Insulin Injection Practice and Injection Complications – Results from the 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: The 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 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 the 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 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 to be 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. Healthcare providers should pay more attention to insulin education and re-evaluate injection practices from time to time.

Keywords
Diabetes, insulin injection, injection technique, lipohypertrophy, insulin education

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Diabetes mellitus (DM) is a major global health problem. The national prevalence of diabetes in Bangladesh is 6.9% and is increasing at an alarming rate. Though the prevalence of type 1 diabetes mellitus (T1DM) is low in this area, the prevalence of gestational diabetes and young-onset type 2 DM (T2DM) is very high. Insulin is an indispensable component of diabetes management. 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. 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. Insulin storage is also important as it may affect the potency of insulin, influencing its efficacy. Faulty injection technique is associated with injection-site complications including lipohypertrophy (LH). 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. Many guidelines have been published for ideal insulin injection practice, but unfortunately, there is a large gap between the guideline recommendations and actual practice of insulin use throughout the world. Data from Bangladesh specifically 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 endocrine clinics. 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 consenting 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 convenience and better understanding in our settings. 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. 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 Declaration of Helsinki. 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. 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 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. Premixed human 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 4 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 given 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 at room temperature, and 1.7% kept insulin in an earthen pitcher 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 626 patients keeping insulins in the refrigerator in between 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 one subject (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
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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 disinfector 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 did not want to inject (23.8%), too low glucose (20.6%), did not 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 doctors (endocrinologists in 32.1% and other specialists or general physicians

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### 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 injection | | |
| 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) | | |
| <7% | 45/758 (5.9) |
| ≥7% | 713/758 (94.1) |

Data are presented as n (%) unless otherwise stated.

*Specific types of diabetes due to other causes.

GDM = gestational diabetes mellitus; NPH = neutral protamine Hagedorn; SD = standard division; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus.
in 36.8% of cases) in most of the instances. Nurses (21.5%), pharmacists (3.5%), medicine shopkeepers (2.9%), medical representatives (0.8%), and other insulin-injecting patients 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% of study subjects could not remember whether their injection site(s) were ever checked. Almost half (49.6%) of the patients never or rarely performed self-monitoring of 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
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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 | 2.083 (1.336–3.233) | 0.002 |
| | ≥5 years | 2.204 (1.331–3.648) |
| Number of injections/day | ≤2 | Referent |
| | >2 | 0.792 (0.427–1.490) | 0.477 |
| Total daily dose of insulin | ≤50 units Referent | 0.934 (0.488–1.787) | 0.836 |
| | ≥50 units | 0.934 (0.488–1.787) |
| Insulin device | Pen device Referent |
| | Syringe and vial | 1.657 (0.850–3.152) | 0.141 |
| Needle length | ≤6 mm Referent | 0.607 (0.343–1.075) | 0.087 |
| | >6 mm | 0.607 (0.343–1.075) |
| Needle reuse frequency | ≤10 times Referent | 3.147 (1.668–5.937) | <0.001 |
| | >10 times | 3.147 (1.668–5.937) |
| Use multiple sites for injection | Yes Referent |
| | No | 0.887 (0.507–1.549) | 0.673 |
| Rotate injection site(s) | 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 skinfold | Yes Referent |
| | No | 0.769 (0.309–1.917) | 0.574 |
| Injection education | Yes Referent |
| | No | 1.375 (0.632–2.995) | 0.422 |

CI = confidence interval.

The glycaemic control of the study subjects (mean HbA1c 9.5%) was worse than the Indian ITQ (8.6%) and global averages (8.5%). 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%). 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 in India and the ROW, including Nigeria. 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. Previous studies report a shifting trend from using longer-sized insulin needles to shorter ones worldwide, due to the increasing use of pen devices. 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.

