ORIGINAL RESEARCH



Turkish Insulin Injection Technique Study: Population Characteristics of Turkish Patients with Diabetes Who Inject Insulin and Details of Their Injection Practices as Assessed by Survey Questionnaire

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ABSTRACT

Introduction: Over 7 million people in Turkey have diabetes. Of the 1 million who inject insulin little is known of their habits and injection techniques.

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For centers participating in the ITQ Turkey Study Group and their location, see Table 1. For types of insulin used in Turkey, see Table 12).

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Z. O. Siva

Department of Endocrinology, Diabetes and Metabolism, Istanbul University Cerrahpasa School of Medicine, Cerrahpasa Mah. Kocamustafapasa Cad. No:53, Fatih, 34098 Istanbul, Turkey Methods: We conducted an Injection Technique Questionnaire (ITQ) survey throughout Turkey that involved 1376 patients from 56 centers. Turkish values were compared with those from 41 other countries participating in the ITQ, known here as Rest of World (ROW). **Results**: The majority (50.4%) of Turkish insulin users give four injections/ day as opposed to ROW, where only 30.9% do. The abdomen is the most common injection site used by Turkish patients, but they also inject insulin in multiple body sites more often than do patients in ROW. Body mass index values in Turkey were 0.75 units higher than those in ROW as was the mean total daily dose (average daily dose [ADD]) of insulin (54.0 IU in Turkey vs. 47.4 IU

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M. Kulaksizoglu · A. Kaya Faculty of Medicine Department of Endocrinology and Metabolism, Necmettin Erbakan University Meram, Yunus Emre Mah. Beysehir Cad. No:281, Meram, 42080 Konya, Turkey in ROW). Mean glycated hemoglobin (HbA1c) in Turkey was 9.1%, which is higher than in ROW and possibly related to the higher BMI and ADD. Turkish patients use insulin analogs (short and long-acting) more frequently than do patients in ROW. The shortest pen needles (4 mm) are used by about one-third of patients in Turkey, but the longer ones (8 mm) are equally common. Needles are reused in Turkey at a rate of 3.4 injections/single needle. However, needle reuse, whether with pens or syringes, is lower in Turkey than ROW, as is the number of times a reused needle is used. More than 75% of used sharps in Turkey go into the rubbish, with nearly 6% having no protection of the tip.

Conclusion: The continued use of 8-mm needles raises the risk of intramuscular injections in Turkish patients. Despite full reimbursement, needle reuse still remains an important issue. More focus needs to be given to dwell times under the skin, reconstitution of cloudy insulant, correct use of skin folds and safe disposal of sharps.

Funding: BD Diabetes Care.

Keywords: Infusions; Injections; Insulin; Lipodystrophy; Lipohypertrophy; Needles; Needlestick; Subcutaneous

Abbreviations

BMI Body mass index
DKA Diabetic ketoacidosis
DM Diabetes mellitus

FIT Forum for injection technique

FITTER Forum for injection technique and

therapy: expert recommendations

C. A. Gürlek

BD Diabetes Care, Ruzgarlibahce Mah. S.Sinan Eroglu Cad. No:6, Akel Is Merkezi A Blok -3. Kat 34805 Kavacik Beykoz, Istanbul, Turkey

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K. W. Strauss (☑) BD Diabetes Care, POB 13, Erembodegem-Dorp 86, 9320 Erembodegem, Belgium e-mail: kenneth.strauss@bd.com GCP Good clinical practice HbA1c Glycated hemoglobin HCP Health care professional

ID Intradermal IM Intramuscular

ITQ Injection Technique Questionnaire IU International Unit (of insulin)

LH Lipohypertrophy

NPH Neutral protamine hagedorn (also

known as Insulin N)
PD Pharmacodynamics
PK Pharmacokinetics
SC Subcutaneous

SD Standard deviation T1DM Type 1 diabetes T2DM Type 2 diabetes

TDD Total daily dose (of insulin)

INTRODUCTION

According to the 2017 International Diabetes Federation Atlas the prevalence of diabetes is increasing worldwide and that by 2045 Turkey will be among the top ten countries in the world in terms of total number of people with diabetes [1]. The most recent TURDEP II study, which evaluated the prevalence of and risk factors for diabetes in Turkish adults, found that 13.7% of the general population has diabetes [2]. This translates into more than seven million Turks having diabetes, of whom 13.6% are on insulin therapy (more than a million people in total).

The insulin Injection Technique Questionnaire (ITQ) is a survey tool that is written in simple layman's terms which assesses all important aspects of insulin injection, from the choice of injecting device to the disposal of used sharps, and from the essential techniques of injecting to the psychological and social aspects of the experience. The ITQ includes one questionnaire for patients and another for the diabetes healthcare professional caring for them. Both are administered in the healthcare setting during routine patient visits and usually took 30-45 min to complete.

