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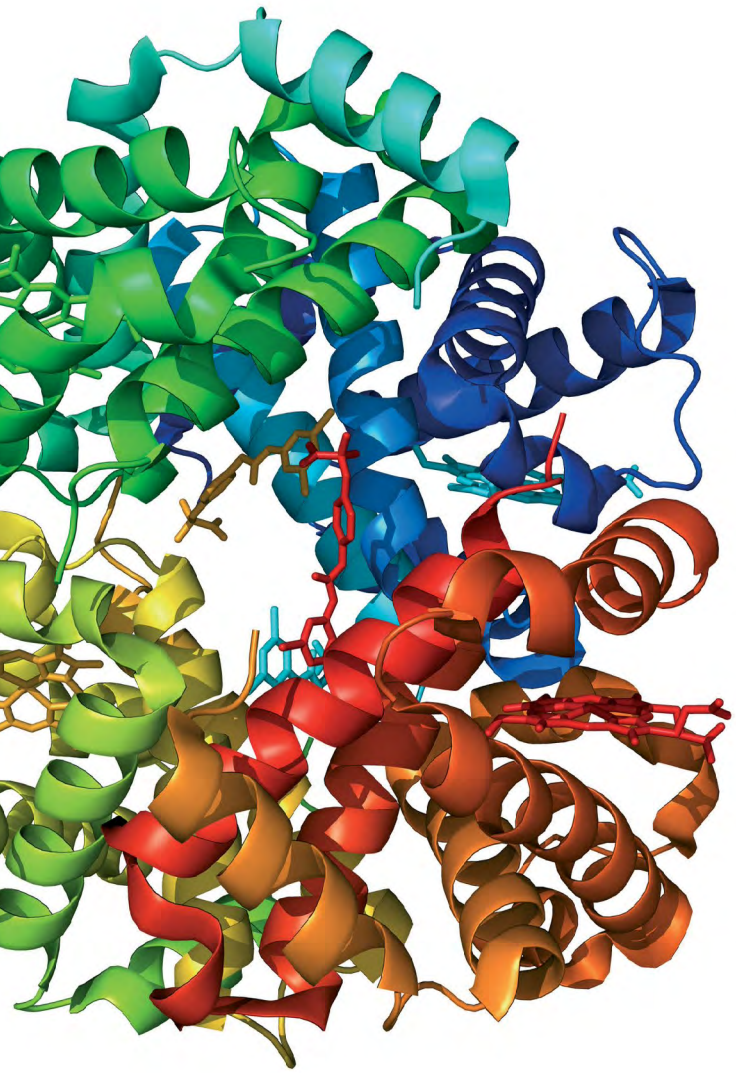

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Za prenumeratę czasopisma „Clinical Diabetology" przysługuje 5 pkt edukacyjnych*

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CLINICAL DIABETOLOGY

JOURNAL OF THE DIABETES POLAND

2019, Vol. 8, No. 3

Contents

The Voice of the Editor-in-Chief

Dear Colleagues,

Just before the publication of this issue of "Clinical Diabetology", the largest diabetes meeting in the world — 79th Scientific Sessions of the American Diabetes Association (ADA) — was held on June 7–11, 2019 in San Francisco, USA. During this congress, all clinical and scientific aspects of diabetes were raised in countless lectures, oral presentations and poster sessions. It is impossible to mention all of them, but I would like to draw your attention to the reports of the greatest interest of the congress participants. These were the reports presenting detailed analysis of the results of large clinical trials, such as PIONEER, REWIND, DECLARE-TIMI 58, CREDENCE, CAROLINA, assessing potential cardio- and nephroprotective effects of new classes of antidiabetic drugs, such as SGLT2 inhibitors or GLP1 analogs, as well as the cardiovascular and renal safety of linagliptin compared with a sulfonylurea. Thanks to these trials we now know for certain that the drugs assessed are safe in terms of cardiovascular and renal function in different patient populations. In addition, the analysis of the results of the CREDENCE study with canagliflozin, for the first time since the proven nephroprotective effect of RAA blockers, ACE inhibitors and sartans, proved that this is another nephroprotective drug for diabetic patients. Soon, we will also learn about the results of the trials assessing kidney function in patients treated with two other SGLT2 inhibitors, dapagliflozin and empagliflozin, which are also expected to confirm the class effect in this respect. This would allow the indications for their use in everyday practice to be extended. In addition, the results of the DECLARE-TIMI 58 trial showed that dapagliflozin therapy is associated with benefits in primary prevention of heart failure in diabetes, a complication that until recently was underestimated and now is considered as one of the major challenges of modern medicine due to the increasing number of affected patients.

It should also be stressed here that this issue is being released in convergence with the next, large and very important scientific meeting of our community — the 20th Scientific Congress of Diabetes Poland that this year was held on May 16–18, in Lublin. During this meeting, apart from the very high scientific level, there was also space for interesting cultural events.

Among papers included in this issue of "Clinical Diabetology", there is a particularly interesting paper by the authors from Egypt who discuss the correlations between microangiopathic complications in type 2 diabetes. Another article that is worth mentioning is the article about the DAWN (Diabetes Attitudes, Wishes and Needs) study. This article does not address the most frequently discussed aspects of organic complications in diabetes but focuses on the mental sphere of patients.

This very issue of "Clinical Diabetology" is special to me because this is my last issue as Editor-in-Chief. Managing "Clinical Diabetology" was a great adventure to me and now I am handing over the helm to the person who guarantees the further development of our journal, and, what I deeply believe, will soon introduce "Clinical Diabetology" into the PubMed and MEDLINE databases and then into a list of journals indexed in the ISI databases, Master Journal List, known in Poland as the Philadelphia List. The next Editor-in-Chief, appointed to this honorable position by the newly elected Main Board of Diabetes Poland, is Professor Leszek Czupryniak.

As usual, I would like to thank all the authors for submitting so many interesting manuscripts and I encourage you to further cooperation with the new Editor-in-Chief of "Clinical Diabetology", a journal that is constantly growing thanks to your support.

Editor-in-Chief

Prof. Janusz Gumprecht

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ORIGINAL ARTICLE
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Correlation of awareness of the disease with glycaemic control and diabetic complications among patients attending a tertiary care hospital

ABSTRACT

Introduction. The awareness level among diabetic patients varies across patient population based on many factors such as differences in the literacy of the study population, socioeconomic status, availability of diabetes education. Hence, it is important to study the same in our set-up to plan appropriate preventive strategies. The present research work attempted to assess the awareness level about diabetes and its complications among diabetic patients attending a tertiary care teaching hospital.

Materials and methods. This is a hospital based, cross-sectional study, done in diabetic patients attending a tertiary care teaching hospital in South India. The awareness level of the patient was assessed using a pretested questionnaire. The questionnaire had 25 questions (knowledge — 18, attitude — 4 and practice — 3) and each correct answer was given a score of 'one' and each wrong answer was given a score of 'zero'. Patients were assessed clinically for the presence of micro and macrovascular complications and basic investigations were carried out. Metabolic control is assessed by HbA_{1c} level.

Results. A total of 150 patients were included in the study. Approx. 52.6% of patients scored between 14 and 18 (sufficient awareness), 6.6% of patients had satisfactory awareness (KAP score 19–20) and 4% of patients had highly satisfactory awareness (KAP score > 20). Only eight patients had a score less than 10 (highly insufficient awareness) and 31.3% had insufficient awareness (KAP score 10–13). A positive correlation between educational qualification and awareness level was observed ($r = 0.495$, $p < 0.001$). Mean awareness score of patients who received diabetes education from physician and dietitian was significantly high when compared to other sources of patient education. Mean awareness scores were lower for those with various diabetic complications. There is a statistically significant negative correlation observed between awareness and HbA_{1c} values ($r = 0.527$, $p < 0.001$).

Conclusion. Majority of the patients had sufficient awareness about the disease and about one-third of the patients had insufficient awareness about diabetes. The awareness level of the patients about the disease had a strong influence on the metabolic control, diabetic complications and also correlated with their educational status. (Clin Diabetol 2019; 8, 3: 143–153)

Key words: awareness, diabetes, KAP score

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Introduction

India being the diabetes capital of the world, mortality and morbidity related to diabetic complications poses a great threat and burden to the economy. Chronic complications are the major outcome of type 2

diabetes mellitus, which reduces the quality of life, incur heavy burden to health care system, and increase diabetic mortality [1, 2]. Diabetes is a lifelong disease and the health care providers have almost no control over the extent to which the patients adhere to the treatment regimen. The appropriate role of the health care providers is to serve as a coach to the patient, who has primary responsibility for delivery of daily health care. Diabetes self-management education has gained importance over the past decade as research has documented the benefits of such interventions in improving glucose control and reducing diabetes related complications. The acquisition of the relevant skills for successful self-management may play a key role in tackling beliefs about health and optimizing metabolic control, risk factors, and quality of life. Hence, comprehensive patient education in diabetics is the corner stone in diabetes management. Diabetes education leads to more informed choices and beneficial changes in behavior which, in turn, improves motivation for self-care and reduces the risk of diabetic complications, thereby reducing the economic cost of diabetes [3]. Even in general population, possessing a good awareness regarding the risk factors for diabetes may help them to take appropriate preventive measures [4]. There are many studies exploring the awareness and its possible associations with metabolic control and complications. However, it is obvious that awareness varies across the patient population. Hence, it is important to study the same in our set-up, to plan appropriate preventive strategies. The present research work attempted to assess the awareness level about diabetes and its complications among patients attending a tertiary care teaching hospital and also to correlate the same with metabolic control and diabetic complications.

Materials and methods

This is a hospital based cross-sectional study, performed among diabetic patients attending a tertiary care teaching hospital in South India. The study was performed after obtaining approval from the institutional ethics committee and the written informed consent of the patients. The participants were selected through convenient sampling, with a sample size of 150 which included both inpatients and outpatients of either gender with age above eighteen years. All consecutive type 2 diabetic patients who visited the hospital during the study period were included. Patients with type 1 diabetes and gestational diabetes were excluded. Demographic details, details of diabetes such as duration, treatment and diabetes education received etc. were collected from the patients. Educational status of the patients was assessed by noting down their educational qualifications. This study was planned to assess their existing awareness on the disease which was assessed using a pretested questionnaire. Questions were made available in vernacular languages according to the patient's preferences. The questionnaire had 25 questions (knowledge — 18, attitude — 4 and practice — 3) and each correct answer was given a score of 'one' and each wrong answer was given a score of 'zero'. The maximum possible scores for knowledge, attitude and practice are 18, 4, and 3 respectively. The total number of correct answers was converted into a KAP score for each patient. The KAP score was classified into five categories and coded as:

- < 10 (≤ 40%): highly insufficient;
- 10–13 (40–52%): insufficient;
- 14–18 (56–72%): sufficient;
- 19–20 (76–80%): satisfactory;
- > 20 (> 80%): highly satisfactory.

Patients were assessed clinically and basic investigations were carried out. Metabolic control is assessed by HbA_{1c} level. Patients were also assessed for the presence of micro and macrovascular complications. Presence of peripheral neuropathy was determined by vibration test using 128 Hz tuning fork, monofilament test using 10 g monofilament, ankle reflex and power assessment. Resting tachycardia and postural hypotension were used as the indicators of autonomic neuropathy. The fundoscopic examination was carried out to look for the presence of retinopathy and the presence of macro/microalbuminuria were the indicators of nephropathy. History of coronary heart disease and cerebrovascular accidents, the presence of peripheral vascular disease and absence of peripheral pulse were the indicators of macrovascular diseases.

Statistical analysis

The analysis of the data was performed using SPSS version 11.5. Categorical variables were shown as frequencies/percentages and the continuous variables were presented as mean ± standard deviation. To compare KAP scores, Student t test and one way ANOVA were used. Correlation between two variables was performed by Pearson correlation. P value < 0.05 considered statistically significant.

Results

Table 1 summarizes the demographic characteristics of the patients. Majority of the patients were in the age group of 51–60 years (36.7%) and 61–70 years (30%). Prevalence of smoking was seen in 32 (21.3%) patients and the alcohol consumption was seen in 18 (12%) patients. All these patients who consumed alco-

Table 1. Demographic characteristics of the patients

Variables	Values
Age (years), mean ± SD	58.05 ± 10.20
Gender, n (%)	
Male	81 (54)
Female	69 (46)
Body mass index [kg/m^2], n (%)	
< 18	3 (2)
18–23	71 (47.3)
23–30	70 (46.7)
> 30	6 (4)
Duration of diabetes (years) mean ± SD	8.83 ±.5.85
Educational status, n (%)	
Illiterate	7 (4.7)
Primary school	14 (9.3)
High school	28 (18.7)
Pre-degree	37 (24.7)
Graduation	56 (37.3)
Post-graduate	5 (3.3)
Professional	3 (2)
Occupation, n (%)	
Unemployed	7 (4.7)
House wife	50 (33.3)
Daily wages	15 (10)
Service	74 (49)
Professional	4 (2.7)
Family history of diabetes, n (%)	
Yes	96 (64)
No	54 (36)
Hypertension, n (%)	
Yes	69 (46)
No	81 (54)

hol and smoking were males. Majority of the patients had the duration of diabetes between 5–10 years (50%) and 26% of patients had the duration diabetes of 11–20 years. Only 15.3% of patients were eating a diet which was rich in vegetables, avoiding sugars and fats. More than one-fourth (26.7%) of the patients were leading a sedentary life, but the majority were doing moderate exercise (38%). Majority of the patients (46%) were using both insulin and oral antidiabetic agents and 28% were on oral antidiabetic drugs and the rest were on insulin only. Adherence to the treatment regimen was reported by 86% of patients.

Table 2 shows the metabolic control (as assessed by HbA_{1c} level) and diabetic complications seen in the patients. Around 16% of patient had a good control

Table 2. Metabolic control (HbA_{1c} level) and complications of diabetes

Variables	Values
HbA_{1c} (%), n (%)	
< 6.5	24 (16)
6.5–8	40 (26.7)
8.1–10	42 (28)
> 10	44 (29.3)
Diabetic complications, n (%)	
Peripheral neuropathy	95 (63.3)
Autonomic neuropathy	35 (23.3)
Retinopathy	67 (44.7)
Nephropathy	59 (39.3)
Peripheral vascular disease	31 (20.07)
Coronary heart disease	16(10.2)
Cerebrovascular accident	5 (3.3)

Table 3. Distribution of scores for knowledge, attitude and practices among patients

Attribute	Score category	Number of patients n (%)
Knowledge	5–7	17 (11.3)
	8–10	45 (30)
	11–13	65 (43.3)
	14–16	22 (14.6)
	> 16	1 (0.6)
Attitude	1	18 (12)
	2	88 (58.7)
	3	43 (28.7)
	4	1 (0.7)
Practices	1	69 (46)
	2	67 (44.7)
	3	14 (9.3)
KAP score	< 10 (< 40%)	8 (3.3)
	10–13 (40–52%)	47 (31.3)
	14–18 (56–72%)	79 (52.6)
	19–20 (76–80%)	10 (6.6)
	> 20 (> 80%)	6 (4)

with HbA_{1c} less than 6%. Peripheral neuropathy is the most common complication (63.3%), followed by retinopathy (44.7%) and nephropathy (39.3%).