Both frequency of needle reuse and the number of times needles were reused were much higher than in ROW, India and Nigeria.
Table 6: Insulin injection-related factors influencing the frequency of hypoglycaemia and hyperglycaemia

| Variables                              | Category | N=847 (n=311) | % with hypoglycaemia | p* | N=571 (n=571) | % with hyperglycaemia | p* |
|----------------------------------------|----------|---------------|----------------------|----|---------------|-----------------------|----|
| Duration of insulin treatment (years)  | <5 (n=582) | 66.6          | 0.318                | 63.9 | <0.001        | 36.1                  |    |
|                                        | ≥5 (n=265) | 33.4          |                      |     |               |                       |    |
| HbA1c (%)                              | <7 (n=45) | 5.8           | 1.000                | 4.3  | 0.008         | 95.7                  |    |
|                                        | ≥7 (n=713) | 94.2          |                      |     |               | 44.7                  | 0.106|
| Diabetic complication(s)               | Absent (n=395) | 40.8        | 0.010                | 59.2 | 0.55         | 55.3                  |    |
|                                        | Present (n=452) | 59.2          |                      |     |               |                       |    |
| Number of injections/day                | ≤2 (n=606) | 70.4          | 0.581                | 71.3 | 0.871         | 28.7                  |    |
|                                        | ≥2 (n=241) | 29.6          |                      |     |               |                       |    |
| Total daily dose of insulin (IU)       | <50 (n=621) | 72.7          | 0.748                | 70.2 | 0.004         | 29.1                  |    |
|                                        | ≥50 (n=226) | 27.3          |                      |     |               |                       |    |
| Insulin device                         | Syringe (n=577) | 70.1          | 0.360                | 70.9 | 0.015         | 29.1                  |    |
|                                        | Pen (n=270) | 29.9          |                      |     |               |                       |    |
| Needle length (mm)                     | ≤6 (n=461) | 55.0          | 0.830                | 45.0 | <0.001        | 55.0                  |    |
|                                        | >6 (n=383) | 45.0          |                      |     |               |                       |    |
| Main injection site                    | Abdomen (n=539) | 57.9          | 0.009                | 62.0 | 0.170         | 38.0                  |    |
|                                        | Others (n=308) | 42.1          |                      |     |               |                       |    |
| Rotate injection site(s)               | No (n=131) | 16.7          | 0.490                | 15.6 | 0.920         | 84.4                  |    |
|                                        | Yes (n=716) | 83.3          |                      |     |               |                       |    |
| Inject into a skinfold                 | Yes (n=760) | 91.3          | 0.291                | 89.0 | 0.335         | 11.0                  |    |
|                                        | No (n=87)  | 8.7           |                      |     |               |                       |    |
| Angle of needle entry                  | 90 degrees (n=547) | 61.1          | 0.118                | 62.3 | 0.055         | 37.7                  |    |
|                                        | Other than 90 degrees (n=300) | 38.9          |                      |     |               |                       |    |
| Needle reuse                           | No (n=11)  | 1.9           | 0.225                | 1.1  | 0.351         | 98.9                  |    |
|                                        | Yes (n=836) | 98.1          |                      |     |               |                       |    |
| Number of times needles reused         | ≤10 (n=496) | 56.4          | 0.214                | 56.3 | 0.011         | 43.7                  |    |
|                                        | >10 (n=340) | 43.6          |                      |     |               |                       |    |
| LH                                     | Absent (n=769) | 88.4          | 0.084                | 89.0 | 0.008         | 11.0                  |    |
|                                        | Present (n=78) | 11.6         |                      |     |               |                       |    |
| Injects into LH (n=78)                 | No (n=48)  | 52.8          | 0.166                | 55.6 | 0.037         | 44.4                  |    |
|                                        | Yes (n=30) | 47.2          |                      |     |               |                       |    |
| Skip injection(s)                      | Yes (n=446) | 69.5          | <0.001               | 65.3 | <0.001        | 34.7                  |    |
|                                        | No (n=381) | 30.5          |                      |     |               |                       |    |
| Education on injection technique       | Yes (n=780) | 96.8          | <0.001               | 92.6 | 0.416         | 7.4                   |    |
|                                        | No (n=67)  | 3.2           |                      |     |               |                       |    |
| Education provider                     | Doctors (n=537) | 59.8          | <0.001               | 64.5 | <0.001        | 35.5                  |    |
|                                        | Others (n=242) | 40.2          |                      |     |               |                       |    |
| SMBG frequency                         | At least 1/day (n=73) | 10.6          | 0.223                | 7.9  | 0.509         | 92.1                  |    |
|                                        | At least 1/week (n=354) | 42.4          |                      |     |               |                       |    |
|                                        | Never (n=420) | 46.9          |                      |     |               |                       |    |

*p-value comparing the column proportions by Chi-square test.