A worldwide insulin ITQ study was conducted from February 2014 to June 2015. This

Table 1 The Insulin Injection Technique Questionnaire Turkey Study Group, 2014-2015

City	Center	Patients
Adana	Çukurova Üniversitesi Tip Fakültesi Balcali Hastanesi	32
Afyon	Afyon Kocatepe Üniversitesi Hastanesi	31
Amasya	Amasya Sabuncuoğlu Şerafettin Eğitim Ve Araştırma Hastanesi	25
Ankara	Ankara Atatürk Eğitim Ve Araştirma Hastanesi	25
Ankara	Dr. Sami Ulus Kadin Doğum, Çocuk Sağliği Ve Hastaliklari Eğitim Ve Araştırma Hastanesi	37
Ankara	Hacettepe Üniversitesi Tıp Fakültesi ErişkiinHastanesi	32
Ankara	Hacettepe Üniversitesi Tıp Fakültesi İhsan Doğramaci Çocuk Hastanesi	21
Ankara	Özel Bayındır Hastanesi	35
Ankara	Dişkapi Yildirim Beyazit Eğitim Ve Araştırma Hastanesi	25
Antalya	Akdeniz Üniversitesi Hastanesi	25
Denizli	Denizli Devlet Hastanesi	29
Antalya	Antalya Eğitim Araştırma Hastanesi	6
Balikesir	Ayvalik Devlet Hastanesi	18
Balikesir	Devlet Hastanesi	25
Bolu	Abant İzzet Baysal Üniversitesi Tip Fakültesi Hastanesi	25
Bursa	Bursa Şevket Yilmaz Eğitim Ve Araştirmahastanesi	19
Bursa	Uludağ Üniversitesi Tip Fakültesi Hastanesi	33
Bursa	Bursa Yenişehir Devlet Hastanesi	25
Çanakkale	Çanakkale Devlet Hastanesi	16
Diyarbakir	Çocuk Hastaliklari Hastanesi	25
Düzce	Atatürk Devlet Hastanesi	31
Edirne	Trakya Üniversitesi Tip Fakültesi Hastanesi	31
Erzurum	Atatürk Üniversitesi Yakutiye Araştırma Hastanesi	7
Eskiş ehir	Acibadem Eskişehir Hastanesi	23
Eskiş ehir	Eskişehir Osmangazi Üniversitesi Tip Fakültesi Hastanesi	26
Giresun	Giresun Devlet Hastanesi	5
İstanbul	Acibadem Hastaneleri	11
İstanbul	İstanbul Kanuni Sultan Süleyman Eğitim Ve Araştırma Hastanesi	6
İstanbul	Marmara Üniversitesi Eğitim Ve Araştırma Hastanesi	25
İstanbul	Bağcilar Eğitim Ve Araştırma Hastanesi	30
İstanbul	İstanbul Üniversitesi Cerrahpaşa Tip Fakültesi Hastanesi	25
İstanbul	Haseki Eğitim Ve Araştırma Hastanesi	30
İstanbul	İstanbul Üniversitesi İstanbul Tip Fakültesi Hastanesi	24

Table 1 continued

City	Center	Patients
İstanbul	Dr. Lütfi Kirdar Kartal Eğitim Ve Araştirma Hastanesi	25
İstanbul	Pendik Kaynarca Semt Polikliniği Diyabet Merkezi	32
İstanbul	Medeniyet Üniversitesi Göztepe Eğitim Ve Araştırma Hastanesi	26
İstanbul	Şişli Hamidiye Etfal Eğitim Ve Araştırma Hastanesi	25
İstanbul	Ümraniye Eğitim Ve Araştırma Hastanesi	28
İzmir	Dokuz Eylül Üniversitesi Tip Fakültesi Hastanesi	26
İzmir	Ege Üniversitesi Tip Fakültesi Hastanesi	31
Kayseri	Erciyes Üniversitesi Tip Fakültesi Hastanesi	25
Kayseri	Kayseri Eğitim Ve Araştırma Hastanesi	36
Kocaeli	Kocaeli Devlet Hastanesi	25
Kocaeli	Kocaeli Üniversitesi Tip Fakültesi Hastanesi	25
Konya	Konya Eğitim Ve Araştırma Hastanesi	25
Konya	Necmettin Erbakan Üniversite Hastanesi Meram Tip Fakültesi	29
Malatya	Malatya Devlet Hastanesi Dahiliye Servisi	7
Mersin	Mersin Devlet Hastanesi	25
Mersin	Mersin Üniversitesi Tip Fakültesi Hastanesi	31
Ordu	Ordu Devlet Hastanesi	30
Samsun	Ondokuz Mayis Üniversitesi Tip Fakültesi Hastanesi	25
Sivas	Cumhuriyet Üniversitesi Tip Fakültesi Hastanesi	36
Sivas	Sivas Numune Hastanesi	26
Tekirdağ	Tekirdağ Devlet Hastanesi	30
Trabzon	Karadeniz Teknik Üniversitesi Tip Fakültesi Farabi Hastanesi	25
Zonguldak	Bülent Ecevit Üniversitesi Uygulama Ve Araştırma Hastanesi	32
TOTAL		1376