Table 3 shows the distribution of scores for knowledge, attitude and practices among the study population. The lowest KAP score for awareness was 7 and the highest score was 22. Around 52.6% of patients scored between 14 and 18 (sufficient awareness), 6.6% of patients had satisfactory awareness (KAP score 19–20)

Table 4. Correlation between educational status and awareness level

Educational status	No of patients	KAP score (mean ± SD)	Correlation coefficient	p value
Illiterate	7	11.3 ± 3.6	0.495	< 0.001
Primary school	14	10.86 ± 2.25		
High school	28	13.86 ± 3.01		
Pre degree	37	15.43 ± 2.85		
Graduate	56	15.38 ± 2.97		
Post-graduate	5	18.60 ± 1.34		
Professional	3	19.33 ± 1.15		

Pearson correlation

Table 5. Correlation between metabolic control (HbA_{1c}) and educational status

Educational status	No of patients	HbA_{1c} (mean ± SD)	Correlation coefficient	p value
Illiterate	7	8.64 ± 1.84	0.003	0.97
Primary school	14	10.24 ± 2.52		
High school	28	8.91 ± 1.94		
Pre degree	37	8.61 ± 2.09		
Graduate	56	8.73 ± 1.95		
Post-graduate	5	5.8 ± 0.37		
Professional	3	10.20 ± 1.40		

Pearson correlation

Table 6. Correlation between source of diabetes education and awareness level

Source of diabetes education	No of patients (%)	KAP score (mean ± SD)	p value
Nil	40 (26.7)	11.42 ± 2.36	< 0.001
Physician	60 (40)	15.27 ± 2.36	
Dietitian	3 (2)	10.67 ± 0.58	
Nurse	7 (4.7)	14.43 ± 1.81	
Advertisement	5 (3.3)	12.8 ± 3.27	
Physician and dietitian	35 (23.3)	18.09 ± 2.0	

ANOVA

and 4% of patients had highly satisfactory awareness (KAP score > 20). Only 8 patients had a score less than 10 (highly insufficient awareness) and 31.3% had insufficient awareness (KAP score 10–13).

Table 4 shows the correlation between educational status and awareness level. A positive correlation between educational qualification and awareness level was observed and it was statistically significant ($r = 0.495$, $p < 0.001$).

Table 5 shows that correlation between metabolic control (HbA_{1c}) and educational status of patients. There was no association between metabolic control and educational status.

Table 6 shows the correlation between the source of diabetes education and awareness level. More than one-fourth (26.7%) of patients did not receive any diabetes education. Around 40% of the patients received education from their treating physicians while 23.3% had both physician and dietitian to advise them. Remaining 3.35 of patients relied on advertisements to obtain information on diabetes. Mean awareness score of patients who received diabetes education from physician and dietitian was significantly high (18.09 ± 2.0) when compared to other groups ($p < 0.001$). Patients who received diabetes education from physicians also had comparatively higher value of awareness score with a mean score of 15.27.

Table 7 shows the correlation of awareness level and presence of complications. Mean awareness scores were lower for those with different types of complications. However, this difference is statistically significant in case of peripheral neuropathy, autonomic neuropa-

Table 7. Correlation between awareness level and presence of diabetic complications

Complications	No of patients	KAP score (mean ± SD)	p value
Peripheral neuropathy			
Yes	95	13.94 ± 3.39	0.001
No	55	15.89 ± 2.90	
Autonomic neuropathy			
Yes	35	13.06 ± 3.52	0.001
No	115	15.18 ± 3.14	
Retinopathy			
Yes	67	13.4 ± 3.37	< 0.001
No	83	15.65 ± 3.01	
Nephropathy			
Yes	59	13.71 ± 3.09	0.004
No	91	15.32 ± 3.36	
Peripheral vascular disease			
Yes	31	13.32 ± 4.0	0.01
No	119	15.04 ± 3.07	
Coronary artery disease			
Yes	16	14.13 ± 5.04	0.48
No	134	14.75 ± 3.10	
Cerebrovascular accident			
Yes	5	11.40 ± 1.34	0.03
No	145	14.80 ± 3.33	

Student t test

thy, retinopathy, nephropathy and cerebrovascular accident. The difference was not statistically significant for coronary artery disease.

Metabolic control was assessed using HbA_{1c} values and compared with the awareness level (KAP scores). There is a statistically significant negative correlation observed between awareness and HbA_{1c} values ($r = -0.527$, $p < 0.001$). Individually, knowledge, attitude and practice also have a statistically negative correlation with HbA_{1c}.

Discussion

The present study was conducted to assess the correlation of awareness of diabetes with the glycaemic control and diabetic complications among type 2 diabetic patients. Our study has shown a statistically significant positive correlation between the educational level of the patient and their awareness level about diabetes. Similar to our findings, Caliskan et al. and Yun et al. also reported that awareness among diabetics is mainly determined by their education levels [5, 6]. In our study population, only 4% were illiterates, 28% had at least high school education and 68% had a formal education level of more than high school. This represents a population of high literacy level when compared to other studies from India like Muninarayana et al. [7] with 43% illiterates reporting a formal education of more than high school. This may be due to the fact that our set up is a tertiary care centre with a paid service wherein most of the patients belong to the high socioeconomic strata.

We were not able to demonstrate a statistically significant correlation with educational level and metabolic control as well as between educational level and the prevalence of diabetic complications. This may be due to the fact that ours is a hospital based study which included even in-patients also and hence, most of the patients likely to have one or more diabetes related complications.

The common perception about dietary modification in diabetes in our study population was to avoid sugars, with 95% of patients avoiding sugar in their diet, of which, 39% of patients also claimed to avoiding fatty foods. A well-balanced diet containing vegetables and fruits, avoiding fats and sugars was taken by only 15% of patients. In a study conducted by Muninarayana et al., 93.5% participants avoided sweets and 87% avoided both sweets and fatty food [7]. Where as in a study done by Badaruddin et al. 54% totally avoided sugars in their diet and 47% considered fruits and vegetables important in their diet [8]. This shows the inadequacy of knowledge about self-care practices and

lifestyle modification, even among patients attending a tertiary care centre.

In the present study, only 38% of patients were engaged in moderate exercise. In a study done at Chandigarh by Kaur et al., only 24% of patients were performing a moderate amount of exercises [9]. Although the importance of exercise in the management of diabetes is often emphasized, the proportion of patients following a strict regimen of at least 30-minute walk for a minimum of 5 days a week was very less in our study. As this is a hospital based study, the participants may be representing a subset with complications of diabetes who were not able to follow a strict exercise regimen.

Analysis of KAP score among our patients showed that the lowest score was 7 and the highest score was 22. Only 6% had a score of more than 20 and 15% had a score of less than 10. 52% of patients scored between 14 and 18. Thus, nearly 35% of patients had insufficient awareness about their disease. Mean awareness score among our patients was 14.69 ± 3.34. Individually, the mean score for knowledge, attitude and practice were 10.8 ± 2.53, 2.18 ± 0.64 and 1.63 ± 0.65 respectively. In a study done by Upadhyay et al. in Nepal, which used a similar type of questionnaire, overall mean score (KAP) of patients was 7.78 ± 3.8, knowledge score was 4.9 ± 3.34, attitude 2.03 ± 0.95 and practice score was 0.84 ± 0.76, which was very low compared to our study [10]. Sabri et al. also used a similar type of questionnaire and demonstrated a mean KAP score as 18 ± 2 among urban patients and 13 ± 2 among rural diabetic patients [11]. The study done by Schillinger et al. used abbreviated s-TOFHILA score to assess the health literacy [12]. They showed mean KAP score as 21. Inadequate health literacy was seen in 38% of patients and 13% had marginal health literacy. The difference in findings between various studies may be due to the differences in the literacy of the study population, socioeconomic status, availability of diabetes education etc.

Though there was a positive correlation between awareness level and adherence to treatment, it was not statistically significant. This could be due to the small number patients who are non-adherent to treatment. We found a statistically significant negative correlation between awareness level and HbA_{1c}. Schillinger et al also reported a significant correlation between health literacy and diabetes control as indicated by HbA_{1c} level [12].

Among our study population, the majority of patients had peripheral neuropathy (63.3%), 44.7 % had retinopathy, 39.3% had nephropathy, 23.3% had autonomic neuropathy and 20.07% had peripheral vascular disease. Coronary artery disease was seen in 10.7% of patients and 3.3% had cerebrovascular accidents. Agrawal et al. reported the prevalence of complications among 11,157 diabetic patients, wherein retinopathy was seen in 32.5%, nephropathy in 30.2%, peripheral neuropathy in 26.8%, coronary heart disease in 25.8% and peripheral vascular disease in 28% of the patients [13]. Rani et al. showed the prevalence of diabetic retinopathy as 18% in the rural areas and 17% in the urban areas. The prevalence of referable retinopathy was 6.8% in rural areas and 4.6% in urban areas [14].

Unnikrishnan et al., showed the prevalence of microalbuminuria in diabetics as 26.9% which was comparable to our value (21%) [15]. Prevalence of coronary artery disease among diabetics as shown by Agrawal et al. was 25.8% which is very high compared to our study [13]. This may be due to the fact that our data for cardiovascular complication was purely based on patients history alone. Our study has shown a statistically significant negative correlation between awareness level and diabetic complications. Schillinger et al. showed a statistically significant association of awareness level with retinopathy and cerebrovascular accident [12]. They have found a negative correlation with regard to other diabetic complications. This difference, when compared to our study could be due to the fact that they had taken into consideration only the self-reported complications.

There were some limitations in the present study. Being a hospital based research, the study population included patients attending a tertiary care hospital and hence their awareness status may not reflect the awareness of general population in the community. Also, the complications rate in our patient population was higher, as many of the patients were referred from primary/secondary care centers. Research at the community level will put more light on the level of awareness in diabetic patient population.

To conclude, educational qualification of the patients has a significant influence on their awareness about diabetes. Majority of the patients had sufficient awareness about the disease and about one-third of the patients had insufficient awareness about diabetes. The patients with higher level of awareness about the disease had better glycaemic control. Both microvascular and macrovascular complications have shown association with the awareness level. The awareness level was better when the patient received diabetes education from physician and dietitian. A common perception about diet is to avoid sugars and very few patients are implementing balanced diet.

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Questionnaire to assess the awareness of the disease with glycaemic control and diabetic complications among diabetic patients

Questions of assessing Knowledge about diabetes (18 questions)

1. Diabetes is a disease in which the body contains:
   a) Higher level of sugar in the blood than normal
   b) Lower level of sugar in the blood than normal
   c) Either a higher or lower level of sugar in the blood than normal
   d) I don't know

2. The major cause of diabetes is:
   a) Increased availability of insulin in the body
   b) Decreased availability of insulin in the body
   c) I don't know

3. The symptom(s) of diabetes is/are:
   a) Increased frequency of urination
   b) Increased thirst and hunger
   c) Increased tiredness
   d) Slow healing of wounds
   e) All of the above
   f) I don't know

4. Diabetes if not treated can lead to:
   a) Eye problems
   b) Kidney problems
   c) Foot ulcers
   d) Heart problems
   e) All of the above
   f) I don't know

5. The most accurate method of monitoring diabetes is:
   a) Checking blood glucose levels
   b) Checking urine sugar
   c) I don't know

6. In a diabetic patient, a high blood pressure can increase or worsen the risk of:
   a) Heart attack
   b) Stroke
   c) Eye problems
   d) Kidney problems
   e) All of the above
   f) I don't know

7. A diabetic patient should measure his/her blood pressure:
   a) Once a year
   b) Once every six months
   c) Once every two months
   d) Once every month
   e) Need not check at all
   f) I don't know

8. The life style modification(s) required for diabetic patients is/are:
   a) Weight reduction
   b) Stopping smoking
   c) Stopping alcohol intake
   d) All of the above
   e) I don't know

9. A diabetic patient should have his/her eyes checked:
   a) Once a year
   b) Every six months
   c) Need not checked at all

10. Regular urine tests will help in knowing:
    a) The status of liver function
    b) The status of kidney function
    c) The control of diabetes
    d) I don't know

11. The important factors that help in controlling blood sugar are:
    a) A controlled and planned diet
    b) Regular exercise
    c) Medication
    d) All of the above
    e) I don't know

12. A regular exercise regimen will help in:
    a) Increasing blood circulation
    b) Enhancing insulin action
    c) I don't know

13. The well balanced diet includes:
    a) Green leafy vegetables
    b) Fiber rich food
    c) Low sugar, oil and fat
    d) I don't know

14. For proper foot care, a diabetic patient:
    a) Should inspect and wash the feet daily
    b) Should select the best possible footwear
    c) Should walk barefoot inside and outside the house
    d) Should not walk barefoot inside and outside the house

15. Treatment of diabetes comprises of:
    a) Antibiotic therapy
    b) Blood transfusions
    c) Substituting insulin
    d) Taking more bitter vegetables
    e) I don't know

16. Diabetes cannot be treated with:
    a) Insulin
    b) Glibenclamide
    c) Metformin
    d) Antibiotics
    e) I don't know

17. Upon control of diabetes, the medicines:
    a) Can be stopped immediately
    b) Can be stopped after one month
    c) Should be continued life-long
    d) I don't know

18. Hypoglycaemic symptoms can be managed by taking:
    a) Sugar
    b) Medicines
    c) Insulin
    d) I don't know

Questions for assessing attitude about diabetes management (4 questions)

1. Do you exercise daily?
    a) Yes
    b) No

    If yes. How often?
    a) Every day
    b) Once weekly
    c) Once monthly

2. Are you following a controlled and planned diet?
    a) Yes
    b) No

    If yes. How often?
    a) Always
    b) Sometimes or rarely

3. Do you miss taking the doses of your diabetic medications?
    a) Yes
    b) No

    If yes. How often?
    a) Occasionally
    b) Once a week
    c) Once a month

4. Are you aware of blood sugar levels falling below normal when you are taking drugs?
    a) Yes
    b) No

    If yes, did you at any time experience any of the following symptoms?
    a) Weakness
    b) Confusion
    c) Visual disturbances
    d) I don't know

Questions for assessing diabetes self-care practices (3 questions)

1. When was your blood pressure checked last?
   a) One week ago
   b) One month ago
   c) Two months ago
   d) Six months ago
   e) One year ago

2. When did you have your last eye examination?
   a) One month ago
   b) Six months ago
   c) One year ago
   d) Two years ago
   e) Not done at all

3. When was your last urine examination?
   a) One month ago
   b) Six months ago
   c) One year ago
   d) Not done at all

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Relation between early stages of diabetic retinopathy and early stages of diabetic kidney disease in patients with type 2 diabetes in Egypt

ABSTRACT

Background. Diabetes mellitus is a pandemic disease. Type 2 diabetes (T2DM) is the most common type. Diabetic retinopathy (DR) and diabetic kidney disease (DKD) are disabling chronic complications. The relation between both is not yet well-established in T2DM. Egypt is considered one of the top ten countries regarding the prevalence of diabetes that makes diabetes and its complications a major health problem. This encouraged us to conduct this research.

Materials and methods. The study included 79 patients with T2DM divided into two groups according to the presence of retinopathy. Both groups were subdivided according to urinary albumin to creatinine ratio (UACR) into normoalbuminuric and albuminuric subgroups. Retinopathy group was further subdivided according to severity of retinopathy into mild, moderate and severe non-proliferative DR (NPDR). Statistical analysis was done and relation between the severity of retinopathy and UACR was studied.

