instances. Nurses (21.5%), pharmacists (3.5%), medicine shopkeepers (2.9%), medical representatives (0.8%), and another insulin-injecting patient with diabetes (2.4%) were also insulin education providers to our study subjects. Such education was reviewed within the previous 6 months in only 39.6% of the patients. The injection sites were checked by the attending physicians in every visit only in 14.9% of the subjects and 48.9% study subjects couldn't remember whether their injection site(s) were ever checked. Almost half (49.6%) of the patients never or rarely performed self-monitoring of

Table 3: Injection practices in 'pain-present' and 'pain-free' subgroups of the study subjects

Parameter	Total patients % (N=847)	Pain present % (n=473)	Pain-free % (n=374)	p*
Insulin device				
Syringe	68.1	73.2	61.8	<0.001
Pen	31.9	26.8	38.2	
Main site of injection				
Abdomen	63.6	60.3	67.9	0.022
Other than abdomen	36.4	39.7	32.1	
Needle reuse				
≤2 times	1.7	1.1	2.5	0.001
3–5 times	22.2	24.6	19.2	
6–10 times	35.4	30.4	41.9	
>10 times	40.7	43.9	36.4	
Needle length				
4 mm	8.3	11.8	3.7	<0.001
5 mm	14.4	10.4	19.5	
6 mm	31.8	26.4	38.5	
8 mm	40.5	44.8	35.0	
12 mm	5.1	6.6	3.2	
Injects into a skinfold				
Yes	89.7	90.1	89.3	0.401
No	10.3	9.9	10.7	
Angle of needle entry				
90 degrees	64.6	59.8	70.6	0.001
Other than 90 degrees	35.4	40.2	29.4	
Bleeding				
Yes	35.5	44.8	23.8	<0.001
No	64.5	55.2	76.2	

*p-value by Chi-Square test.

blood glucose (SMBG) and a few of the subjects performed SMBG for the recommended times.

Hypoglycaemia and hyperglycaemia

More than one-third (36.7%) of the study subjects experienced hypoglycaemia (plasma glucose <3.9 mmol/L with or without hypoglycaemic symptoms) for a median number of two times within the previous 6 months of the study; among them, 9.8% experienced severe hypoglycaemia. A greater number of patients (67.4%) experienced hyperglycaemic episodes (plasma glucose >13.9 mmol/L) in that period and in 4.5% of the instances the hyperglycaemic episodes were severe. The factors contributing to the occurrence of hypoglycaemia and hyperglycaemia in the study are shown in *Table 6*.

Discussion

BIITS covered the entire country and all the sectors (government and private hospitals and specialist OPDs) of healthcare delivery systems in the country. The survey covered all the major aspects of insulin injections, including patient demographic characteristics, key insulin injection practices and parameters, complications, and education. A total of 847 patients from 18 centres participated in this study. Study subjects had been living with diabetes for an average of 9.8 years and had been

Table 4: Factors affecting insulin leakage after injections

Parameter	Total patients (N=847)	Leakage present (n=329)	Leakage absent (n=518)	p*
Insulin device				
Syringe	68.1	69.0	67.6	0.705
Pen	31.9	31.0	32.4	
Dwell time after injection				
<5 s	34.7	39.5	31.7	0.038
5–10 s	44.3	39.8	47.1	
>10 s	7.7	6.1	8.7	
Not aware how long	13.3	14.6	12.5	
Needle length				
4 mm	8.3	13.4	5.0	<0.001
5 mm	14.4	17.0	12.7	
6 mm	31.8	22.5	37.6	
8 mm	40.5	45.3	37.5	
12 mm	5.1	1.8	7.1	
TDD of insulin, IU mean ± SD	41 ± 25	45 ± 29	39 ± 22	<0.001

Data are presented as % unless otherwise stated.
*p-value by Student's t-test or Chi-Square test as applicable.
IU= international unit; s = seconds; SD = standard deviation; TDD = total daily dose.