survey involved 42 countries and 13,289 patients [3, 4]. Turkey was one of the principal countries which participated, with an input of 1376 patients from 56 centers that represented all of the major regions of the country (Table 1). Of interest to Turkish healthcare providers (HCP), this insulin ITQ evaluated the techniques used by Turkish insulin users when injecting themselves. Little was known on this

subject until the present study. The various language versions of the ITQ questionnaire (including Turkish) are available at www. fitter4diabetes.com. The findings of the worldwide insulin ITQ study forms the basis for the New Insulin Delivery Guidelines which were recently published worldwide [5, 6] and in Turkey. A Turkish national guideline based on the results of this study has recently been

published and distributed to all hospitals and HCP involved in diabetes management, with the endorsement and support of the Turkish Ministry of Health [7].

The study reported here was undertaken to improve our understanding of the key injecting parameters of the estimated one million Turkish diabetic patients who use insulin daily. A correct injection technique is critical to achieving optimal insulin action; of equal importance is the type and dose of insulin used (with the latter usually receiving the most attention from the HCP). Unless insulin is delivered correctly. adjustments of dose and insulin type are unlikely to result in clinical improvements. Therefore, an understanding of exactly how Turkish patients inject insulin is essential to improve guidelines aimed at addressing deficiencies in the management of diabetics, to target training and to implement specific educational tools and approaches. The ITQ was administered with the aim of addressing these parameters in Turkish clinical practice and, in the long term, improving patient outcomes and lowering healthcare costs.

METHODS

The ITQ study methodology has been previously described in publications on the worldwide [3] and Indian [8] results. Similar methods for data collection and analysis were used in Turkey as in these previous studies. This study was conducted according to Good Clinical Practice rules and the Helsinki declaration. No information which could lead to the identification of a participant was made available to the sponsor, and participants were informed that their care would not be affected in any way by their participation in the study. They were not put at risk through their participation in the study nor were they paid to participate. Ethics committee approval was therefore not required, but it was obtained whenever specifically requested by a center and/or by local regulations. All 56 participating centers from 29 cities in Turkey (as in the Rest of World [ROW]) did so willingly and without financial incentive. A total of 1376 Turkish participants with diabetes for whom both patient and nurse forms were filled out were included in the ITQ database. Worldwide as well as country-specific ITQ survey data (including Turkey) are available in an interactive form on Tableau Public Adam Young's Profile website [9]. This database contains all of the raw ITQ data, both for Turkey and for ROW (by individual country), and it allows the user to select and view results for specific parameters or combinations of parameters.

RESULTS

Population Descriptors

In order to ensure we had the most representative sample of Turkish insulin injectors, we took patients 'as is', meaning if they injected insulin and had done so for ≥ 6 months, they were included in the survey. Some of these patients had had extensive and best-in-class education and training in their injection technique of choice, while some had had no education or training at all; however, most fell somewhere in between these extremes. This variation in education and training on insulin injection is typical of Turkey and of the ROW.

Overall 82.4% of Turkish participants were adults, 51.3% were female, 33.2% had type 1 diabetes (T1DM) and 66.8% had type 2 diabetes (T2DM). These Turkish patients had had diabetes for a mean of 11.3 years and had been using insulin for an average of 6.9 years. Additional population statistics for the Turkish participants in our study, compared side to side with the ROW data, are given in Table 2. The ROW data are the mean values of the 41 ITO countries combined, excluding data from Turkey, which participated in the worldwide insulin ITQ study. Table 3 shows the breakdown in patient age and identity of the injector, and Table 4 shows the characteristics of Turkish participants compared to ROW data. The majority of Turkish patients used short- and long-acting insulin analogs, and the mean total daily dose (TDD), all insulins included, was 54.0 international units (IU) compared to 47.4 IU in ROW (Table 2). As in ROW, the mean TDD of

Table 2 Population demographics for Turkish and Rest of World patients

Population demographic factors	Mean values for Turkey	Mean ROW values ^a	Turkey (n)	ROW ^a (n)
Age (years)	45.0	52.7	1366	11,859
BMI (kg/m ²)	28.5	26.3	1333	11,473
Mean no. of years with DM	11.3	13.5	1289	7908
Age at diagnosis (years)	33.6	40.6	1331	11,406
Mean no. of years on pills	10.8	8.1	366	6241
Mean no. of years on insulin	6.9	9.0	1235	7007
TDD regular (IU)	35.9	26.1	136	1286
TDD rapid analogs (IU)	36.0	30.9	681	2786
TDD NPH (IU)	29.3	31.7	63	1071
TDD basal analogs (IU)	25.4	28.1	917	3792
TDD premix (IU)	48.7	41.6	343	1453
Overall TDD (IU)	54.0	47.4	1251	6505
HbA1c (%)	9.10	8.35	1298	6365