Results. Patients with retinopathy had significantly higher diabetes duration and UACR than non retinopathy group. Also in subgroups of normoalbuminuria and albuminuria, retinopathy group was significantly higher regarding the same parameters. On subdividing the retinopathy group according to severity, severe NPDR group had significantly higher UACR. The severity of DR was significantly positively correlated with UACR.

Conclusions. The present study identified a significantly positive correlation between early stages of DR and UACR in patients with T2DM in Egypt. Not all cases of DR had DKD especially in early stages and also not all cases of DKD are associated with the presence of DR in T2DM. (Clin Diabetol 2019; 8, 3: 154–160)

Key words: diabetic retinopathy, diabetic kidney disease, type 2 diabetes

Introduction

Diabetes mellitus (DM) is considered a global health problem due to its high prevalence and the high incidence of its chronic complications. It is considered the leading cause of blindness, end stage renal disease (ESRD) and lower limb amputation worldwide [1]. According to recent statistics, the Middle East is considered an emerging hot spot in developing diabetes. Egypt is ranked as one of the top ten countries in the prevalence of diabetes (16.7% of the adult Egyptian population) [2].

Diabetic retinopathy (DR) is one of the major chronic microvascular complications of diabetes.

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Worldwide, the prevalence of DR among people with diabetes is about one third [3]. The duration of diabetes and the level of glycemic control are strongly related to DR. Moreover, chronic hyperglycemia, diabetic kidney disease (DKD), hypertension and dyslipidemia increase the risk of DR [4].

Diabetic kidney disease is another disabling microvascular complication of diabetes. The Diagnosis of DKD is based on the presence of albuminuria and measurement of estimated glomerular filtration rate (eGFR). The pathogenesis of microvascular complications is multifactorial and difficult to understand [5].

The relation between DR and DKD is well-established in type 1 diabetes (T1DM). In type 2 diabetes (T2DM), this association is less clear especially in early stages [6]. The prevalence of DR may reach 63% in patients with T2DM with proteinuria [7]. The presence of DKD in the absence of DR should suspect a nondiabetic renal disease [8]. This study was conducted to study the relation between early stages of DR and early stages of DKD in T2DM in Egypt.

Materials and methods

This cross sectional study was conducted on 79 patients with T2DM recruited from the diabetes outpatient clinic of Alexandria Main University Hospital, Faculty of Medicine, Alexandria University, Alexandria, Egypt. Exclusion criteria were: urinary tract infection, estimated glomerular filtration rate (eGFR) less than 60 ml/min, patients with severely increased urinary albumin excretion (UACR > 300 mg/g), pregnancy and lactation.

This work was done in accordance with the Ethical Principles for Medical Research Involving Human Subjects outlined in the Helsinki Declaration in 1975 (revised in 2008). An approval was obtained from ethics committee of Faculty of Medicine, Alexandria University. Each participant had signed a written informed consent before participating in the study.

Patients were subjected to full history taking including history of smoking, hypertension, dislipidemia and diabetes duration. Complete physical examination was performed including blood pressure measurement, weight, height, body mass index (BMI) that was calculated as body weight [kg] divided by body height squared [m^2] and waist circumference (WC) that was measured from the midpoint between highest point of the iliac crest and lowest point of the costal margin at the end of normal expiration according to the WHO recommendation. Screening for diabetic sensorimotor polyneuropathy was done using: The 10-g monofilament using Semmes-Weinstein 5.07 (10 g) monofilament [9], vibration sense: using a neurothesiometer, the methods were based on the International Working Group on the Diabetic Foot of the IDF [10] and the ankle reflex was also examined.

Fundus examination was done in ophthalmology outpatient clinic of Alexandria Main University Hospital using slit lamp biomicroscope plus fundus lens by the same efficient ophthalmology consultant for all cases.

Eight ml of blood were drawn from the anticubital vein for each patient and a spot of urine sample was taken for complete urine analysis and measurement of urinary albumin to creatinine ratio (UACR). Albuminuria was confirmed by being positive in two of three specimens of UACR collected within a 3 to 6-month period. Each blood sample was divided between K_2-EDTA vacutainer tubes for glycated heamoglobin (HbA_{1c}) and a clot activator serum vacutainer tube for chemistry tests. Routine laboratory tests were done as follows: HbA_{1c}, fasting plasma glucose, blood urea, serum creatinine and measurement of estimated GFR using The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [11], total serum cholesterol, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and serum triglycerides.

Cases were divided according to the presence of diabetic retinopathy into two groups (Table 1): 49 patients without retinopathy and 30 patients with retinopathy (all had nonproliferative diabetic retinopathy (NPDR) divided according to severity into mild (n = 12), moderate (n = 13) and severe NPDR (n = 5) (Table 2).

Each group was further subdivided into two subgroups according to urinary albumin to creatinine ratio (UACR) into normoalbuminuric group (UACR < 30 mg/g) and albuminuric group (with moderately increased urinary albumin excretion UACR 30–300 mg/g [formerly called microalbuminuria]). Within the group without retinopathy, 26 patients had normoalbuminuria and 23 patients had albuminuria while in the retinopathy group, 13 patients had normoalbuminuria and 17 patients had albuminuria. The base line characteristics of each subgroup are presented in Table 3. Correlations between severity of DR and other parameters were measured (Table 4).

Statistical analysis of the data was done using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level.

The used tests were:

1. **Chi-square test:** for categorical variables, to compare between different groups.

2. **Fisher's Exact or Monte Carlo correction:** correction for chi-square when more than 20% of the cells have expected count less than 5.
3. **Student t test:** for normally distributed quantitative variables, to compare between two groups.
4. **F-test (ANOVA):** for normally distributed quantitative variables, to compare between more than two groups, and post hoc test (LSD) for pairwise comparisons.
5. **Kruskal-Wallis test:** for abnormally distributed quantitative variables, to compare between more than two studied groups and post hoc (Dunn's multiple comparisons test) for pairwise comparisons.
6. **Spearman correlation coefficient** was used to identify the correlation between the severity of retinopathy and other parameters.

Results

Among the 79 patients with diabetes included in this study, 49 had no retinopathy and 30 had diabetic retinopathy (all of them had nonprolifirative diabetic retinopathy (NPDR) with different stages). The two groups were comparable regarding different parameters with no statistically significant difference except for few parameters (Table 1).

Regarding duration of diabetes it was highly statistically significantly increased in the retinopathy group than in the no retinopathy group. Regarding peripheral neuropathy assessment (monofilament, ankle reflex and vibration sense (using vibration perception threshold by neurothesiometer)), they were highly significantly different between the 2 groups. Also UACR was highly significantly increased in the retinopathy group than in the group without retinopathy.

Table 1. Comparison between the two studied groups according to different parameters

	No retinopathy (n = 49)	Retinopathy (n = 30)	Test of sig.	P
Gender				
Male	32 (65.3%)	17 (56.7%)	χ^2 = 0.590	0.443
Female	17 (34.7%)	13 (43.3%)		
Age (years)				
Median (min.–max.)	51 (30–65)	52.5 (38–68)	t = 0.902	0.370
Mean ± SD	50.2 ± 8.2	51.9 ± 8		
Diabetes duration (years)				
Median (min.–max.)	3 (0.5–23)	8.5 (1–20)	U = 342.5*	< 0.001*
Mean ± SD	4.3 ± 4	8.9 ± 5.6		
BMI [kg/m^2]				
Median (min.–max.)	30 (20–45)	28.8 (21.5–42)	t = 1.230	0.223
Mean ± SD	30.7 ± 6.1	29.1 ± 4.7		
Waist circumference [cm]				
Median (min.–max.)	100 (71–140)	103 (82–125)	t = 0.756	0.452
Mean ± SD	100 ± 11.9	102 ± 10.9		
Monofilament				
Absent	1 (2%)	4 (13.3%)	χ^2 = 17.417*	< 0.001*
Normal	46 (93.9%)	16 (53.3%)		
Decreased	2 (4.1%)	10 (33.3%)		
Vibration (VPT)				
Median (min.–max.)	15 (6–50)	33.5 (9–100)	U = 318.5*	< 0.001*
Mean ± SD	16.8 ± 9.6	34.1 ± 21.2		
Ankle reflex				
Absent	15 (30.6%)	18 (60%)	χ^2 = 9.709*	0.008*
Normal	29 (59.2%)	7 (23.3%)		
Reinforcement	5 (10.2%)	5 (16.7%)		
FPG [mg/dl]				
Median (min.–max.)	150 (80–390)	156 (102–336)	U = 722.0	0.895
Mean ± SD	164.3 ± 58.9	172.6 ± 66.4		
HbA_{1c} (%)				
Median (min.–max.)	8.1 (5.6–14.5)	9 (6–13.3)	t = 1.300	0.197
Mean ± SD	8.6 ± 1.8	9.2 ± 1.8		

→

Table 1 (cd). Comparison between the two studied groups according to different parameters

	No retinopathy (n = 49)	Retinopathy (n = 30)	Test of sig.	P
Albumin [g/dl]				
Median (min.–max.)	3.7 (2.8–4.8)	3.7 (3–4.9)	t = 0.172	0.864
Mean ± SD	3.7 ± 0.4	3.7 ± 0.4		
Creatinine [mg/dl]				
Median (min.–max.)	0.8 (0.5–1.2)	0.8 (0.5–1.2)	t = 0.688	0.494
Mean ± SD	0.8 ± 0.1	0.8 ± 0.2		
eGFR [EPI] ml/min				
Median (min.–max.)	96 (61–135)	97.8 (61–125.8)	t = 0.178	0.859
Mean ± SD	94.5 ± 17.4	95.2 ± 16.6		
Cholesterol [mg/dl]				
Median (min.–max.)	200 (113–272)	187 (106–285)	t = 1.115	0.268
Mean ± SD	194 ± 39	183.6 ± 42.1		
Triglycerides [mg/dl]				
Median (min.–max.)	162 (46–300)	166.5 (43–336)	t = 0.232	0.818
Mean ± SD	159.5 ± 53.3	163.2 ± 76.9		
HDL-C [mg/dl]				
Median (min.–max.)	45 (24–74)	44.5 (25–55)	t = 1.051	0.297
Mean ± SD	46.5 ± 10	44.2 ± 8.5		
LDL-C [mg/dl]				
Median (min.–max.)	110 (51.8–188)	108 (59–201)	t = 0.414	0.680
Mean ± SD	113 ± 36.2	109.7 ± 32.8		
UACR [mg/g]				
Median (min.–max.)	20 (3.4–91)	91.3 (6–298)	U = 362.5*	< 0.001*
Mean ± SD	31.5 ± 25.9	96.6 ± 84.4		

χ^2 — Chi-square test; t — Student t-test; U — Mann-Whitney test; p — p value for comparing between the studied groups; *statistically significant at $p \leq 0.05$

Table 2. Relation between severity retinopathy and different parameters (n = 30)

	Severity Retinopathy			Test of sig.	p
	Mild NPDR (n = 12)	Moderate NPDR (n = 13)	Severe NPDR (n = 5)		
Diabetes duration (years)					
Median (min.–max.)	6 (1–12)	7 (2–20)	10 (3–20)	H = 2.167	0.338
Mean ± SD	6.7 ± 3.7	9.9 ± 6.6	11.2 ± 6.1		
eGFR EPI [ml/min]					
Median (min.–max.)	93 (63.5–123)	97 (61–125.8)	102 (72–110)	F = 0.222	0.802
Mean ± SD	92.7 ± 17.3	96.6 ± 17.6	97.5 ± 15		
UACR [mg/g]					
Median (min.–max.)	32.1 (6–134)	29.9 (27.3–163.5)	270 (179.5–298)	H = 14.155*	0.001*
Mean ± SD	55.7 ± 47.3	79.2 ± 59.6	240[ab] ± 55.9		

F — F for ANOVA test; H — H for Kruskal-Wallis test. Pairwise comparison bet. each 2 groups was done using post hoc test (Dunn's for multiple comparisons test); p — p value for comparing between different categories; *statistically significant at $p \leq 0.05$; a — significant with mild NPDR; b — significant with moderate NPDR; UACR — urinary albumin to creatinine ratio; NPDR — non-proliferative diabetic retinopathy

Subdividing each group according to UACR into normoalbuminuric group and albuminuric group, the duration of diabetes was significantly higher in both retinopathy subgroups than in both subgroups without retinopathy but not between the albuminuric and normoalbuminuric subgroups within each group (Table 3). Regarding UACR it was significantly higher in the albuminuric group with retinopathy than the 3 other subgroups while there was no statistically significant difference between the 2 normoalbuminuric

Table 3. Comparison between the four studied subgroups according to different parameters

	No retinopathy (n = 49)		Retinopathy (n = 30)		Test of sig.	p
	Normoalbuminuria (n = 26)	Albuminuria (n = 23)	Normoalbuminuria (n = 13)	Albuminuria (n = 17)		
Diabetes duration						
Median (min.–max.)	4 (0.5–23)	2 (0.5–10)	7 (1–20)	10 (1.5–20)	H = 17.646*	0.001*
Mean ± SD	5.2[a] ± 4.8	3.3[a] ± 2.5	8.4[b] ± 5.2	9.2[b] ± 6.1		
Monofilament						
Absent	1 (3.8%)	0 (0%)	2 (15.4%)	2 (11.8%)	χ^2 = 20.217*	< 0.001*
N	25 (96.2%)	21 (91.3%)	8 (61.5%)	8 (47.1%)		
Dec	0 (0%)	2 (8.7%)	3 (23.1%)	7 (41.2%)		
Vibration (VPT)						
Median (min.–max.)	12 (6–40)	16 (6–50)	30 (9–90)	34 (10–100)	H = 20.215*	< 0.001*
Mean ± SD	14.8[c] ± 8.2	19[ac] ± 10.7	31.8[ab] ± 20.7	35.9[b] ± 22.1		
Ankle reflex						
Absent	10 (38.5%)	5 (21.7%)	7 (53.8%)	11 (64.7%)	χ^2 = 13.564*	0.024*
Normal	15 (57.7%)	14 (60.9%)	3 (23.1%)	4 (23.5%)		
Reinforcement	1 (3.8%)	4 (17.4%)	3 (23.1%)	2 (11.8%)		
FPG [mg/dl]						
Median (min.–max.)	150 (89–306)	150 (80–390)	130 (102 –336)	168 (102 –300)	H = 0.725	0.867
Mean ± SD	162.4[b] ± 56.1	166.5[b] ± 63.1	166.2[b] ± 71.9	177.6[b] ± 63.7		
HbA_{1c} (%)						
Median (min.–max.)	7.8 (5.6–12.4)	8.5 (6.5 – 14.5)	9 (7.1–13.3)	9 (6–12.2)	F = 1.254	0.296
Mean ± SD	8.3 ± 1.7	9 ± 2	9.2 ± 1.6	9.2 ± 1.9		
Creatinine [mg/dl]						
Median (min.–max.)	0.8 (0.6–1.1)	0.9 (0.5–1.2)	0.8 (0.5–1)	0.9 (0.5–1.2)	F = 0.850	0.471
Mean ± SD	0.8 ± 0.1	0.9 ± 0.2	0.8 ± 0.2	0.9 ± 0.2		
eGFR EPI [ml/min]						
Median (min.–max.)	96 (61–123)	98 (61–135)	97 (63.5125.8)	98 (61–123)	F = 0.107	0.956
Mean ± SD	93.6 ± 13.8	95.4 ± 21.1	96.6 ± 15.8	94.1 ± 17.7		
UACR [mg/g]						
Median (min.–max.)	9.3 (3.4–20.5)	52 (30.4–91)	27.3 (6 – 29.9)	149 (39.5–298)	H = 67.948*	< 0.001*
Mean ± SD	10.7[c] ± 5.8	55.1[a] ± 18.3	22.5[c] ± 8.2	153.3[b] ± 70.5		

χ^2 — Chi-square test; F — F for ANOVA test; H — H for Kruskal Wallis test; p — p value for comparing between the studied groups; *statistically significant at p ≤ 0.05. Means with common letters are not significant (i.e. means with different letters are significant)

subgroups regarding UACR although the mean value of UACR was higher in the normoalbuminuric group with retinopathy.