Table 5: Binary logistic regression analysis for the predictors of lipohypertrophy in the study subjects

Variables	Sub-groups	Odds ratio (95% CI)	p
Duration of insulin use	<5 years	Referent	
	≥5 years	2.204 (1.331–3.648)	0.002
Number of injections/day	≤2	Referent	
	>2	0.797 (0.427–1.490)	0.477
Total daily dose of insulin	<50 units	Referent	
	≥50 units	0.934 (0.488–1.787)	0.836
Insulin device	Pen device	Referent	
	Syringe-vial	1.637 (0.850–3.152)	0.141
Needle length	≤6 mm	Referent	
	>6 mm	0.607 (0.343–1.075)	0.087
Needle reuse frequency	≤10 times	Referent	
	>10 times	3.147 (1.668–5.937)	<0.001
Use multiple sites for injection	Yes	Referent	
	No	0.887 (0.507–1.549)	0.673
Rotate of injection sites	Yes	Referent	
	No	1.082 (0.524–2.236)	0.832
Angle of needle entry	90 degrees	Referent	
	Not at 90 degrees	2.203 (1.322–3.672)	0.002
Injects into skin-fold	Yes	Referent	
	No	0.769 (0.309–1.917)	0.574
Got injection education	Yes	Referent	
	No	1.375 (0.632–2.995)	0.422

CI = confidence interval.

using insulin for a mean of 3.8 years. These timeframes should reflect sufficient experience regarding diabetes management including insulin injection technique.

The mean daily dose of insulin in this study (41 units) was higher than the Indian ITQ Study (36.9 units) and another Indian study (33.36 units) but lower than the rest of the world (ROW; 50.2 units).[10–12] The use of <50 units of insulin per day by about three-quarters of the study subjects and their uncontrolled blood glucose indicates the inadequate adjustment of insulin dose in these patients. Olamoyegun et al., in Nigeria, found around 90% of the insulin users taking ≤40 units of insulin per day.[13] The frequency of subjects taking a fewer number of injections (1 or 2) per day was higher, and the frequency of the subjects having at least four injections/day was lower, in this study than observed in Indian- and the World ITQ studies. These are the reflections of greater use of premixed insulins and lesser use of basal-bolus insulin regimen by the subjects of the current study in comparison to those studies.[10,11] Four daily injections of basal-bolus insulin are more costly and require more degrees of patient education and motivation than twice daily premixed insulins. In developed countries, basal-bolus insulin is more acceptable than developing and underdeveloped countries of the world.

Another important observation was that many (31.8%) of the study subjects in the current study were dependent on others (family members and paramedics) for injections, which may be a barrier to multiple daily insulin injections. Furthermore, the people who assist with the injections may not always be available and this may lead to skipping insulin injections, also injections by paramedics create extra costs for diabetes care. A similar picture was observed in a Nigerian study, in which 28.2% did not inject themselves.[13] The global scenario is better in this aspect (~98% self-inject).[10]

The glycaemic control of the study subjects (mean HbA1c 9.5%) was worse than Indian ITQ (8.6%) and global averages (8.5%).[10,11] Selim et al., in a previous study, found similar mean HbA1c (9.56%) among Bangladeshi patients with T2DM, though more patients (18.9%) had HbA1c <7% in their study than ours (5.9%).[14] This is frustrating and alarming as insulin is considered to be the most potent weapon for diabetes control and in patients with T2DM; insulin is often used when oral anti-diabetic drugs fail to control diabetes. The study subjects were on insulin for a mean of 3.8 years, a long time for necessary adjustment and intensification of insulin dose. The reason behind this high HbA1c, despite sufficient time for insulin adjustment, must be discovered to get the benefit of insulin treatment in these patients.

Most of the subjects in the present study used insulin syringes; the use of pen devices was less frequent than India and the ROW, including Nigeria.[10,11,13] The pen devices are costly and many of our patients are unlikely to be able to afford them. The greater use of medium length (6 mm and 8 mm) needles and less use of shorter needles in this study are the reverse of ROW and Indian data.[10,11] Previous studies report a shifting trend from using longer-sized insulin needles to shorter ones worldwide, due to the increasing use of pen devices.[10] Shorter needles are as effective as longer ones in terms of insulin delivery and confer some additional benefits including reduction of injection pain and avoidance of intramuscular injections.[2]

Both the frequency of needle reuse and the number of times the needles were reused were much higher than ROW, India and Nigeria.[10–13] Reusing makes needles distorted and bent, as a result, injection-related complications including pain, bruising, local bleeding,

Table 6: Insulin injection-related factors influencing the frequency of hypoglycaemia and hyperglycaemia