BMI Body mass index, DM diabetis mellitus, TTD total daily dose (combined total of all insulin used in 1 day in international units (IU), NPH neutral protamine hagedorn (also known as Insulin N), HbA1c glycated hemoglobin ^a ROW (Rest of World) values refer to the mean values of the 41 other ITQ participating countries combined (excluding Turkey)

Table 3 Identity of patient (or healthcare provider) who filled out the Injection Technique Questionnaire (ITQ) for the Turkey insulin ITQ survey (n = 1306) and for the Rest of World ITQ survey (n = 8225)

Patient/HCP identifier	Turkey ITQ (%)	ROW ITQ (%)	Turkey (n)	ROW (n)
Self-injecting adult (≥ 18 years)	82.4	91.8	1076	7551
Self-injecting adolescent (13-17 years)	10.1	4.1	132	337
Self-injecting child (< 13 years)	3.5	2.2	46	180
Parent who gives injections to his/her child	4.0	1.9	52	157

HCP Healthcare provider

Turkish adolescents was nearly the same as that of adults (52.1 IU), while school-age children used an average of only 37.0 IU/day, and children receiving injections from parents used only 24.7 IU/day (Table 4). The TDD was not significantly associated with body mass index (BMI).

Devices and Key Injection Practices

The injection devices used and needle reuse practices in Turkey versus ROW are shown in Table 5. These data clearly show that insulin pens are much more commonly used in Turkey than in ROW and that needle lengths differ significantly between Turkey and ROW. The 4-mm needle is used more commonly in Turkey (35.1%) than ROW (21.8%), while the 5-mm

Table 4 Comparison	of patient	characteristics	in	Turkish	ITQ	survey	(n = 1376)	and	Rest	of World	ITQ	survey
(n = 11,913)	_					•						-

Mean values	Mean values Self-injecting adult (> 18 years old)		Self-injecting adolescent (13–17 years old)		Self-injecting child (< 13 years old)		Child receiving Injections from parent	
	Turkey (n = 1076)	ROW (n = 7530)	Turkey (n = 132)	$ \begin{array}{c} \text{ROW} \\ (n = 336) \end{array} $	Turkey (<i>n</i> = 46)	ROW (n = 180)	Turkey (<i>n</i> = 52)	ROW (n = 156)
Age (years)	51.0	53.7	15.0	15.0	10.8	10.6	7.6	7.6
BMI (kg/m ²)	30.1	27.9	21.8	21.9	18.3	19.0	17.0	17.4
HbA1c (%)	9.20	8.28	8.75	9.29	8.44	8.57	7.26	8.71
TDD (IU)	56.0	48.1	52.1	55.4	37.0	37.8	24.7	22.3
Years on insulin	7.3	9.3	5.8	6.1	4.3	4.3	3.4	3.7
Needle length								
4 mm (%)	28.1	23.3	51.0	38.1	70.7	44.3	76.1	53.7
5 mm (%)	7.9	25.6	17.0	26.6	14.6	23.5	13.0	13.4
6 mm (%)	21.1	21.9	26.0	20.2	12.2	19.1	10.9	14.6
8 mm (%)	42.9	29.3	6.0	15.1	2.4	13.0	0.0	18.3
> 4 mm combined (%)	71.9	76.8	49.0	61.9	29.3	55.6	23.9	46.3

needle is used by < 10% of adult Turkish patients on insulin. However, in Turkey use of the 8-mm needle is still almost as common as that of the 4-mm needle. The average number of times an individual pen needle is used is significantly lower in Turkey (3.42) than in ROW (4.98) (Table 5) Furthermore, among patients still reusing needles, the number of reuse times is lower among Turkish patients than among those in ROW. When asked why they reused, over 66.9% of Turkish patients who answered said that it was 'for convenience'.

Injections/day and Injection Sites

The number of injections per day in both Turkey and ROW is shown in Table 6. More than one-half of Turkish patients inject themselves or others four times per day, which is a far higher percentage than found in ROW. The percentages of Turkish patients giving

themselves or others two or five injections/day are similar to those for ROW, while the percentages giving one or three injections/day are considerably lower.

The recommended injection sites are the abdomen, thigh, arm and buttocks [10–14]. Table 7 shows the sites used by Turkish patients and compares them to those used by patients in ROW, and Table 8 presents percentages for specific injecting zones or combinations of zones for both Turkey and ROW. Note that the combination of zones most commonly used are different for the bottom two rows (shown in italics), with a larger percentage of Turkish patients using a combination of abdomen/thigh/arm sites or all four sites.

Injecting Process

Turkish patients using pens were asked how long they left the needle under the skin after the

Table 5 Comparison of devices used and reuse practice in Turkey (n = 1366) and in Rest of World (n = 11,712)

Devices used and reuse practice	Turkey	ROW
Device (% used)		
Syringe	0.4	10.8
Pen	97.3	83.9
Pump	1.5	2.3
Pen and syringe	0.8	3.0
Needle length used (mm)		
4	35.1	21.8
5	9.6	39.6
6	20.6	17.7
8	34.7	20.8
Needle reuse (%)		
Pen	24.2	59.9
Syringe	6.3	44.5
Number of times pen needle reused		
2	56.8	28.4
3–5	32.3	40.4
6–10	6.8	16.8
> 10	4.0	14.4
Mean times a used pen needle is used	3.42	4.98

plunger had been completely pushed down (dwell time; recommendations suggest 10 s or longer). Compliance with this guideline by Turkish patients was 48.3%, which is much higher than the average compliance rate in ROW (Table 9). The size of the injection sites, skin folds and injection angles for both patients of Turkey and ROW are compared in Table 10.