Regarding severity of retinopathy (Table 2) the three subgroups were comparable regarding different parameters without statistically significant difference except for UACR that was highly significantly higher in cases of severe NPDR.

On performing correlation between severity of retinopathy and different parameters, it was highly significantly positively correlated with UACR with no significant correlation with other parameters (Table 4, Figure 1).

Table 4. Correlation between severity of retinopathy and different parameters (n = 30)

	Severity retinopathy	
	r_s	p
UACR	0.642*	< 0.001*
eGFR EPI	0.137	0.472
Diabetes duration	0.273	0.144
Systolic blood pressure [mm Hg]	0.097	0.612
Diastolic blood pressure [mm Hg]	–0.034	0.858

r_s — Spearman coefficient; *statistically significant at p ≤ 0.05; UACR — urinary albumin to creatinine ratio; eGFR — estimated glomerular filtration rate

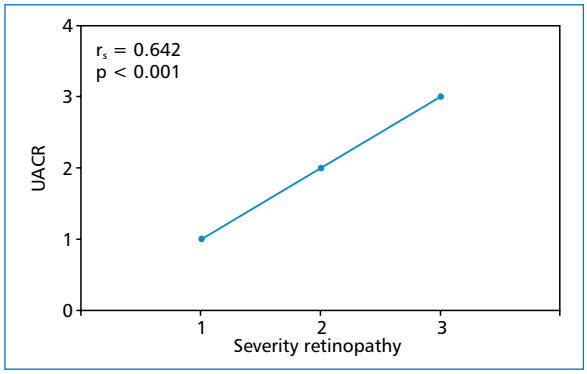

Figure 1. Correlation between severity of retinopathy and UACR (n = 30). Severity of retinopathy: 1 — mild NPDR; 2 — moderate NPDR; 3 — severe NPDR. UACR — urinary albumin to creatinine ratio; NPDR — non-proliferative diabetic retinopathy

Discussion

Although the association between diabetic retinopathy and DKD is well established in T1DM, it is less evident in T2DM especially in early cases of DKD with moderately increased UACR. To the best of our knowledge, no previous studies clearly discussed the relation between early stages of diabetic retinopathy and early stages of DKD in T2DM in Egypt. That's why we conducted the present study.

In the present study, the patients with retinopathy had significantly higher UACR, significantly longer diabetes duration and significantly higher prevalence of peripheral neuropathy. Otherwise, groups and subgroups were comparable regarding other parameters.

Regarding the severity of DR, severe NPDR cases had significantly higher UACR than the other 2 groups. The severity of retinopathy was highly significantly positively correlated with UACR.

Sanyal et al. [12] studied the association between retinopathy and nephropathy in diabetic patients with advanced renal disease. They concluded that retinopathy without nephropathy is common while nephropathy without retinopathy is rare. However, their patients had had advanced renal disease (ESRD) and this explains the discordance between their results and ours as we studied patients with diabetes with early stages of DKD and DR.

A meta-analysis involving 2012 patients from 26 studies found that DR is useful in screening for or diagnosing DKD in patients with T2DM and renal disease, and they recognized proliferative DR as a highly specific indicator for DN [13]. The present study had similar results but regarding early stages of both complications.

In agreement with the results of the present study, Kotlarsky et al. [14] concluded that the degree of renal impairment is proportional to the degree of eye damage. In addition, they statistically proved the chronological relation between retinopathy and DKD; that the renal injury precedes the retinopathy.

Romero-Aroca et al. [15] studied the relationship between DR and DKD in T2DM and concluded that both UACR and eGFR are important risk factors of DR, although UACR has a better association. The present study revealed similar results regarding the relation between DR and UACR but not regarding eGFR, this may be due to the early stages of the disease included in the present study.

Zhang et al. [16] studied the relationship between DR and the DKD progression in patients with T2DM. They concluded that in patients with T2DM and DKD, DR may predict the renal prognosis. They found a significant association between the severity of glomerular lesions and DR.

Although the pathogenesis of all microvascular complications is similar (polyol pathway, protein kinase C pathway and advanced glycation end products) [17], this difference in the time of the beginning of each complication may be a result of genetic factors determining the susceptibility to DR irrespective to DKD. Many studies reported specific genes associated with or protective against DR [18–21]. Further studies are needed to prove the association between DR and DKD in T2DM with the identification of chronological sequence which occurs first.

Conclusions

The present study revealed significant relation between the severity of DR and the degree of albuminuria in early stages of DKD in cases with T2DM. Further studies are needed to confirm this relation and to reveal the chronological sequence of diabetic microvascular complications in T2DM.

Not all cases of DR have DKD especially in early stages and also not all cases of DKD are associated with the presence of DR in T2DM. Genetic predisposition may be present.

The study also concluded that patients with DR have significantly longer diabetes duration than patients without DR.

Conflict of interest

The authors declare no conflict of interest.

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Study of the type 2 diabetic patients' status of care and control in rural areas of Ardabil Province in 2017, Iran

ABSTRACT

Introduction. Diabetes mellitus includes a group of metabolic disorders diagnosed by increased serum glucose concentration. It causes major changes in most systems of the body, which lead to acute and chronic complications of the disease which results in disability, medical costs, and high mortality. This research was conducted to assess type 2 diabetic patients' status of care and control in rural areas of Ardebil province in order to improve the care indicators by presenting results to regional authorities.

Materials and methods. In this cross-sectional descriptive-analytic study, 360 patients identified as type 2 diabetes in rural areas of Ardabil province were selected through cluster sampling and data was collected through a questionnaire by interviewing patients and reviewing their files, and 3 categories of demographic, clinical and socio-economic factors were studied. The data was analyzed by Chi-square and Friedman statistical tests using SPSS software version 20.

Results. According to Chi-square test, there was a significant relationship between the patients' marital status (p = 0.032) and their complications of diabetes (p = 0.10) and the level of care and between the number of patients' family members (p = 0.001) and body mass index (p = 0.006) and the level of control and also, between the use of ordered drug by patient and the level of care and control (p = 0.003). The results of the mean ranking based on the Friedman statistical test showed that the age variable has the highest mean score and the greatest impact on the care and control of the disease and the lowest score and impact was of the nutrition education variable.

Conclusion. This study revealed that in order to control the complications of the disease, lifestyle changes, dietary observation, weight control, ordered drug use and self-care programs are very effective. (Clin Diabetol 2019; 8, 3: 161–166)

Key words: care and control, type 2 diabetes, rural areas

Introduction

Diabetes mellitus includes a group of metabolic disorders that all are diagnosed by increased serum glucose concentration. Different types of the disease are due to various reasons caused by genetic factors, environmental factors and lifestyle [1]. 59 percent of all deaths in the world and 46 percent of the burden of illness are due to non-infectious diseases, and statistics demonstrate an increase in the prevalence of these diseases. The damage of these diseases and their costs for health systems has always been a serious and strong incentive to design and implement prevention programs at various levels [2]. Despite the advances of medical science, not only the spread of the disease is not reduced but also it is increasing every day [3]. Diabetes is an ice burg-like disease that afflicts around 30 million people around the world and its abundance in most adult societies is between 2 to 5 percent [4]. According to the World Health Organization classifi-

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cation, variety of diabetes includes type 1 or insulin dependent, type 2 or non-insulin dependent which is the most common type of diabetes, gestational diabetes and specific types of diabetes [5]. More than 90% of diabetic patients are suffering from type 2 diabetes [6]. Type 2 is a disease with severe difficulties and complications and problems both in terms of the cost of care and financial burden of disability [7]. Due to statistics and global increasing trend, the World Health Organization (WHO) has reported diabetes as a latent epidemic, and since 1993, called all countries in the world to cope with this epidemic. The prevalence of diabetes, especially type 2, has increased significantly in recent decades [1]. Recent studies in Iran reported prevalence of 5.5% and 7.7% of diabetes among adults [8]. Diabetes causes dangerous complications such as atherosclerosis, retinopathy, and nephropathy leading to renal failure, and peripheral neuropathy with the risk of complications of diabetic foot [9]. Progress of complications and the cost of treatment among diabetic patients are mainly due to inappropriate blood glucose control [10]. According to the studies, half of the type 2 diabetic patients are unaware of their disease and are diagnosed totally random. Almost in all health systems, a diabetic patient costs 2 to 4 times more than a non-diabetic person. Its direct costs takes 1.5–2.5% of the total health budget and its indirect costs (due to the cost of hospitalization, the occurrence and exacerbation of chronic complications) are manifold and its subtle costs are unpredictable. On the other hand, while preventing complications of diabetes, many costs and deaths can be reduced by proper care and implementing preventive measures regarding complications of the disease, such as proper control of blood glucose, proper nutrition and exercise among diabetic patients [5].

As a developing country, Iran faces a massive and salient increase in the population of diabetic patients by approximate increase of 195% compared with the current prevalence [8]. In Iran, in 1996, after a comprehensive review, the national program to prevent and control the diabetes was designed to integrate into the health network system. The program was aimed to combat this global problem through primary, secondary and tertiary preventive measures [5]. In addition to drug use and diet observance, among the factors influencing blood glucose control, the role of other variables such as age, sex, economic status, educational level and family factors in controlling blood glucose cannot be ignored. Identification of these factors can be effective in designing necessary interventions to control blood glucose [11]. Among the factors influencing on the control of diabetes, there are patient related factors, such as the socio-economic class and the patient's lifestyle, and the duration of engagement and awareness and attitude toward diabetes and physician related factors such as knowledge, personality and counseling style and facilities of the health center are mentioned. The evidence suggests that controlling blood glucose can reduce the risk of debilitating and even lethal complications of diabetes [12]. One of the most important goals in treatment of diabetic patients is to achieve proper blood glucose control. An important indicator of blood glucose control is glycosylated hemoglobin (HbA_{1c}), and in fact the best target for controlling and treating diabetes is to maintain the level of glycosylated hemoglobin in normal range. Unlike other indicators, this indicator is not affected by daily fluctuations of blood glucose [11].

This research was conducted to investigate the effective factors of management to control of type 2 diabetic patients in rural areas of Ardabil province in order to provide results for the regional authorities to improve care indicators.

Method

This is a descriptive-analytic study that has been conducted to study type 2 diabetic patients' status of care and control in rural areas of Ardebil province. The samples of this study were diabetic patients from rural areas of Ardabil province which the number of them in these areas was 5,608. The sample size was determined 360 by sample estimation formula. In this research, the patients were divided into 10 clusters and clusters were assigned relative to all patients in each city, then, the clusters considered for each city were randomly allocated among the covered villages by simple random sampling and the required information was collected by interviewing and reviewing their files thorough a questionnaire and the results were analyzed by Chi-square and Friedman statistic tests using version 20 of the SPSS software.

Findings

The results of the Chi-square test indicated that there is no significant relationship between gender, age, educational level, occupation, income, hypertension, smoking, vegetable consumption, exercise, nutrition education, training the complications of the disease, and the level of care and control of diabetes, but there is a significant relationship between the marital status of the patients and the complications of diabetes and the level of care, but there is no significant relationship with the level of diabetes control. There is also a significant relationship between the patients' number of family members, body mass index and the family history of diabetes and the diabetes control level, but no

Table 1. Demographic characteristics of the studied samples regarding care and control

Variable	Care	p	Control	p
Gender				
Male	93	NS	28	NS
Female	202		73	
Age				
39–30	19	NS	4	NS
49–40	37		12	
59–50	106		40	
69–60	71		29	
Above 70	62		16	
Marital status				
Single	21	p = 0.03	274	NS
Married	9		92	
Education				
Illiterate	224	NS	77	NS
High school diploma	63		21	
University graduated	8		3	
Occupation				
Housewife	196	NS	70	NS
Farmer	67		23	
Manual worker	13		4	
Unemployed	16		3	
Employee	3		1	
Family size				
Below 5	186	NS	78	p = 0.001
5 to 10	106		23	
10 to 15	3		0	

NS — not significant

significant relationship with the level of care, and finally, there is a significant relationship between the use of ordered drug and the level of diabetes care and control.

The results of Friedman statistical test revealed that there is a relationship between the care and control of diabetes mellitus and the patients' epidemiologic factors, and also the results of mean ranking showed that the highest mean scores of the patients' questionnaire included age, body mass index, marital status, complications of illness, smoking, drug discontinuation, incomes, and consumption of vegetables respectively which had the greatest impact on the control and care of the disease, and the mean of the nutrition education variable has the lowest score (Tables 1–4).

Discussion

In the study by Shiva Heidari et al., the mean glycated hemoglobin of the participants was 9.4 ± 0.9 and most units (57.4%) had no favorable blood glucose control. The results showed a significant relationship between blood glucose control and the marital status ($p < 0.0001$), economic status ($p = 0.003$), duration of diabetes ($p = 0.03$), home glucose test ($p = 0.01$), family structure ($p = 0.01$) and family support ($p < 0.0001$). According to the research, the results of Friedman statistical test showed that age, body mass index, marital status, complications of disease, smoking, drug discontinuation, income, and consumption of vegetables cause the greatest impact on the care and control of the disease, which indicates the consistency of some of these results and the results of the study by Heidari et al. [11].

Gholamreza Sharifirad in a descriptive-analytic study showed that most subjects had one outcome, cardiac complications (22.2%), two outcomes, cardiovascular and ophthalmic complications (12.7%) and three outcomes, cardiac and ophthalmic complications, and feet wound (14%). The majority of subjects (50%) experienced one outcome of diabetes, while 33.6% had two outcomes and 16.4% had three or more. In the present study, there was at least one complication in most patients [13].