Variables	Category N=847	% with hypoglycaemia (n=311)	p	% with hyperglycaemia (n=571)	p
Duration of insulin treatment (years)	<5 (n=582)	66.6	0.318	63.9	<0.001
	≥5 (n=265)	33.4		36.1	
HbA1c (%)	<7 (n=45)	5.8	1.000	4.3	0.008
	≥7 (n=713)	94.2		95.7	
Diabetic complication(s)	Absent (n=395)	40.8	0.010	44.7	0.106
	Present (n=452)	59.2		55.3	
No. of injections per day	≤2 (n=606)	70.4	0.581	71.3	0.871
	>2 (n=241)	29.6		28.7	
Total daily dose of insulin (IU)	<50 (n=621)	72.7	0.748	70.2	0.004
	≥50 (n=226)	27.3		29.1	
Insulin device	Syringe (n=577)	70.1	0.360	70.9	0.015
	Pen (n=270)	29.9		29.1	
Needle length (mm)	≤6 (n=461)	55.0	0.830	45.0	<0.001
	>6 (n=380)	45.0		55.0	
Main Injection site	Abdomen (n=539)	57.9	0.009	62.0	0.170
	Others (n=308)	42.1		38.0	
Rotate injection site(s)	No (n=131)	16.7	0.490	15.6	0.920
	Yes (n=716)	83.3		84.4	
Inject into a skinfold	Yes (n=760)	91.3	0.291	89.0	0.335
	No (n=87)	8.7		11.0	
Angle of needle entry	90 degrees (n=547)	61.1	0.118	62.3	0.055
	Other than 90 degrees (n=300)	38.9		37.7	
Needle reuse	No (n=11)	1.9	0.225	1.1	0.351
	Yes (n=836)	98.1		98.9	
How many times reuse needles	≤10 (n=496)	56.4	0.214	56.3	0.011
	>10 (n=340)	43.6		43.7	
LH	Absent (n=769)	88.4	0.084	89.0	0.008
	Present (n=78)	11.6		11.0	
Injects in to LH (n=78)	No (n=48)	52.8	0.166	55.6	0.037
	Yes (n=30)	47.2		44.4	
Skip injection(s)	Yes (n=466)	69.5	<0.001	65.3	<0.001
	No (n=381)	30.5		34.7	
Got education on injection technique	Yes (n=780)	96.8	<0.001	92.6	0.416
	No (n=67)	3.2		7.4	
Education provider	Doctors (n=537)	59.8	<0.001	64.5	<0.001
	Others (n=242)	40.2		35.5	
SMBG frequency	At least 1/day (n=73)	10.6	0.223	7.9	0.509
	At least 1/week (n=354)	42.4		42.6	
	Never (n=420)	46.9		49.6	

*p-value comparing the column proportions by Chi-Square test.
HbA1c = glycated haemoglobin; LH = lipohypertrophy; SMBG= self-monitoring of blood glucose.

infections, and LH occurs more frequently with needle reuse.[2] Puder et al. suggested that using pen needles up to five times does not lead to needle tip deformity and does not increase pain or unpleasantness.[15] Furthermore, such limited reuse could help save money for healthcare systems.[15]

Insulin vials and pens, which are not in active use, must be refrigerated, but not frozen. In places where the refrigerator is not available, such as in rural areas, the insulin vial may be kept in water in earthen pitch or wide-mouthed bottle after air-tied in a plastic bag. Storing insulin in room temperature, which may exceed 30°C in summer in this area, may decrease the efficacy of insulin.[2] Though the insulin storage practice was satisfactory in the majority, a good number of subjects in the current study stored insulin at room temperature before use. Olamoyegun et al., in Nigeria, had similar observations.[13] Unfortunately, we found the majority of the pen users to keep the pen devices with needles in the refrigerator in between injections. Pens should never be refrigerated with needles as this practice may cause insulin to precipitate in the needle and the needle may become blocked causing improper dosing.[2]

Cloudy insulins (premixed and Neutral protamine Hagedorn [NPH]) must be suspended by proper tipping or rolling before injection given. Failure to re-suspend NPH and premixed insulins leads to significant variability in action profile particularly the nocturnal plasma insulin concentration resulting in blood glucose variability, including hypoglycaemic episodes.[2] Proper suspension practice was not observed in the majority of our study subjects; though the ROW scenario was better, the Indian ITQ Study had a similar picture.[10,11]