Turkish patients were asked to make a mock injection while a nurse observed the technique. One of the parameters evaluated was whether the patient lifted a skin fold and, if so, whether it was lifted properly and released correctly. In Turkey, 52.3% of patients were observed to lift a skin fold and, of those who do so, 79.2% do it correctly (with one or two fingers plus the

Table 6 Comparison of the number of injections administered by patients in Turkey (n = 1352) and Rest of World (n = 8165)

Number of Injections/day	Turkey (%)	ROW (%)	Turkey (n)	ROW (n)
1	9.5	17.1	129	1394
2	25.6	26.1	349	2131
3	5.4	14.3	73	1167
4	50.4	30.9	688	2525
5	8.3	7.6	113	622
6	0.6	2.3	8	189
>6	0.3	1.7	4	137

ROW refers to values from the 41 other ITQ participating countries combined (excluding Turkey)

thumb). However, less than half were observed to release the fold appropriately (option three in Table 11). We also found (data not shown) that 45.9% of Turkish patients lift a skin fold when using the 4-mm needle (where a fold is not required), while 52.2% do with the 6-mm needle and 60.5% do so with the 8-mm needle (both needle lengths generally require a skin fold).

Insulins

The breakdown of the major categories of insulin used in Turkey compared to ROW is shown in Table 12. The values show that considerably more patients are using the newer analogs in Turkey, both short or long-acting, than in ROW.

Patients were queried about where they stored their insulin prior to opening it; 81.7% of Turkish patients reported storing unopened insulin in the refrigerator. After opening it, 73.3% of Turkish patients continued to store it in the fridge. Of these, only 51.6% let it stand at room temperature prior to injecting.

Turkish patients using cloudy insulin (NPH, N or pre-mixed insulin) were asked if they reconstituted the insulin before injecting, and 54.2% said yes. They were then asked how many times they rolled or tipped their vial or

Table 7 Comparison of injection sites used by Turkish insulin injectors to those used by Rest of World

Injection site used	Turkey (%) ^a	ROW (%) ^a	Turkey (n)	ROW (n)
Abdomen	86.5	91.3	1158	10,449
Thigh	80.1	41.9	1072	4802
Buttocks	20.5	13.3	275	1527
Arm	84.2	28.1	1127	3211
Total no. of patients			1376	11,447
Total sites used by these patients			3881	19,989

^a Percentages add to over 100 because most patients use more than one site

Table 8 Comparison of injection sites used (alone or in combination) by Turkish insulin injectors and those used by Rest of World

Injection sites	Turkey		ROW	•
	% ^a	n	% ^a	n
Abdomen alone	6.5	90	46.1	5275
Thigh alone	1.6	22	3.1	350
Arm alone	2.7	37	2.0	227
Abdomen/thigh	6.7	92	17.8	2033
Abdomen/arm	8.4	116	6.4	736
Thigh/arm	6.6	91	2.3	267
Abdomen/thigh/arm	44.8	616	9.0	1032
Abdomen/buttocks/arm	1.2	16	0.9	101
Thigh/buttocks/arm	1.9	26	0.5	55
All 4	16.1	222	6.8	774

Italics emphasize the different combinations

pen to reconstitute the insulin before injecting it (recommendations suggest 20 rolls or tips are necessary to completely remix crystalline

Table 9 Comparison of dwell times after pen injection in Turkish insulin injectors and those of Rest of World

Dwell time	Turkey (%) (n = 1357)	ROW (%) $(n = 7316)$
< 5 s	11.6	19.9
5–10 s	37.1	47.2
> 10 s	48.3	28.9
I'm not aware of how long	2.9	4.1

Table 10 Comparison of size of injection sites, skin folds and injection angle in Turkish insulin injectors and those of Rest of World

Injection sites/skin folds/injection angle	Turkey	ROW
Size of injection area (Abdomen) ^a		
Postcard	11.6	57.9
Playing card	37.1	19.0
Credit card	48.3	15.4
Postage stamp	2.9	7.7
Injection into a skin fold ^b	52.3	65.9
Injection into skin at 90° angle ^c	89.1	83.5

n = 1214 (Turkey); n = 8394 (ROW)

insulin). Table 13 shows that only 13.6% of Turkish patients using cloudy insulins comply with this guideline. Of these, patients, 80.8% tip or roll them only 10 times or less.