Table 2. Clinical characteristics of the studied samples regarding care and control

Variable	Care	p	Control	p
Body mass index				
Thin	12	NS	6	p = 0.006
Normal weight	71		21	
Overweight	131		39	
Obesity	81		35	
Presence of diabetes in family	152	NS	40	p = 0
Hypertension	132	NS	45	NS
Presence of complications				
Ophthalmic	28	p = 0.01	8	NS
Renal	16		8	
Cardiac	29		12	
Late wound healing	39		9	
No complication	183		64	
Ordered drug use	262	NS	93	p = 0
Nutrition education	269	NS	95	NS
Training complications of the disease	276	NS	97	NS
Instructing drug use	274	NS	93	NS

NS — not significant

Table 3. Socioeconomic characteristics of the studied samples regarding care and control

Variable	Care	p	Control	p
Income				
Low	94	NS	30	NS
medium	188		64	
High	13		7	
Smoking	42	NS	11	NS
Vegetable consumption				
Below 100 g	101	NS	32	NS
20–100 g	171		57	
200–400 g	23		12	
Exercise	191	NS	66	NS

NS — not significant

The results of the study by Nader Esmaeilnasab et al., Showed that according to the results of the measurement of hemoglobin glycosylated, 26.8% of the patients had proper control (glycated hemoglobin less than 6) and 73.2% of moderate control (glycated hemoglobin 6 to 8) or weak (glycated hemoglobin above 8). There was no significant relationship between fasting blood glucose and gender, age, body mass index, duration of onset and duration of referral and insulin injection, but there was a significant relationship between fasting blood glucose and patients' education and occupation. However, in the results of the present study, in most patients, glycated hemoglobin levels were above 7, despite the ordered care by practical nurse and the physician and were classified as uncontrolled patients in accordance with the guidelines of the country. Also, contrary to the results of our study, Nader Esmaeilnasab et al., found a significant relationship between body mass index and control of disease [12].

In 2013, Fosse-Edorh et al., in a cross-sectional study showed that type 2 diabetes in women was correlated with age, body mass index and occupation, but was not related to the level of education. In men, type 2 diabetes was not associated with the birth place. According to the present study, the majority of studied patients were female [14].

Table 4. The mean ranking of the impact of patients' variables on the control and management of diabetes based on Friedman test

Rank	Variable	Mean score
1	Age	38.93
2	Body mass index	38.27
3	Marital status	30.75
4	Suffering from complications	30.15
5	Smoking	28.98
6	Discontinue medication	28.73
7	Income	27.27
8	Vegetable consumption	26.37
9	Hypertension	24.07
10	Sex	21.17
11	Family history of diabetes	20.60
12	Family size	19.96
13	Occupation	19.38
14	Exercise	18.16
15	Education	15.18
16	Residence	13.91
17	Regular visits for caring	13.88
18	Instructing drug use	13.85
19	Training of the complications	13.58
20	Nutrition education	12.98

A study by Zeng Bin et al., in 2014, revealed that the most associated factors of self-management of diabetes included five groups: social characteristics, behavioral and psychological characteristics, social support, language barriers, and cultural characteristics. Also, according to the results, factors such as quality of life, glycated hemoglobin, and blood pressure and other cardiovascular risk factors were potentially associated with improving self-management of diabetes. According to the results of the research, there is a significant relationship between the use of the ordered drug by patient and the level of diabetes care and control, which suggests patients' self-management in this regard [15].

The study by Kumar and Sandhya, in 2018, about blood glucose control, lipid profile and blood pressure among type 2 diabetic patients in northern Kerala, India, showed that the high average of blood glucose levels, resulted in a predictable increase of vascular disease, which In turn, affects the quality of health and efficiency. Generally, this study suggests that individual and community economic growth for therapeutic interventions to improve glycemic control can reduce the risk of cardiovascular and fungal diseases. The study showed that there is a need for more drugs, better strategies and more emphasis on glycemic control, to increase the level of control on diabetes which was undesirable in Kerala [16].

The study by Sanjoy K Paul et al., in 2018, found that among type 2 diabetic patients with normal weight, the white European population had a significantly higher incidence of cardiovascular disease than South Asian populations. Overweight and obese diabetic patients from South Asia and the Caribbean region had the same prevalence of cardiovascular disease, while the white European population that was obese had a significant higher prevalence of cardiovascular disease. Among patients of South Asia and South Africa who were obese, the risk of major cardiovascular events was significantly higher among overweight people compared to European white peers during a mean period of 7 years follow up. However, there were similar levels of risk for the white population of Europe and South Asia in normal weight. The risk of developing chronic kidney disease among European and South Asian population with a BMI ≥ 25 was high and the same, while among the African-Caribbean population only overweight patients were at high risk of chronic kidney disease [17].

Conclusion

The mentioned studies, as well as other researches, indicate that factors such as age, body mass index, marital status, economic status, and complications of the disease affects the control of the disease. The results of the distribution of variables by Kolmogorov Smirnov test showed that the distribution of variables was not normal ($p = 0.05$) and also, in order to determine the reliability of the questionnaire, Cronbach's alpha of SPSS software was used, and the alpha value showed that the reliability of the questionnaire was decent ($\alpha = 0.7$). Investigating the results of the chi-square test of the patients' questionnaire showed that there is no significant relationship between the gender, age, education, occupation, income, hypertension, smoking, vegetable consumption, exercise, nutrition education, drug use training, and the level of care and control of diabetes, but there is a significant relationship between the patients' marital status and the complications of diabetes, and the level of care, despite any significant relationship with the level of diabetes control. Also, there is a significant relationship between the number of family members and the body mass index and the diabetes control, but, there is no significant relationship with a level of care and finally, there is a significant relationship between the use of the ordered drug by the patient and the level of diabetes care and control. The results of Friedman statistical test showed that there is relationship between the care and control of diabetes and patients' epidemiologic factors, and also the results of mean ranking, revealed that the highest mean scores

in the patients' questionnaire were age, body mass index, marital status, smoking, The amount of income and consumption of vegetables respectively, which has caused the greatest impact on the control and care of the disease and the mean of the nutrition education variable is the lowest score.

Conflict of interest

The authors affirm that there is no conflict of interest involved in the writing of this paper.

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Psychological well-being and diabetes-related distress in states of type 2 diabetes in the first multi-national Diabetes Attitudes, Wishes and Needs (DAWN) Study

ABSTRACT

Purpose. To examine well-being and diabetes-related distress across several common states differentiated in the course of type 2 diabetes.

Material and methods. Random samples of adults with type 2 diabetes were obtained from multiple countries in the first DAWN (Diabetes Attitudes, Wishes, and Needs) Study (n = 3432). All data were obtained during structured interviews. Criteria for defining states of diabetes included time since diagnosis of diabetes, the timing and nature of anti-hyperglycaemic medication regimens, and the timing and number of complications.

Results. Duration of diabetes closely corresponded to a set of typical states based on the criteria. Using analysis of covariance to control for confounding factors, diabetes-related distress and psychological well-being were significantly ($p < 0.05$) worse for persons with diabetes with more complications and more intense medication regimens. Longer duration of insulin use was significantly associated with more diabetes-related distress. Worse distress and well-being were significantly associated with the accumulation of complications over time, but were more strongly associated with recently diagnosed complications than with more distally diagnosed complications.

Conclusions. Well-being and distress varied over states as defined by the nature and timing of diagnoses and medications. The observed patterns were more complex than a linear model of disease staging would suggest. (Clin Diabetol 2019; 8, 3: 167–175)

Key words: psychological well-being, diabetes, type 2 diabetes, diseases states, diagnosis, complications, treatment regimen

Introduction

It is well-recognized that type 2 diabetes is a progressive disease [1]. It has been proposed that diabetes can be conceptualized in terms of stages, but differentiation of its stages is less clear than in other life-long illness. Stages of overt type 2 diabetes have been identified based on the need for insulin, including not insulin requiring and requiring insulin for control [2, 3]. Similar staging was accepted by the Japan Diabetes Society [4]. Disease staging by Gonnella [5] included complications as a criterion. Because the course of type 2 diabetes may not follow consecutively all described states, our notion of "states" occurring over the course of diabetes de-emphasizes the requirement that there be a fixed order of progression across the states. The majority of cases can be classified into several states

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according to concrete criteria reflecting the progression of diabetes, including duration of diabetes diagnosis, therapeutic regimen — lifestyle intervention, oral antihyperglycemic medications (OAM), and injections — and occurrence of complications.

What is less clear is how the progression of diabetes disease severity manifests itself in the psychological life of people with diabetes — how do the states in the progression of diabetes affect their psychological adjustment to having diabetes? The early work on this topic conceptualized the progression in terms of the predictable crises of diabetes [6], starting with the diagnosis of diabetes through changes in the intensity of medication regimens necessary to control blood glucose levels, and the onset of diabetic complications, hospitalization and the threat of imminent death. This work suggested that these events are associated with changes in psychological adjustment, with the implication that for each event there is a crisis period followed by a period of accommodation.

In this paper we seek to develop a multi-dimensional typology of the states in the course of type 2 diabetes and examine the impact of these states on two indicators of psychological adjustment in people with diabetes — psychological well-being and diabetes-related distress.

Our typology is based on two criteria that define the different states. The first criterion is the *type of event*. We identify three such events:

— diagnosis of diabetes;
— major intensification of glucose lowering treatment (first oral medication, first injected medication);
— diagnosis of a diabetic complication.

The second criterion is the *recency/latency* of a criterion event (diagnosis or major treatment intensification). For the purpose of this paper we define a recent event as one that has occurred within the last year, while events having occurred more than a year ago are not recent.

There is evidence to support an association of psychological adjustment with each of the criteria noted above. Having type 2 diabetes is associated with higher levels of depression [7], and type 2 diabetes is associated with greater severity of depressive symptoms among those newly diagnosed than those previously diagnosed [8]. Among people with type 2 diabetes those treated with insulin have higher levels of depression than those not using insulin [9, 10], although insulin initiation may be associated with a short-term reduction in depression [11, 12]. Complications are associated with greater depression or diabetes-related distress [7, 13–16], with some evidence that depression rises at onset and resolves over time [17, 18].

Another formal property of our typology is the nature of progression across states: 1) Mechanical models define the progression as entirely predictable; the next state to be occupied is entirely determined by the current state, with no reversal in the progression, no skipping of states, etc. 2) Probabilistic models regard the progression as only partially predictable; state reversal and skipping may occur. Hybrid typologies, like the one proposed here, are a combination of the two models. Treatment intensification involves probabilistic progression; the exact progression is not predetermined, but given a current level of treatment intensity some next states are more likely than others. Complications involves a mechanist progression; a person with diabetes must have one complication before they have two complications, and for the most part complications do not reverse themselves (although they may be successfully treated). Recency/latency involves a mechanistic progression in that an event must have been recent before it becomes non-recent, and a non-recent event cannot become recent (although additional events may occur, thereby adding another recent event to existing events, e.g., new complications).

The criteria defined above were used to generate a set of nine states representing a typical progression of diabetes ("typical" in that actual progression of any given patient may not follow the progression hypothesized here). In addition to the logical requirements of mechanical progression, we make two probabilistic assumptions based on empirical considerations:

— for treatment intensification no medication precedes oral medication, and oral medication precedes insulin;
— for the relationship between treatment intensification and complications insulin initiation precedes complications.

Thus, the resulting typical diabetes states (in order from earliest to latest) are:

— new diagnosis of diabetes, no medication, no complications;
— old diagnosis of diabetes, no medication, no complications;
— old diagnosis of diabetes, oral medication, no complications;
— old diagnosis of diabetes, recent initiation of insulin, no complications;
— old diagnosis of diabetes, old initiation of insulin, no complications;
— old diagnosis of diabetes, old initiation of insulin, recent complication only;

— old diagnosis of diabetes, old initiation of insulin, one old complication;
— old diagnosis of diabetes, old initiation of insulin, one old complication and one recent complication;
— old diagnosis of diabetes, old initiation of insulin, two old complications.

Additional states beyond the last one could be postulated but they would involve the replication of the pattern represented by the last several states — onset of a third complication and its transition to an old complication, followed by a fourth cycle of complications, etc. For the purpose of simplification, and given the difficult of obtaining a sample large enough and with a high enough level of complications to be able to examine additional states, we limit ourselves to these nine states.

Using the proposed multi-dimensional typology of disease states, we assess:
— the impact of our criteria on the psychological adjustment of people with diabetes;
— the degree to which the order of the states corresponds to the actual duration of diabetes for the people with diabetes occupying those states (i.e., represent a progression);
— the degree to which these states of diabetes capture variation in the indicators of psychological adjustment.

Material and methods

Study background

The study design of the first Diabetes Attitudes, Wishes and Needs (DAWN) Study, described in detail elsewhere [19, 20], was a cross-sectional survey. In 2001 telephone or face-to-face interviews (in respondents' native language) were conducted in 13 countries representing 11 regions in Asia, Australia, Europe, and North America. There were three independent surveys of random samples of respondents: 5,426 adults who self-identified as having diabetes (~500 per region), 2,750 physicians (~200 primary care physicians and ~50 diabetes specialists per region), and 1,122 nurses (~50 diabetes specialists and 50 generalists per region).

The study was conducted according to the Joint Guidelines on Pharmaceutical Research Practice of the British Healthcare Business Intelligence Alliance and the Association of the British Pharmaceutical Industry. Verbal informed consent was obtained from all respondents and participation was voluntary. Ethical approval of the study protocol and use of these data was obtained from the institutional review board at Loyola University Maryland (the Human Subjects Research Committee).

Study subjects

Inclusion criteria were age 18–80 and self-identified as diagnosed with diabetes for at least six months. Exclusion criteria were severe physical or mental illness. The selection quota was for approximately equal numbers of people with self-reported type 1 and type 2 diabetes mellitus. This paper uses data from all people with diabetes who could be classified as having type 2 diabetes mellitus according to the following criteria: diagnosed at or after age 40, and not treated with insulin both at diagnosis and at the time of the survey.

Measures

Respondent demographics

In addition to country of residence, respondent demographic characteristics included sex, age, marital status (married or not), and residential urbanicity (rural, suburban, small urban, large urban).

Diabetes states

There were three main criteria for defining disease states:
— time since diagnosis of diabetes (up to one year *vs.* more than one year);
— glucose control medication regimen (none, oral only, insulin and oral, insulin only);
— pattern of complications (absence/presence of complications with onset of more/less than one year).

There were two secondary criteria: time since insulin initiation (up to one year *vs.* more than one year) and number of complications. The number of complications was a count of conditions reported as being under treatment from a list including 15 possibilities.

Psychological outcomes

Well-being was assessed by the WHO-5 measure [21] (alpha = 0.83). It has adequate validity both as a screening tool for depression and as an outcome measure in clinical trials [20]. The raw score is calculated by totaling the figures of the five answers. The raw score ranges from 0 to 25, 0 representing worst possible and 25 representing best possible quality of life. To obtain a percentage score ranging from 0 to 100, the raw score is multiplied by 4. A percentage score of 0 represents worst possible, whereas a score of 100 represents best possible well-being. Diabetes-related distress was assessed with a multi-item scale developed for this study and using the following seven items (alpha = 0.79): being stressed about diabetes, burned out from coping with diabetes, tired of complying with medications, afraid diabetes is getting worse, diabetes-related worry about family responsibilities, diabetes-related worry

about financial future, worry about hypoglycemia. Response options (Fully disagree = 0, Mainly disagree = 1, Mainly agree = 2, Fully agree = 3) were multiplied by 100/3 and the score was calculated as the mean of completed items. Scores could range from 0 to 100.

Statistical analysis

The main analyses of well-being and diabetes--related distress used analysis of covariance (ANCOVA) and controlled for all respondent characteristics listed in Table 1 (country, residential urbanicity, age, gender, marital status).