Though arms and thighs were more frequently used as a single injection site in this study than observed in India, ROW and Nigeria, the abdomen was the most frequent site of insulin injection used by our patients.[10,11,13] The lower risk of intramuscular injection and more rapid absorption due to the presence of a thick subcutaneous fat layer have made the abdomen the first choice for insulin injection. Thigh injections carry a higher risk of intramuscular injection.[2,10,11] Systematic intra-site and inter-site rotation helps to maintain healthy injection sites, optimises insulin absorption and reduces the chance of LH.[2] Most of the participants in the present study used multiple sites for injections and followed some form of rotation pattern while injecting; the rotation practice was similar to those observed in ROW, and better than Indian patients observed by Baruah et al. but not as good as the Nigerian insulin users.[10,12,13]

Around two-thirds of the study subjects cleaned their injection site(s), a better picture than observed among previously reported Nigerian patients.[13] The majority used disinfectants for the purpose and only a few used alcohol pads or water. The injection should always be given at a clean site with a clean hand. Though insulin can be injected provided the site is considered 'socially clean', the site should be thoroughly cleaned with either with alcohol swabs or with a cotton ball dipped in water always, especially if the injection site is found unclear.[2] Almost half (42.7%) of the study subjects who used alcohol pad and disinfectants did not wait until those evaporate before injecting; this practice may cause injection pain.

We observed the majority of the study subjects to inject into a skinfold lifted correctly but most of them released the skinfold inappropriately. Pinching up skin decrease the chance of intramuscular injection.[2,11] The angle of needle insertion was 90 degrees in the majority of the study subjects and only a few injected intradermally. Insulin must be injected at the subcutaneous fat layer for proper absorption, intradermal injections not only fail to deliver insulin at this site resulting in therapeutic ineffectiveness, but also increases the risk of local complications.[2]

Almost half of the patients skipped insulin injections, though frequent injection skipping was less common. A similar picture was observed in the ROW, and the main reasons for injection skipping in this study were also similar to the ROW study.[10] Nigerian insulin users skipped injections less frequently than our study.[13] The sharp disposal practice by our patients was poor, and worse than that observed in India.[11] Such practice increases the risk of sharp injuries to anyone who comes near the rubbish or handle those.

Pain was an important injection complication among the insulin users in the current study and pain was commonly associated with bleeding. Longer needles and higher frequency of needle reuse were associated with painful injections. Pen users had less painful injections due to the use of shorter needles. These findings were similar to the World- and the Indian ITQ Study results.[16,17] Patient awareness of injection pain and discomfort has been studied extensively and is found to be related to three key factors: needle length, needle diameter and injection

context.[18,19] Subjects injecting into the abdomen experienced less frequent pain in our study, as was also observed by Heise et al.[20]

The ideal practice of keeping the needles under the skin for 10 seconds or longer after injecting was not followed by most of the subjects in this study.[2] A shorter dwell time of the needles after injection is found to be associated with a higher frequency of insulin leakage from the site of injection by some researchers. It is also observed that the amount of leakage increased with increased dosage administered.[21] There were similar observations in the present study. We also observed that smaller length needles were associated with a higher frequency of insulin leakage than the longer ones. Previous studies found no meaningful influence of needle length on the insulin leakage.[21]

Insulin LH, which remains a serious local problem of insulin therapy, denotes a benign tumour-like swelling of fatty tissue at the injection site secondary to the lipogenic effect of insulin.[22] The observed prevalence of LH in the current study (9.2%) was lower than the previous studies done worldwide, which may be due to the shorter duration of insulin use in study subjects in the present study.[12,16,17] The site distributions of LH (abdomen being the most common site) were similar to the World ITQ Study, though the most common sites of LH among Indian insulin injectors were thighs followed by arms and abdomen.[16,17] In the present study, longer duration of insulin use, higher frequency of needle reuse, and injecting at an oblique angle were found to be the important predictors of LH. The presence of LH was associated with higher HbA1c values, with a mean HbA1c 0.5% higher in patients with LH than those without LH among Bangladeshi injectors. Previous investigators had similar observations.[23–25] This is important in the setting of diabetes control because LH is a preventable complication of insulin injection and only by its prevention, can we lower HbA1c and reduce diabetes complications.