Patients were queried about whether they ever skipped injections and, if so, how often and why. In Turkey, 48.8% of patients admitted they skip injections; the frequency of skipping injections is shown in Table 14. The most common reason given was 'I forgot' (49.1%). Patients were also asked if they disinfected the skin before injections, and 28.3% said they did. Only 2.5% of Turkish patients give their injections through clothing.

^a Percentages add to less than 100 because other combinations if sites were reported, but at percentages < 1%

^b n = 1349 (Turkey); n = 6904 (ROW)

 $^{^{}c}$ n = 1358 (Turkey); n = 6950 (ROW)

Table 11 Timing of release of skin fold

When released?	Turkey (%) (n = 708)	% ROW ($n = 4737$)
(1) Once the needle is in the skin	8.5	20.0
(2) Once the insulin is totally injected	44.2	31.9
(3) Once the insulin is injected and the needle is removed from the skin	47.3	48.0

Table 12 Type of insulins used in Turkey and Rest of World

Type of Insulin	lin Percentage of injections in Turkey given with this insulin Percentage of injections in ROW given with this insulin		Turkey (n)	ROW (n)
Short-acting human R or Regular)	5.2	19.8	111	2217
Rapid-acting analogue	33.0	25.5	702	2863
NPH	2.9	9.4	62	1055
Long-acting analogue	43.2	32.6	917	3649
Pre-mix human or analog	15.7	122.7	333	1425
Total injections	100.0	100.0	2125 ^a	11,209 ^b

 $^{^{\}rm a}$ Total number of injections is > 1307 (number of Turkish patients responding) since many were using more than one type of insulin

 Table 13 Number of times cloudy insulin tipped or rolled

 before Injecting

Number of rolls/tips	Turkey (%) $ (n = 396)^{a} $	$ \begin{array}{l} \text{ROW (\%)} \\ (n = 2746)^{\text{a}} \end{array} $
2	4.0	7.8
3	4.8	7.7
4	3.8	5.7
5	14.6	16.4
8	4.5	3.2
10	43.7	33.2
15	5.6	4.2
20	13.6	9.7

 $^{^{\}rm a}$ Percentages add up to <100 because other numbers of rolls/tips were reported, but at percentages of <1%

Table 14 Frequency of skipping injections

Frequency	Turkey (%) (n = 672)	ROW (%) $(n = 4230)$
Often (several times a week)	14.6	7.6
Sometimes (several times a month)	37.1	35.7
Almost never (several times a year)	48.4	56.7

Needlestick Injuries

When asked if there was anyone in their immediate surroundings who might accidentally receive a sharps injury, 10.9% of Turkish patients said yes (Table 15). Over 16% of patients reported a sharps injury had already

^b Total number of injections is > 6506 (number of ROW patients responding) since many were using more than one type of insulin

Table 15 Persons in household at risk for sharps Injury

Who?	Turkey (%) (n = 194)	ROW (%) (n = 1897)
Children	36.1	33.2
Other family members (e.g. spouse)	52.6	47.4
Nurse or other healthcare professional	3.6	5.4
House keeper or rubbish collector	7.7	14.0

occurred to one of these persons. The conditions patients may have which might put others at risk for a blood-borne pathogen are shown in Table 16. Table 17 shows how used sharps are disposed, and Table 18 shows what happens to containers when they are full.

DISCUSSION

Until our ITQ survey little was known about where, when and how Turkish patients use insulin. Our study covered the entire country, with 1376 patients surveyed from 56 centers in 29 cities (Table 1). Our demographic data (Table 2) shows that our patient population is representative of Turkish T1DM and T2DM patients who inject insulin.

We found a HbA1c of 9.1%, which is consistent with the results of the other multicenter studies conducted in Turkey [15, 16] and higher than the mean HbA1c of 8.35% reported for ROW (Table 2). This higher value could be attributable to higher levels of obesity among

Table 17 Disposal habits for used sharps

Where are sharps disposed?	Turkey (%) (n = 1359)	ROW (%) (n = 11,426)
Into a container specially made for used sharps	7.9	22.2
Into a home container such as an empty bottle	13.5	24.2
Into the rubbish with the cap on	70.0	45.5
Into the rubbish without recapping	5.8	7.0
I clip off the needle and it stays in the clipper	2.8	1.1

Turkish diabetics patients as the BMI values were 0.75 units higher in Turkey than in ROW. Most of this difference in BMI value is attributable to the adult patients (BMI of 30.1) vs. 27.9 for ROW), while Turkish children and adolescents had BMI values equivalent to those in ROW (Table 4). Turkish patients use insulin analogs (short and long-acting) more frequently than patients in ROW (Tables 2, 12). The majority of Turkish insulin users give four injections/day, which is higher than the number reported in ROW. Turkish patients inject insulin in multiple body sites, which is also more often than do patients in ROW. The two most popular injection site combinations are the abdomen/thigh/arm and abdomen/thigh/ buttocks/arm (Tables 7, 8). These combinations, both involving the use of thighs and arms, are especially relevant when considering the shallow subcutaneous depth in the limbs with reference to the needle lengths used (Table 5).