Table 1. Sample profile

Measures	% (N) or M + SD
Country	
Australia	9.2 (317)
France	7.3 (249)
Germany	8.7 (299)
India	8.7 (299)
Japan	10.8 (370)
Netherlands	10.0 (344)
Poland	7.2 (247)
Scandinavia	8.7 (300)
Spain	7.7 (264)
United States	11.2 (386)
United Kingdom	10.4 (357)
Female	54.2 (1861)
Married	72.1 (2473)
Residential urbanicity	
Rural	22.5 (772)
Suburban	20.5 (705)
Small urban	18.2 (626)
Large urban	38.3 (1316)
Age (years)	59.28 ± 11.84
Diabetes diagnosed in last year	6.8 (232)
Duration of diabetes	11.22 ± 9.49
Medications	
None	12.4 (425)
Oral medications only	47.7 (1636)
Insulin	39.9 (1371)
Start insulin in last year	4.5 (155)
Complications	
None	71.2 (2444)
New complications only	6.7 (229)
Old complications only	16.0 (549)
New and old complications	6.1 (210)
Number of complications	0.29 ± 0.63
WHO-5 well-being	54.90 ± 23.54
Diabetes-related distress	33.74 ± 22.95

A single multivariate model was estimated to identify independent (additive) relationships of diabetes-related distress and psychological well-being with each of the three state-defining criteria (duration of diabetes diagnosis, type and duration of medication use, and duration/number of complications). Several ancillary analyses were conducted using multiple regression. Two of these analyses examined whether each of the secondary criteria (duration of insulin use and number of complications) were related to the study outcomes. Two other ancillary analyses examined whether there was (a) a nonlinear relationship between number of complications and study outcomes, and (b) an interaction between number of complications and presence of a new complication.

Effect parameters (unstandardized coefficients) from multiple regression equations were used to estimate distress and well-being for each of nine states defined by combinations of the three criteria. Then these estimated levels of psychological adjustment were compared with actual levels of psychological adjustment for those classified into the states. To validate the temporal ordering of the typical diabetes states the mean duration of diabetes for people with diabetes in those states was examined; the hypothesis is a monotonic increase in duration across the nine states.

Results

Sample profile

The final sample consisted of 3432 adults with type 2 diabetes mellitus (see Table 1). Slightly over half (54%) were female, with a median age of 59, and most (72%) were married. Country samples ranged from 247 to 386, and respondents were mostly from urban locales (57%) [23].

Most respondents (93%) had been diagnosed with diabetes over a year (mean duration of 11 years). Only 12% did not take medication to control blood glucose, and 40% took insulin (5% had started insulin in the last year). A third of respondents (29%) had one or more diabetes complications, with 13% having new complications (less than 1 year duration) and 22% had complications of longer duration. The maximum number of complications was 4, with mean of less than a third of a complication per respondent; the modest level of complications reflects the fact that respondents have a mean age of only 59 and a mean diabetes duration of only 11 years.

Outcomes by state criteria

Results are reported in Table 2. Neither well-being nor diabetes-related distress was significantly associ-

Table 2. Least square means of well-being and diabetes-related distress for disease state markers

Disease state markers	WHO-5 well-being		Diabetes-related distress	
	Mean	Std. error	Mean	Std. error
DM Dx < 1 year past	53.19[a]	1.62	40.08[a]	1.52
DM Dx > 1 year past	50.50[a]	0.68	38.44[a]	0.64
No medication	52.07[a, b]	1.39	33.89[a]	1.31
Oral medication only	52.74[b]	1.01	40.39[b]	0.95
Insulin	50.71[a]	1.06	43.49[c]	0.99
No complications	58.15[c]	0.83	29.75[a]	0.77
New complications only	48.26[a]	1.65	45.30[c]	1.55
Old complications only	53.14[b]	1.23	36.56[b]	1.16
Old and new complications	47.80[a]	1.76	45.42[c]	1.66

Note: Least Square means adjusted for country, age, sex, marital status, residential urbanicity, and all diabetes state markers. Means with the same superscript are not significantly different ($p > 0.05$); means without the same superscript are significantly different [$p < 0.005$ except insulin *vs.* oral medication only for well-being ($p = 0.018$) and new complications only *vs.* old complications only for well-being ($p = 0.006$)]

ated with diagnosis of diabetes within the last year (given the exclusion criteria, this actually refers to diagnosis between 6 and 12 months ago). However, because the direction of association was in opposite directions for the two outcomes we conducted an additional analysis. We first reverse scored well-being so that it was an indicator of general psychological distress, then we performed a MANOVA to assess whether there was an interaction between time of diagnosis (new versus old diagnosis of diabetes) and type of distress (general versus diabetes-related). The result was a statistically significant interaction ($p = 0.008$), with *less* general distress and *more* diabetes-related distress among those with a recent diagnosis of diabetes.

Well-being and diabetes-related distress were associated with the intensity of the glucose lowering medication regimen at different levels ($p = 0.061$ and $p < 0.001$, respectively). The level of well-being was lowest among those taking insulin only and highest among those taking oral medications only, with those taking no medication or both insulin and oral medications intermediate; only the two groups with the most extreme values were significantly different. Diabetes-related distress in those taking insulin was significantly higher than the group taking only oral medication, which was significantly higher than among those not taking glucose lowering medication.

Well-being and diabetes-related distress both differed significantly ($p < 0.001$) across complication subgroups. Well-being was highest among those with no complications and significantly lower among those with only complications of more than a year's duration; those with a complication of recent onset (less than 12 months ago), with or without complications of longer duration, were significantly lower than the other groups. Diabetes-related distress followed a similar pattern — lowest among those with no complications and significantly higher among those with only complications of more than a year's duration; those with complication of recent onset (less than 12 months ago), with or without complications of longer duration, were significantly higher than the other groups.

Although our primary ANCOVA assumed only additive relationships we conducted additional ANCOVA to determine whether there were interactions (two-way or three-way) among the three main criteria. For well-being there were no significant interactions. For diabetes-related distress there was one significant ($p = 0.005$) interaction, between duration of diabetes and type of complications; new complications were associated with a greater elevation in distress among those with recently diagnosed diabetes.

Another ancillary analysis examined whether number of complications of over a year's duration ("old" complications) was a more powerful predictor of well-being and distress than merely the absence/presence of such complications. While the effect of a single old complication was much less than that of a new complication, the effect of two, or three, old complications was greater than that of a new complication (for well-being and diabetes-related distress, respectively). Another ancillary analysis demonstrated that the relationship of psychological adjustment with number of complications was linear rather than nonlinear. We also examined whether there was a significant interaction between number of old complications and the presence of a new complication; for diabetes-related distress the interaction was significant ($p = 0.002$) as the number of old complications had a much stronger impact among those with no new complication (effect

Table 3. Duration of diabetes, well-being, and diabetes-related distress for typical states of diabetes

DM diagnosis	Medications	Complications	N	DM duration	Well-being	Distress
New	None	None	55	0.9	59 (64)	29
Old	None	None	314	7.7	57	24
Old	Oral only	None	1107	8.8	58	30
Old	New insulin	None	80	12.2	56	29
Old	Old insulin	None	745	14.9	57	32
Old	Old insulin	New only	105	17.4	46 (48)	48
Old	Old insulin	One old only	183	18.1	54 (52)	38
Old	Old insulin	One old and new	73	18.7	49 (47)	49
Old	Old insulin	Two old only	39	20.5	40	48

Note: Values for N and duration are actual values for those who fall into the groups representing each state. Values for well-being and distress are least square means obtained from regression models including diagnosis, medications, and complications. Where the actual mean for the group differs from the least square mean by more than 1 point, the actual group mean is shown in parentheses. New diagnosis, new insulin and new complications represent events taking place within one year prior to the study

parameter = 5.63, $p > 0.001$) than among those with a new complication (effect parameter = 2.22, p = ns).

Assessment of typical states of diabetes

Table 3 shows that the 2701 of the 3432 participants (79%) fell into one of the nine typical states (80% of those with two or less complications).

Over half of those not falling into one of the typical states were people who had complications but had not yet started insulin therapy. The hypothesized temporal ordering of the typical diabetes states exactly corresponds to the actual ordering of the states as measured by the mean duration of diabetes for those in each state. Similarly, the estimated levels of well-being and diabetes-related distress based on the model parameters correspond closely to the actual levels, especially in the intermediate states which represent the majority of the data used to generate the estimated effect parameters.

Discussion

The findings of this study indicate that both psychological wellbeing and diabetes-related distress have similar significant independent relationships with several components of our multi-dimensional typology, including the timing (recency/latency) of events, the level of treatment intensity, and the number of complications. Moreover, the ordered set of typical states represented by a combination of these components seems to correspond closely to the actual occurrence of these states in the study sample, as indicated by the duration of diabetes for people occupying those states.

There was evidence to support the three-level categorization of treatment intensity, with each level being significantly different from another level for at least one indicator of psychological adjustment. Greater treatment intensity generally was associated with worse psychological adjustment, although those taking oral medication had slightly (i.e., not significantly) higher well-being than those not taking glucose-lowering medication.

Number of complications had the strongest relationship with psychological adjustment. Each additional complication was associated with a decrement in psychological adjustment about twice the size of the decrement associated with insulin treatment. This finding is consistent with previous research indicating that complications are associated with declines in psychological adjustment. However, recent research suggests that this relationship may be bi-directional, with depression increasing the risk of complications [24, 25] as well as the reverse [24, 26]. There is also evidence to suggest that the association between psychological adjustment and the state-defining events (change in treatment and occurrence of complications) is dependent on the timing of the events. Although time since diabetes diagnosis was not significant in the multivariate analyses based on all patients, there were substantial decrements in both indicators of psychological adjustment for those with longer time since diagnosis when the comparison was limited to those with no other risk factors (no medication and no complications). There was a similar relationship with time since initiation of insulin treatment; this was significant in multivariate analyses that controlled for occurrence of complications. Conversely, psychological adjustment was better for those whose complications were further in the past. Thus, the timing of events does not have a universal association with psychological adjustment; sometimes less recent events have a stronger association than more recent events, and sometimes vice-versa.

The temporal ordering of the typical states identified here was validated by the duration of diabetes

associated with being in those states; the actual duration was entirely consistent with the hypothesized temporal ordering. When comparing estimated and actual levels of psychological adjustment the differences between them were mostly at the extremes and for smaller groups of people with diabetes. Since there were relatively few participants in these groups we must be cautious in making conclusions regarding these groups and the effects giving rise to differences among these groups. This is especially true for two sets of findings. For the comparison of states one and two the actual well-being scores of those with more time since diabetes diagnosis show a greater *worsening* than estimated scores; moreover, these states exhibit one of the few inconsistencies between the findings for well-being and distress, as the latter shows a substantial *improvement* for the same group. The second finding to view with caution is the finding regarding well-being for the onset and duration of a second complication. The estimated data necessarily shows the pattern to be the same for the initial and second complications (well-being *improves* as the complication recedes in time); for the actual data this pattern is replicated for the first complication, but for the second complication well-being *worsens* with time since the event. The pattern for actual diabetes-related distress scores is consistent with the pattern for estimated well-being scores; adjustment *improves* as the second complication recedes in time.

A final comment about the multivariate analyses; they demonstrate few non-additive or non-linear relationships. Number of complications did not exhibit a non-linear relationship with well-being or distress. Of the eight two-way or three-way interactions among the three main criteria for the two outcomes, only one was significant. Perhaps the most interesting departure from simple additive effects is the interaction between having a new complication and number of complications for diabetes-related distress. For patients with recent onset of a complication the number of existing complications is not associated with an increase in distress; this is confirmed by the equal levels of actual distress for those with only a new complication and those with a new complication as well as one old complication.

Study strengths and limitations

The major strength of this study is the availability of a large sample with a diverse population which allows us to compare people with diabetes with various combinations of the characteristics defining the typical states of diabetes. The fundamental limitation of this paper is the cross-sectional nature of the data used to evaluate the proposed multi-dimensional typology of diabetes states. Ideally, we would be able to follow people with diabetes over time to see whether they experience events in the order our typology hypothesizes, and prospectively observe changes in psychological adjustment associated with the transition from one state to another. Absent longitudinal data, our results are suggestive rather than definitive (although this is the first large study to comprehensively examine this issue). Another limitation is that we do not have enough people with diabetes in some states to be able to obtain reliable estimates of the differences among states; this is particularly true for assessment of the impact of newly diagnosed diabetes and recent initiation of insulin (or oral medication) therapy (fortunately, other studies provide evidence regarding the impact of these events on psychological adjustment). In addition, this study used a newly developed measure of diabetes--related distress which has not been fully validated; however, it had good reliability in assessing many of the same diabetes-related feelings (stress, worry, fear, burnout) as other measures of the same construct [14].

Research implications

Additional longitudinal studies are needed to assess the impact of the events studied here on the psychological adjustment to having diabetes. Moving beyond the issues addressed in the present research, we need to understand what factors are associated with variation in the impact of these events on the psychological adjustment of people with diabetes, e.g., outcome expectations, coping strategies, etc. Does the patient's response to events early in the progression of diabetes (e.g., acceptance of diagnoses) alter the trajectory of the progression? This knowledge would permit us to develop a more patient — centered understanding of the progression of diabetes. Research also should determine whether different complications have different consequences for psychological adjustment. Relatedly, do the benefits of treatment intensification in term of preventing complications outweigh any psychological impact of increased treatment burden? What factors in current treatment intensification, if any, contribute to psychological impact and how might new developments in diabetes therapies diminish negative impact? And while our primary analyses simply regarded diabetes-related distress and psychological well-being as independent outcomes, it is likely that they are differentially sensitive to the events studied (e.g., as shown for time since diagnosis of diabetes) and that each affects the others' course of development, a topic that warrants further research. Finally, research should examine whether the progression of states changes over time.

Clinical implications

This study suggests that state transitions in diabetes (treatment intensification and occurrence of complications) are associated with sustained deterioration in psychological adjustment. While the psychological impact of a complication tends to wane somewhat over time, it does not disappear entirely, and it is not clear what processes produce this (partial) remission. Nevertheless, the results of this study suggest that people with diabetes experiencing these potentially traumatic events should be monitored and receive psychological treatment and support as appropriate to restore quality of life [27].

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Practical guidance on insulin injection practice in diabetes self-management in the Indian setting: an expert consensus statement

ABSTRACT

This consensus statement aimed to provide a simple and easily implementable practical educational guideline for healthcare professionals (HCPs) and patients regarding insulin injection practice in diabetes self-management in the Indian setting.

A group of experts analysed published data from guidelines, clinical trials and real world evidence to reach consensus recommendations on optimal insulin injection practices in terms of a) the injection sites (preparation of site of injection, choosing the injection site, site rotation), b) choice of device and storage of insulins, and c) safety precautions, sharp disposal practice and complications.

Findings from Global and Indian arm of 2014-2015 ITQ Study were considered to emphasize a need for improved practice by HCPs covering all the vital topics essential to proper injection habits.

The consensus statement provides a simple and easily implementable practical educational guideline for HCPs and patients to optimize insulin injection practices in accordance with recent advances in device manufacturing, newer research findings, and updated international guidelines as well as widespread concerns about neglected safety precautions such as single-patient use of pens and appropriate sharp disposal practices. (Clin Diabetol 2019; 8, 3: 176–194)

Key words: insulin injection practices, guidelines, injection site, site rotation, storage, disposal, safety, complications

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Introduction

Insulin self-administration is an indispensable component of diabetes management and the importance of guiding patients towards best injection practice has increasingly been recognized in accordance with growing awareness of the critical role of the correct injection technique in achieving optimal control of diabetes [1–7].