HbA1c = glycated haemoglobin; LH = lipohypertrophy; SMBG= self-monitoring of blood glucose.

Reusing makes needles distorted and bent, as a result, injection-related complications including pain, bruising, local bleeding, infections and LH occur more frequently with needle reuse. 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. Furthermore, such limited reuse could help save money for healthcare systems.

Insulin vials and pens that are not in active use must be refrigerated, but not frozen. In places where a refrigerator is not available, such as in rural areas, the insulin vial may be kept in water in an earthen pitcher or wide-mouthed bottle after being air-tied in a plastic bag. Storing insulin at room temperature, which may exceed 30°C in summer in this area, may decrease the efficacy of insulin. 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. Unfortunately, we found the majority of the pen users kept 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.
Cloudy insulins (premixed and neutral protamine Hagedorn (NPH)) must be suspended by proper tapping or rolling before the injection is 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. 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.15

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 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. 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.9,10-12

Around two-thirds of the study subjects cleaned their injection site(s), a better picture than observed among previously reported Nigerian patients.10 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. Almost half (42.7%) of the study subjects who used alcohol pads and disinfectants did not wait until those evaporated before injecting; this practice may cause injection pain.

We observed the majority of the study subjects who injected into a skinfold lifted correctly, but most of them released the skinfold inappropriately. Pinching up skin decreases 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 into the subcutaneous fat layer for proper absorption; intradermal injections not only fail to deliver insulin at this site resulting in therapeutic ineffectiveness, but also increase 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.12 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 or handles the rubbish.

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 worldwide- and the Indian ITQ Study results.12,13 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.12,15 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! 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.10,11-12 The site distributions of LH (abdomen being the most common site) were similar to the Worldwide 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.20-25 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 in recent months; similar scenarios were observed in the worldwide- and Indian-ITQ studies.10-11 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.2,4 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 Worldwide 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 Worldwide ITQ Study when the abdomen is used
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. 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. Subjects using smaller needles had less chance of hyperglycaemia in our study; this may be due to using smaller needles in pen devices, which were associated with lower hyperglycaemia risk. Previous studies found higher frequencies of unexplained hyperglycaemia 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 worldwide- and Indian-ITQ studies found higher frequencies of unexplained hyperglycaemia and glucose variability in those with the incorrect rotation of sites, and with needle reuse.16,24

1. We observed no differences in hypo- and hyperglycaemic events between subjects who rotate injection sites and who do not. Though using needles did not impart a significant influence on the occurrences of hypo- and hyperglycaemic events in our study, subjects using needles >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 hyperglycaemia and glucose variability in the Worldwide ITQ Study.14

2. 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 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.

3. 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 to be insufficient and almost ineffective. There is scope for improving these, lessening injection complications and improving 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.