Table 16 Risk factors for sharps injury

Reason	Turkey (%) $(n = 236)$	ROW (%) $(n = 2448)$
I don't use devices that prevent injuries to others (safety devices)	18.2	29.4
I don't have appropriate disposal containers for my used sharps	55.5	40.6
Used sharps are sometimes left where others might get stuck	19.1	25.8
I'm positive for hepatitis or another blood-borne illness	7.2	4.2

Table 18 Ultimate disposal of sharps waste

What do you do with the waste?	Turkey (%) (n = 589)	ROW (%) (n = 5594)
Put it into the rubbish	61.5	38.0
Take it to a pharmacist	0.8	14.1
Take it to a doctor's office	0.5	6.9
Take it to a laboratory	0.2	0.4
Take it to the hospital or clinic	14.9	22.9
Take it to a local deposit or collection service	7.3	11.4
None of the above	14.8	6.3

Syringe use has almost disappeared in Turkey; at the present time syringes alone are used by less than half a percent of injectors while another 0.8% use them in combination with pens (Table 5). Thus, in the remainder of this discussion we focus on insulin pen use. The shortest pen needles (4 mm) are used by about one-third of patients in Turkey, but the longer ones (8 mm) are equally common. Our 2015 ITQ revealed that there has been a great change in the size of insulin needles used in Turkey. As recently as 2008, by far the majority (83.5%) of Turkish patients used 8-mm needles. While it is encouraging to see the 'shift to shorts' among Turkish patients, it is still worrying to find such high percentages of patients still using the 8-mm needle (Tables 4, 5). In all, more than half of Turkish patients (55.3%) are still on long pen needles.

A study of a large and heterogeneous population (four ethnic groups) of American adults with diabetes revealed that skin thickness at injection sites differed minimally by BMI (obese patients have equivalent skin thickness to thin and normal-weight ones) [17]. Strollo and Gentile recently summarized the influence of ethnic origin and skin thickness [18] and found that fat thickness (dimensions of the subcutaneous space) varies widely from individual to individual as a function of BMI, gender and injection site. Another recent study confirmed these anatomic findings in Chinese patients [19].

Hirsch at al. [20] showed that the risk of intramuscular (IM) injections with 8-mm needles is considerable in adults. This risk as a function of the length of the needle is shown in Table 19. The risk is especially high in those using the thigh and arm sites as injection sites (see values in italics in Table 19), where as many as one-fourth to one-fifth, respectively, of injections with the 8-mm needle may go into muscle. Many more Turkish patients use these sites for injections than those in ROW, with 80.1% using the thigh and 84.2% using the arm (Table 7). Our survey showed that 42.9% of adult Turkish injectors are still using the 8-mm needle, a figure much higher than the 29.3% in ROW (Table 4). Of these, 60.5% achieve a level of safety from IM injections by using a lifted skin fold, but that still leaves nearly two out of five injectors who do not.

Table 19 Estimated intramuscular injection risk by body site

Needle length	Body sites combined	Thigh	Arm	Abdomen	Buttock
4 mm	0.4%	1.6%	1.0%	0.3%	0.1%
5 mm	1.8%	4.7%	3.1%	1.1%	0.5%
6 mm	5.7%	10.0%	7.0%	2.8%	1.3%
8 mm	15.3%	25.0%	19.5%	9.7%	5.5%
12.7 mm	45.0%	63.0%	55.0%	38.0%	26.9%

Assumption is made that the injection is made straight in at 90°, without a pinch-up Italics indicate the injection sites and needle length associated with high risk Table is adapted from Hirsch et al. [39], with permission

Almost 18% of our survey population was in the pediatric age range (Table 3). The risk of IM injections with the 8-mm needle in children is strikingly high. Lo Presti et al. [21] reported that in children aged less than 7 years, more than four of five injections would go into the muscle when the 8-mm needle was used perpendicularly. For school-age children (7-13 years old) and for adolescents (14-18 years old), two of three injections with the 8-mm needle would go into muscle. These higher than expected percentages of Turkish children in these age groups were found by our survey to be still using needles longer than the recommended 4 mm: 49.0, 29.3 and 23.9% of adolescents, children and those receiving injections from their parents. respectively, used needles longer than 4 mm (Table 4).

Our worldwide ITQ data [3] shows that 4-mm needles are associated with lower TDD, fewer hospitalizations for hypoglycemia, lower needle reuse rates and fewer cases of lipohypertrophy (LH) (all with p < 0.05 by multivariate analysis). In a large, randomized, prospective controlled crossover study of obese subjects taking large insulin doses, with two arms (4 vs. 8 mm and 4 vs. 12.7 mm), the 4-mm needles provided equivalent glycemic control (by HbA1c) as the 8-mm and 12.7-mm needles [22]. No additional skin leakage was seen with the 4-mm needles compared to the other sizes of needles. Furthermore, patients reported less pain with the 4-mm needle.