Incorrect selection of injection site or delivery device and inappropriate injection technique are considered to modify insulin absorption parameters, leading

to higher amount of insulin use and higher glycated haemoglobin (HbA_{1c}) values as well as to glycaemic variability, unexplained hypoglycaemia and poor long-term outcomes [8–10]. Therefore, correct insulin injection technique and correct choice of injection site and delivery devices have been considered as important as providing optimal (type and dose) insulin therapy in achievement of glycaemic goal in diabetes [5, 11].

Identification of patient, provider, and healthcare system based barriers of initiating and adhering to insulin injection therapy is a critical step toward successful diabetes self-management [5, 12–16]. Optimal delivery and effect of all injectable agents rely on correct injection technique [17], emphasizing the role of enhanced awareness of the good injection practices among healthcare professionals (HCPs) as well as patients [5, 9, 18]. Several guidelines on insulin self-administration are available across the world as well as in India, whereas as consistently reported by several studies across the globe, there is a significant gap between the recommendations of the guidelines and actual insulin injection practice [5, 8, 10, 19–21].

Moreover, recent advances in device manufacturing, newer research findings and updated international guidelines necessitate renewed commitment toward optimizing insulin injection practices [5].

Therefore, this consensus statement aimed to review the current guidelines and available evidence to provide a simple and easily implementable practical educational guideline on insulin injection practice for both HCPs and patients in terms of preparation and selection of injection sites, site rotation, selection of the device, storage of insulins, safety precautions, sharp disposal practice and complications.

Materials and methods

An expert panel consisting of 9 endocrinology specialists from university and state hospitals met to develop consensus on insulin injection practices in insulin-treated patients with diabetes in the Indian setting. The panel critically analysed published data from guidelines, clinical trials and real world evidence and agreed on a series of recommendations supported by scientific evidence and experts' clinical opinion. The proposed consensus planned to provide a simple and easily implementable practical educational guideline for insulin injection practice for both HCPs and patients, in terms of a) the injection sites (preparation of site of injection, choosing the injection site, site rotation), b) choice of device and storage of insulins, and c) safety precautions, sharp disposal practice and complications (Figure 1).

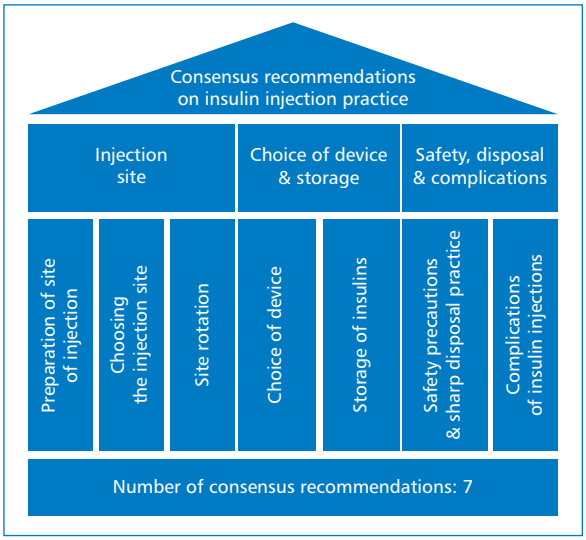

Figure 1. Framework for consensus recommendations

Injection site

Injection site preparation

Current guideline recommendation on injection site preparation indicates the injection site should be clean and dry, and soap and water can therefore be used for unclean sites with no need for disinfection, whereas whenever use of alcohol swabs is needed, the site should be dried before injecting (Table 1) [5, 22–25]. However, disinfection is required in institutional settings such as hospitals and nursing homes, particularly if the site is found to be unclean. If alcohol is used, it must be allowed to dry completely before the injection is given [26].

Consensus statement on injection site preparation

The expert panel recommends that the injection must be given to clean site using clean hands and after inspection and palpation, with use of soap and water when it is necessary to clean the site of injection. Disinfection of the site or the device is not recommended, while if alcohol swabs are used, then the area must be allowed to dry before the injection.

Consensus statement 1. Injection site preparation

- Injection must be given to clean site using clean hands
- Disinfection of the site or the device is not recommended
- Cleaning of the site of injection with soap and water can be done
- If alcohol swabs are used, then the area must be allowed to dry before the injection
- The site should be inspected and palpated by the individual prior to injection

Table 1. Guidelines recommendations on injection site preparation

Guideline	Recommendation
Canadian Forum of Injection techniques (FIT) Recommendations for Best Practice in Injection Technique (2012) [22]	• Site should be clean and free of infection, oedema, bruising or lipohypertrophy • Alcohol swabs may be used, but should be dried before injecting
UK FIT Recommendations for Best Practice in Injection Technique (2015) [23]	• Site inspection and palpation before use • Avoid site with infection, lipohypertrophy, inflammation • Inject in clean site with clean hands • If unclean — use soap and water • Disinfection usually not required; alcohol swabs may be used
American Association of Diabetes Educators (AADE) Strategies for Insulin Injection Therapy in Diabetes Self-Management (2011) [24]	• Site should be clean and dry • Injection through single layer of clothing — clinical judgment
American Diabetes Association (ADA) Insulin Administration Guidelines (2004) [25]	• Wait until topical alcohol (if used) has evaporated completely before injection
Australian Diabetes Educators Association (ADEA) Clinical Guiding Principles for Subcutaneous Injection Technique (2015) [26]	• If site requires cleaning, soap and water is adequate • Alcohol usually not required, increases skin toughening
Indian FIT Recommendations for Best Practice in Injection Technique (2017) [5]	• Clean site properly • Alcohol if used, let it evaporate, as dry surface minimizes pain • Do not use soap-based detergent, chloroxylenol, and cetrimide/chlorhexidine • Inject if site is considered "socially clean"

Choosing the injection site

Rate of insulin absorption depends on multiple factors including insulin related factors (physicochemical properties, excipients, injected volume, concentration, and dosage) and the clinical conditions during injection [orthostatic position, injection site, depth of injection, exercises, local massage, heat exposure, smoking, subcutaneous tissue thickness (SCT) and subcutaneous adipose tissue blood flow] [27–29].

Overall, gender (higher risk in males), BMI (higher risk for < 25 kg/m^2), and injection site (higher risk for thigh) as combined with needle length (higher risk for ≥ 8 mm) and insertion angle (90°), are considered to determine estimates of risk of intramuscular insulin injection [30–32].

Abdomen and buttock are the site of injections associated with fastest and slowest rates of insulin absorption, respectively, while lateral side of the thigh, not proximal to the knee, and upper arm have moderate absorption rates [25, 33–35].

Available guidelines on insulin injection practice consider abdomen as the commonest injection site followed by buttocks and thigh [5, 22, 23] or arm, [24–26] and recommend selection of thigh [5, 23, 24, 26] and buttocks [5, 23, 26] for NPH, abdomen for soluble human insulin, [23, 26] abdomen (morning) and thigh or buttock (evening) for premixed insulins [23], while no specific site selection was considered for insulin analogues [23, 26] (Table 2).

Consensus statement on injection site selection

The expert panel recommends that abdomen (the site with the most consistent absorption) as followed by thighs and buttocks as the appropriate injection sites for adults, whereas the arm is not considered a preferred site for self-injection due to risk of intramuscular administration. Abdomen is considered to be potentially better choice of injection site for soluble human insulin due to characteristic fastest absorption, while thigh and buttocks are considered more appropriate for NPH injection since absorption is slowest from these sites. For rapid or long acting basal insulin analogues and GLP 1agonists, using any of the injection sites is possible as absorption rates do not appear to be site-specific.

Consensus statement 2. Injection site selection

- Abdomen, thighs and buttocks are the recommended injection sites for adults, with abdomen offering most consistent absorption
- The arm is not a preferred site for self-injection due to risk of intramuscular administration
- The thigh and buttocks may be preferred injection sites when using the NPH, since absorption is slowest from these sites
- The abdomen may be the preferred site for soluble human insulin since absorption is fastest there

Table 2. Guideline recommendations on injection site selection

Guideline	Recommendation
Canadian FIT Recommendations for Best Practice in Injection Technique (2012) [22]	• Abdomen, thighs and buttocks are the recommended sites • Abdomen — most consistent absorption • Arm not preferred — difficult access, less SC fat and ↑ risk of IM injection
UK FIT Recommendations for Best Practice in Injection Technique (2015) [23]	• Thigh and buttocks — preferred for NPH • Abdomen preferred — soluble human insulin • Premixed insulin — abdomen (morning) and thigh or buttock (evening) • Insulin analogues — any site
American Association of Diabetes Educators (AADE) Strategies for Insulin Injection Therapy in Diabetes Self-Management (2011) [24]	• Thigh — NPH • Absorption fastest — abdomen > arms > thighs > buttocks
American Diabetes Association (ADA) Insulin Administration Guidelines (2004) [25]	• Upper arm & anterior and lateral aspects of thigh, buttocks, and abdomen (exception — circle with 2-inch radius around the navel)
Australian Diabetes Educators Association (ADEA) Clinical Guiding Principles for Subcutaneous Injection Technique (2015) [26]	• Abdomen — commonest site followed by buttocks, thigh and arm • Abdomen — no injection within 5 cm of umbilicus • Human insulin — abdomen, NPH — thigh and buttocks • Modern analogue insulin — any site • GLP-1 — abdomen, thigh or upper arm
Indian FIT Recommendations for Best Practice in Injection Technique (2017) [5]	• Indian women — discuss site beforehand, so that their sensibilities are not offended • Abdomen preferred • If risk of nocturnal hypoglycaemia with NPH — evening dose into thigh or buttock • Buttock — for infants and toddlers, not preferred in adults

- Rapid-acting and long acting basal insulin analogues may be given at any of the injection sites, as absorption rates do not appear to be site-specific
- When injecting rapid and long acting analogue insulin these should be given in different sites even if given at different times during the day
- Injection site showing signs of oedema, inflammation must be avoided
- GLP 1 agonists are absorbed equally from each of the usual injection sites (abdomen, arm and thigh)

Site rotation

Correct site rotation, defined as always injecting at least 1 cm from a previous injection, has been consistently shown to be the best way to safeguard normal tissue [4, 34, 36, 37].

Worldwide Injection Technique Questionnaire (ITQ) 2014–2015 data reported that patients who rotate correctly tend to have lesser rates for hyperglycaemia, LH, unexplained hypoglycaemia and glucose variability [10, 38]. Incorrect rotation of sites was reported to be associated with 0.57% higher HbA_{1c} levels, 4.7 IU higher total daily insulin dose and higher frequencies of unexpected hypoglycaemia and glucose variability [10, 38].

In a recent study comparing findings from Indian arm *vs.* rest of the world (ROW) in the ITQ 2014–2015 global study, correct site rotation was reported to be applied by similar percentage of patients in the India setting (68.1%) and rest of the world (ROW) (71.0%), whereas much higher percentage of patients in India than in ROW (48.7 *vs.* 18.4%) identified that they were never trained on correct site rotation [36].

Notably, despite its association with lower HBA_{1c} levels, less LH, and more correct injection site rotation; routine inspection of injection sites by the HCP at least once a year was not met by nearly 80% of patients in India as well as in ROW [36, 38].

Implementation of an easy-to-follow rotation scheme from the onset of injection therapy is considered important in acquisition of an appropriate site rotation practice. One scheme with proven effectiveness involves dividing the injection site into quadrants (or halves when using the thighs or buttocks), using one quadrant per week and moving always clockwise. Injections within any quadrant or half should be spaced at least 1 cm from each other in order to avoid repeat tissue trauma. Pump cannula should be placed at least 3 cm away from previous sites. HCPs should verify that the rotation scheme is being followed at each visit and give help and advice where needed (Figure 2, 3) [4, 36, 39–41].

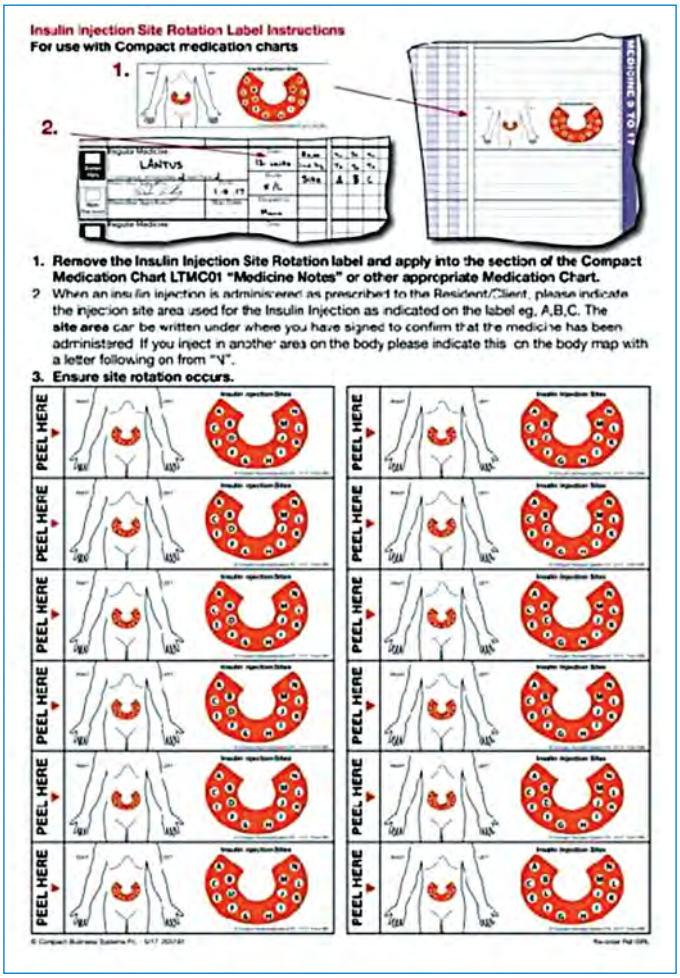

Figure 2. Insulin injection site rotation label

Available guidelines on site rotation recommend teaching a structured and easy-to-follow rotation scheme to patients, and emphasize rotating within one area rather than rotating to a different area and with dividing the injection site into quadrants (abdomen) or halves (buttock or thigh), using 1 quadrant/week and moving clockwise and spacing injections at least 1 cm from each other. Patient education and inspection at each visit is considered essential, while use of site rotation grids is considered useful in patients forgetting injection sites (Table 3) [5, 22–26, 42].

Consensus statement on site rotation

The expert panel recommends teaching an easy-to-follow rotation scheme to patients from the onset of injection therapy, use of a structured rotation plan including one quadrant per week and moving always in the same direction with spacing subsequent injections within the quadrant at 1 cm to avoid repeated trauma and review and emphasize the importance of discussing site rotation with patient at each visit.