References

1. International Diabetes Federation. IDF Diabetes Atlas Ninth Edition 2019. Available at: www.idf.org/sa-activities/advocacy-awareness/resources-and-tools/159-idf-diabetes-atlas-ninth-edition-2019.html (accessed 28 January 2020).
2. Tandon N, Kalra S, Bahara YP, et al. Forum for injection technique and therapy expert recommendations, India: the Indian recommendations for best practice in insulin injection technique, 2017. Indian J Endocrinol Metab. 2017;21:605–17.
3. Siddiqui NJ, Kamrul-Hasan M, Hassan MA, et al. Ramadan perspective epidemiology and education in diabetes (RAPEED) study. Mymensingh Med J. 2017;26:256–65.
4. Grassi G, Sciconte P, Trevisacchi R, et al. Optimizing insulin injection technique and its effect on blood glucose control. J Clin Parl Endocrinol. 2014;1:143–50.
5. Vimalavathini R, Gitarajili B. Effect of temperature on the potency & pharmacological action of insulin. Indian J Med Res. 2009;130:166–9.
6. Deng N, Zhang X, Zhao F, et al. Prevalence of hypophysectomy in insulin-treated diabetic patients: a systematic review and meta-analysis. J Diabetes Investig. 2018;9:536–43.
7. Majumdar A, Sahoo J, Roy G, Kamalanatha S. Improper sharp disposal practices among diabetes patients in home care settings: need for concern? Indian J Endocrinol Metab. 2015;19:02–5.
8. Frid AH, Khegutal G, Grassi G, et al. New insulin delivery recommendations. Mayo Clin Proc. 2016;91:1231–55.
9. Spollett G, Edmunds SJ, Metherf P, et al. Improvement of insulin injection technique: examination of current issues and recommendations. Diabetes Educ. 2016;42:379–94.
10. Frid AH, Hirsch L, Menzies AR, et al. Worldwide injection technique questionnaire study: population parameters and injection practices. Mayo Clin Proc. 2016;91:1221–23.
11. Kalra S, Mithal A, Sahay R, et al. Indian injection technique study: population characteristics and injection practices. Diabetes Ther. 2017;8:637–57.
12. Barash ME, Kalra S, Bisce S, Deiki L. An audit of insulin usage and insulin injection practices in a large Indian cohort. Indian J Endocrinol Metab. 2017;21:443–52.
13. Galavoyyan MA, Akbariade AT, Ala OA. Audit of insulin prescription patterns and associated burden among diabetics in a tertiary health institution in Nigeria. Afr Health Sci. 2018;18:852–55.
14. Selim S, Patel S, Safdarian M, et al. The challenge of proper glycaemic control among patients with type 2 diabetes in Bangladesh. SGMEM. 2016;6:56–20.
15. Funder J, Almar M, Muller B, et al. Using insulin pen needles up to five times does not affect needle tip shape nor increase pain intensity. Diabetes Res Clin Pract. 2006;71:199–202.
16. Frid AH, Hirsch L, Menzies AR, et al. Worldwide injection technique questionnaire study: injecting complications and the role of the professional. Mayo Clin Proc. 2016;91:1224–30.
17. Kalra S, Mithal A, Sahay R, et al. Indian injection technique study: injecting complications, education, and the healthcare professional. Diabetes Ther. 2017;8:659–72.
18. Brady KA, Aamer JR, Khine H. Perception and attitude of providers towards pain and anxiety associated with pediatric vaccine injection. Cln Pediatr. 2015;50:140-3.
19. Diamond S, Matok I. Pharmacists’ anticipated pain compared to experienced pain associated with insulin pen injection and fingernip. Can J Diabetes. 2011;35:282–8.
20. Hesse T, Nossek D, Deiwag S, et al. Impact of injection speed and volume on perceived pain during subcutaneous injections into the abdomen and thigh: a single-centre, randomized controlled trial. Diabetes Obes Metab. 2014;16:971–6.
21. Wittmann A, Köver I, Kral N, et al. Insulin leakage value in relation to pen needle length and administered dose after subcutaneous injection. Diabetes Technol Ther. 2010;12:587–90.
22. Rodermudeker RP, Pielard GE, Siehen AI. Lipodystrophy reactions to insulin: effects of continuous insulin infusion and new insulin analogues. Am J Clin Dermatol. 2007;8:1–8.
23. Vardar IF, Kızılık S. Incidence of lipohypertrophy in diabetic patients and a study of influencing factors. Diabetes Res Clin Pract. 2007;77:231–6.
24. Saez-de Barra L, Gallego F. Factors related to lipohypertrophy in insulin-treated diabetic patients: role of educational intervention. Pract Diab Int. 1999;15:9–11.
25. Bianco M, Hermann DT, Stauso KF, Amaya M. Prevalence and risk factors of lipohypertrophy in insulin-injecting patients with diabetes. Diabetes Res. 2013;99:445–53.
26. American Diabetes Association. Glycaemic targets: standards of medical care in diabetes-2019. Diabetes Care. 2019;42(suppl. 1):1–76.
27. Singh R, Samuel C, Jacob I. A comparison of insulin pen devices and disposable plastic syringes – simplicity, safety, convenience and cost differences. Eur Endocrinol. 2018;4:47–51.
28. Xie L, Zhou S, Pinsky WA, et al. Impact of initiating insulin glargine disposable pen versus vial/needle on real-world glycaemic outcomes and persistence among patients with type 2 diabetes mellitus in a large managed care plan: a claims database analysis. Diabetes Technol Ther. 2014;16:567–73.