These results are consistent with those from other comparative studies of 4-, 5- or 6-mm needles [23-30]. Miwa et al. [29] compared 4-mm needles with their 6-mm counterparts and reported equivalent safety and effectiveness results. These authors reported that their Japanese subjects found the 4-mm needle to be less painful than the 6-mm needle as well as simpler and easier to use. Nagai et al. [30] compared 4and 5-mm needles and reported similar results. Hirose et al. [31] conducted pharmacokinetic/ pharmacodynamic (PK/PD) studies and determined bioequivalent maximum concentrations and similar areas under the curve for the 4-, 6and 8-mm needles. A crossover study using the euglycemic clamp measuring PK/PD in both normal-weight and obese, healthy adults showed similar insulin uptake and action when insulin lispro was injected with a 5-mm needle on 1 day and an 8-mm needle on the next day [32].

Needle reuse has been a contentious subject, with financial interests being a confounding issue on both sides of the debate. However, a Spanish study [33] showed an association between LH (which the authors found in 52% of T2DM and 72% of T1DM patients) and the reuse of needles (p < 0.05). There was a clear trend to greater frequency of LH as the number of uses (reuse) of the needle increased. The presence of LH was highest when the needle was used six times or more. Of those who reused needles, 70% had LH (84% in T1DM) [33]. A more recent Chinese study has confirmed these findings [34].

Needle reuse, whether with pens or syringes, is lower in Turkey than in ROW, as is the number of times a reused needle is used (Table 5). When Turkish patients do reuse needles, the principal reason given is not cost as the needles have already ben fully reimbursed, but rather convenience [35].

Pen needles, syringes and lancets used in the treatment of diabetes are the most frequently used sharps in the world. Most of these are employed in the home setting, where their safe disposal after use is of critical public health importance. In Turkey, the ITQ data revealed that many persons are in the immediate surroundings of the person who is injecting/being injected, often children, who might accidentally be injured by the used sharps (Table 15). Appropriate disposal containers are not available to more than half of Turkish patients (Table 16), and conditions favorable to contamination exist even in the home setting; this includes a sero-positive rate for hepatitis and other blood-borne illnesses of 7.2% of patients. by indicated by self-reporting (Table 16). More than 75% of used sharps in Turkey go into the rubbish, with nearly 6% not even having the minimum protection of a cap (Tables 17, 18). This represents a risk for children, home healthcare nurses, maids and household cleaners, rubbish collectors, street animals and others in the community. Furthermore, 10.9% of our survey population reported that a needlestick

injury had already occurred sometime during their years of injecting insulin. Hence, more safety measures, including a wider use of safetyengineered devices, are clearly needed in Turkey.

CONCLUSIONS

In summary, based on our comparison of ITQ data, many of the parameters of injection practice are better in Turkey than in ROW, but we are still far from achieving our goals The continued use of 8-mm needles by approximately one-third of Turkish patients increases the risk during IM injections. Additionally, more focus needs to be given to dwell times under the skin, reconstitution of cloudy insulins, correct use of skin folds and safe disposal of sharps. The Turkish Injection Delivery Guidelines, named the 'Insulin Injection Techniques and Treatment Guideline for Health Care Professionals', are a welcome step in this direction. These should be made available to all patients and professionals involved in insulin therapy in Turkey and should followed by all as a road map to optimal therapy. The authors plan to conduct another ITQ approximately 1 year after these guidelines are published with the aim to assess their impact on Turkish injection practice.

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Prior Publications. This article is another in a series of country-specific analyses of the worldwide ITQ survey results. Two previous publications appeared in an issue of *Diabetes Therapy* in 2017 entitled "Indian Injection Technique Study: Population Characteristics and Injection Practice" [37] and "Indian Injection Technique Study: Injecting Complications, Education, and the Health Care Professional" [38], both in volume 8.

Disclosures. Cansu Aslan is an employee of BD, a manufacturer of injecting devices. Laurence J. Hirsch is an employee of BD, a manufacturer of injecting devices. Kenneth W. Strauss is an employee of BD, a manufacturer of injecting devices. All other authors (Selcuk Dagdelen, Oguzhan Deyneli, Nermin Olgun, Zeynep Osar Siva, Mehmet Sargin, Sükrü Hatun, Mustafa Kulaksizoglu and Ahmet Kaya) have nothing to disclose.

Compliance with Ethics Guidelines. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study. No participant identifying information was made available to the sponsor and participants were informed that their care would not be affected in any way by their participation. They were not put at risk in any way by the study and were not paid to participate. Ethics committee approval was therefore not generally required but was obtained whenever specifically requested by a

center and/or by local regulations. All 56 participating centers from 29 cities in Turkey (as in Rest of World [ROW]) did so willingly and without financial incentive.

Data Availability. Worldwide as well as country-specific ITQ survey data (including Turkey) are available at Tableau Public Adam Young's Profile website (http://tabsoft.co/23V6ofi). This database contains all of the raw ITQ data, both for Turkey and ROW (by individual country), and allows the user to select and view results for specific parameters or combinations of parameters. This site allowed the generation of all datasets used in the current study.

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