It is very important to provide education on insulin injection whenever a patient is prescribed with insulin, and such education should be repeated periodically for better therapeutic outcomes. Patients in the present study received such education at the beginning of their insulin treatment, though this was not repeated in the majority within the recent months; similar scenarios were observed in the World- and the Indian ITQ studies.[16,17] Thus the discrepancy in given education and current injection practice is the reflection of inadequacy and ineffectiveness of the education provided. Guidelines also recommended checking injection sites at least annually, and more frequently when the risk of LH and other injection-related complications are high.[2,8,9] Unfortunately, around half of the patients in the present study never had their injection sites checked by their physicians as reported by the study subjects; this is alarming and the situation is worse than observed in India.[17]

The prevalence of both hypoglycaemia and hyperglycaemia among patients in the present study were high, even higher than the World ITQ Study and the Indian ITQ Study.[16,17] The study subjects with diabetes complication(s), those who injected in abdomen, skipped injections, got education about insulin injection, and those who got insulin education from the doctors had higher frequency of hypoglycaemia than their counterparts. In addition to more stringent glycaemic control, other known risk factors for hypoglycaemia in diabetes include the use of insulin and insulin secretagogues, non-adherence to recommended diet and exercise, renal and hepatic impairment, longer duration of diabetes, alcohol ingestion and others.[26] In contrast to our findings, rates of unexplained hypoglycaemia and glucose variability were found to be lower in the World ITQ Study when the abdomen is used

exclusively as an injection site, but as one added the use of the limbs, the rates of both disorders increased.[16]

The higher hypoglycaemic frequency among the insulin-educated subjects in our study is the reflection of the inadequacy and ineffectiveness of the education provided. We observed higher frequency of hyperglycaemic episodes among the subjects with higher duration of diabetes, those using higher doses of insulin, among syringe users than pen users, those using longer needles, those with a higher frequency of need reuse, those with LH and whom inject into their LH, those who skipped injections, and those who received insulin education from the doctors.

T2DM is a progressive disease with progressive loss of endogenous insulin secretion. Gradual up-titration of insulin dose is needed with increasing duration of diabetes in the majority of the patients; failure of proper insulin adjustment will result in uncontrolled diabetes.[20] Subjects injecting insulin with pen devices demonstrated better glycaemic control in the previous studies, moreover, insulin analogues are more commonly used with pens which provide better glycaemic efficacy in comparison to human insulin.[27,28] Subjects using smaller needles had less chance of hyperglycaemia in our study, which may be due to using smaller needles in pen devices which were associated with lower hyperglycaemia risk. Previous studies found higher frequencies of unexplained hypoglycaemia and glucose variability in those with LH and those injecting into LH.[16,17,25] We also observed significantly higher frequencies of hyperglycaemia in subjects with LH than without LH. More subjects with LH had hypoglycaemic events than those without LH though the difference was not statistically significant. The World ITQ and the Indian ITQ studies found higher frequencies of unexplained hypoglycaemia and glucose variability in those with the incorrect rotation of sites, and with needle reuse.[16,17] We observed no differences in hypo- and hyperglycaemic events between subjects who rotate injection sites and who do not. Though reusing needles did not impart a significant influence on the occurrences of hypo- and hyperglycaemic events in our study, subjects reusing the needles for >10 times had more chance of hyperglycaemic episodes. In contrast to our observation, receiving injection training from a trained person, e.g., a diabetes nurse, was found to be associated with less frequent unexpected hypoglycaemia and glucose variability in the World ITQ Study.[16]

Limitations of the study

This study has several limitations. The vital data input in this study involved recall by the patients (about events in recent months), which may have an inherent bias. Though during the interview the questions were translated to Bengali (the mother tongue of the study subjects) by the investigators, the questionnaire was in English. The study subjects were interviewed by multiple investigators conferring the risk of observer bias. HbA1c was not measured by the same method in all the study centres. Nevertheless, this one is the first multi-centre study which evaluated the insulin injection practices nationwide in Bangladesh and a fair number of patients were investigated. The study result may serve as a baseline for comparison of the injection practices in the future in this area.

Conclusion

Most of the patients in this area are not following the ideal insulin injection practice as per recommendations. The complications of insulin injection including LH were also high. The insulin education that was provided to most of them, was found insufficient and almost ineffective. There is scope for improving these and lessen the injection complications and improve glycaemic status. The results of the current study may serve as the backbone of the template on which different corrective strategies may be developed in the future. ❑

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