Consensus statement 3. Site rotation

- Individuals should be taught an easy-to-follow rotation scheme from the onset of injection therapy
- Structured rotation plan of one quadrant per week and moving always in the same direction is proven and effective
- Injection within the quadrant must be spaced at 1 cm to avoid repeated trauma
- Site rotation at each injection is the most appropriate strategy for prevention of lipohypertrophy. It also ensures consistent absorption
- It is recommended to discuss the rotation of site with patient during each visit

Choice of device and storage of insulins

Selection of the device

Factors underlying the choice of right device include biomechanical factors (accuracy, length of needle, degree of dose increment and suitability for children/visually/dexterity-challenged people), psychosocial factors (attractiveness, discreteness/

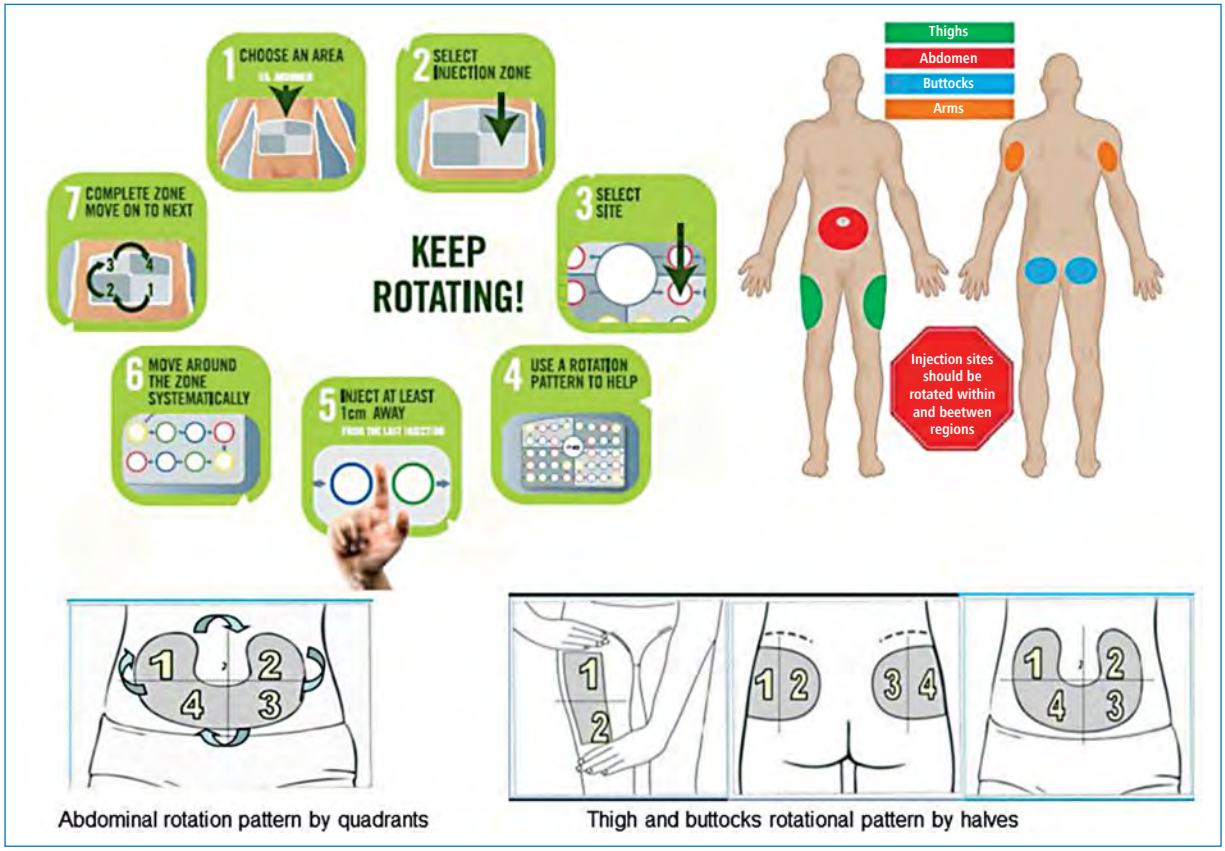

Figure 3. Ways for optimal site rotation. Adapted from Frid A. et al. Diabetes and Metabolism 2010; 36 (Suppl 2): S3–18, Kaira et al. Diabetes Ther. 2017; 8: 659–672. Diagrams courtesy of Lourdes Saez-de Ibarra and Ruth Gaspar, DNSPE from La Paz Hospital, Madrid, Spain, Spollett G. et al. The Diabetes Educator 2016; 42 (4): 379–394

Table 3. Guideline recommendations on site rotation

Guideline	Recommendation
Canadian FIT Recommendations for Best Practice in Injection Technique (2012) [22]	• Teach & demonstrate "structured rotation" to patient • Same anatomical region, same time of day, 2 to 3 cm apart injections • Rotation of site — discuss and check at each patient visit
UK FIT Recommendations for Best Practice in Injection Technique (2015) [23]	• Teach easy-to-follow rotation scheme at onset of therapy • Divide site into quadrants, 1 quadrant/week, move always in same direction (clockwise or anti-clockwise) • Space injections at least 1 cm from each other • Teach and demonstrate for detection of lipohypertrophy
American Association of Diabetes Educators (AADE) Strategies for Insulin Injection Therapy in Diabetes Self-Management (2011) [24]	• Rotation within an area — critical for optimal absorption • Rotation — within the same area, rather than from major site to site • Patient education and inspection at each visit essential
American Diabetes Association (ADA) Insulin Administration Guidelines (2004) [25]	• Rotation — important to prevent lipohypertrophy • Rotate within one area rather than rotating to a different area • Helps to decrease variability in absorption from day to day
Australian Diabetes Educators Association (ADEA) Clinical Guiding Principles for Subcutaneous Injection Technique (2015) [26]	• Teach, demonstrate and document rotation in drug chart at visit • Rotation within one area rather than into a different area • Divide into quadrants (abdomen) or halves (buttock or thigh), 1 quadrant/week and move clockwise • Site rotation grids — for pts forgetting injection sites
Indian FIT Recommendations for Best Practice in Injection Technique (2017) [5]	• Divide into quadrants (abdomen) or halves (buttock or thigh), use 1 quadrant/ /week and move clockwise • New injection site should be at least 1–2 cm apart from the previous site • HCPs — review site rotation scheme at least once a year

Table 4. Available pen devices in the market

Pen	Insulin types	D/R	Dosing increments	Max dose	Colours/other features
Novo Nordisk					
NovoPen® 4	NovoMix® 30; NovoRapid®; Levemir®; Actrapid®; Mixtard® 30/70; Mixtard® 50/50	R	1.0	60	Silver or blue
FlexPen®	NovoMix® 30; NovoRapid®; Levemir®	D	1.0	60	Blue (NovoMix®30), orange (NovoRapid®), green (Levemir®)
FlexTouch®	Tresiba, Ryzodeg, Xultophy	D	1	50 (Xultophy) 80	Blue (Ryzodeg), green (Tresiba), pink (Xultophy)
Lilly					
Humapen® Savvio™	Humalog®; Humalog® Mix 25®; Humalog® Mix 50®; Humulin® R; Humulin® NPH; Humulin® 30/70	R	1.0	60	Grey, blue, green, pink, red and graphite
Humapen® Luxura HD™	Humalog®; Humalog® Mix 25®; Humalog® Mix 50®; Humulin® R; Humulin® NPH; Humulin® 30/70	R	0.5	30	Green
Kwikpen®	Humalog®; Humalog® Mix 25®; Humalog® Mix 50®	D	1.0	60	Grey
Sanofi					
Solostar®	Apidra®; Lantus®; Toujeo®	D	1.0	80	Grey (Lantus®), blue (Apidra®), grey and green (Toujeo®)
AllStar™	Apidra®; Lantus®	R	1.0	80	Violet

D — disposable; R — reusable

/size, comfort/ease of use and ease of transport/storage), environmental factors (temperature stability, biodegradability/"green devices", availability of compatible insulins and availability of ancillary supplies), pragmatic factors (cost of device/insulin refills/needles, expected duration of insulin therapy with prescribed regimen and monthly dose requirement vis a vis capacity of device) and medication-counselling factors (time taken to reach, time taken to learn, risk of error in delivery and availability of post-prescription follow-up).

The modern pen devices have various advantages over the conventional insulin delivery methods such as user-friendliness, comfort of injection, higher accuracy specially at low doses, the flexibility of incorporating insulin injections into a busy lifestyle which may improve diabetes control with much less effort, while maintaining the quality of life for the diabetic patients [43, 44]. Pen devices available in the market are summarized in Table 4.

In a past study on the accuracy and precision of low-dose insulin administration via various devices including NovoPen® (3.0 mL), BD-Mini Pen® (1.5 mL), Humalog Pen® (100 U/mL), 30G Precision Sure-Dose® Insulin Syringes, 30G BD Ultra-Fine II® Short Needle Syringes, and H-TRON-plus V100® insulin pump; the pen and pump devices were reported to be more accurate, and the pump to be more precise, than the syringes at the 1U and 2U doses. Syringes were considered to be dangerously inaccurate clinically, at the 1U dose (Figure 4) [44].

In a past study addressing dose accuracy of NovoPen® 4 with respect to ISO tolerance limits [0.0–2.0 for a target dose of 1 U, 28.5–31.5 for 30 IU and 57.0–63.0 for 60 U, SD: ± 2.67 for each), NovoPen® 4 was reported to be accurate before and after simulated lifetime use of 5475 injections in 5 years with mean dose of test medium delivered remained within the ISO tolerance limits at all doses tested and under conditions of mechanical and temperature stress (Figure 5) [45].

Comparison of minimum, medium, and maximum doses of FlexTouch® (1/40/80 U), KwikPen® (1/30/60 U) and SoloSTAR® (1/40/80 U) in terms of dose accuracy in a past study revealed that FlexTouch® delivered all doses consistently, as demonstrated by low standard deviations [46]. FlexTouch® showed similar accuracy to KwikPen® at 1 U and to SoloSTAR® at 40 and 80 U and provided equivalent accuracy at medium and maximum doses with all tested pens, whereas it was significantly more accurate at delivering 1 U of insulin than SoloSTAR® (Figure 6) [46].

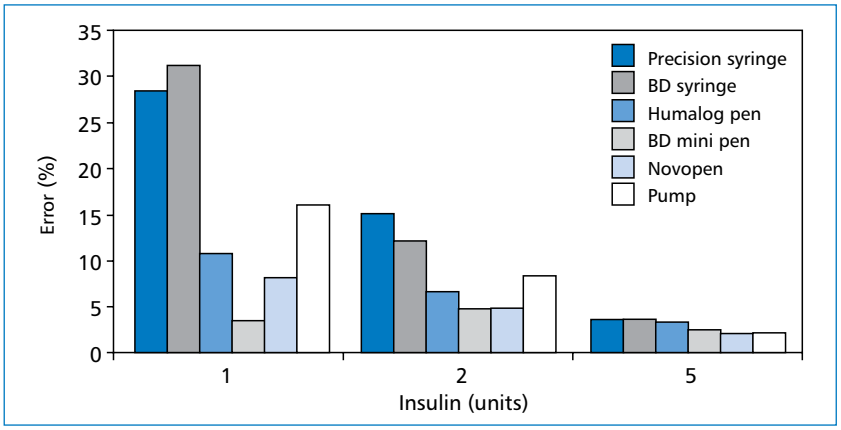

Figure 4. Accuracy and precision of low-dose insulin administration via different devices. Adapted from Keith K. et al. Clin Pediatr (Phila) 2004; 43 (1): 69–74

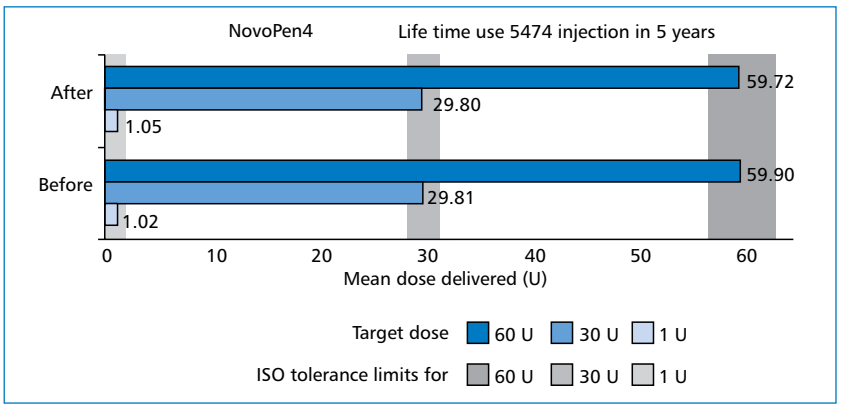

Figure 5. Dose accuracy and durability of the NovoPen®4 insulin delivery device. Adapted from Kristensen CM, Donsmark M. Clin Ther. 2009; 31 (12): 2819–2823

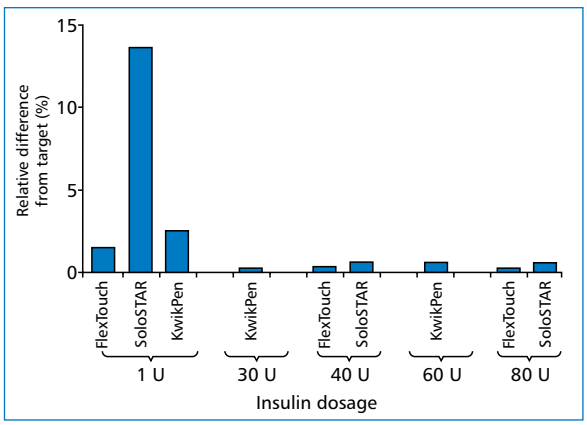

Figure 6. Mean relative percentage difference from target dose for FlexTouch, SoloSTAR, and KwikPen. Adapted from Wielandt JO. et al. J Diabetes Sci Technol. 2011; 5 (5): 1195–1199

Available guidelines consider insulin pens as the injection devices of choice due to shorter needle size, psychological advantages, convenience, accuracy and adherence as well as cost benefits due to treatment adherence (Table 5) [22–24, 26].

Consensus statement on choice of device

The expert panel recommends use of insulin pens over syringes for the convenience, ease of use, reduced fear of injections, greater treatment adherence and greater social acceptance. There are pen injectors dedicated to insulin preparations manufactured by different companies which may be used because they are compatible with insulin cartridges. However, Novo Pen® 4 and Flex Touch® are recommended over other devices for the ease of use, accuracy and lower dose force *vs.* other pen devices.

Consensus statement 4. Choice of device

- Insulin pens are recommended over syringes for the convenience, ease of use
- Pen devices are preferred over syringes for reduced fear of injections and greater treatment adherence
- Pen devices are recommended over syringes as they offer greater social acceptance

Table 5. Guideline recommendations on choice of device

Guideline	Recommendation
Canadian FIT Recommendations for Best Practice in Injection Technique (2012) [22]	Insulin pens are the injection devices of choice due to shorter needle size
UK FIT Recommendations for Best Practice in Injection Technique (2015) [23]	Pen devices may have psychological advantages over syringes and therefore maybe more acceptable
American Association of Diabetes Educators (AADE) Strategies for Insulin Injection Therapy in Diabetes Self-Management (2011) [24]	Cost benefits for using pens versus syringes due to improved treatment adherence
Australian Diabetes Educators Association (ADEA) Clinical Guiding Principles for Subcutaneous Injection Technique (2015) [26]	Convenience, accuracy and adherence

Figure 7. Improvised practical methods of storage in India — rural

- Novo Pen 4 and FlexTouch are recommended over other devices for the ease of use, accuracy and lower dose force vs other pen devices

Storage of insulins

For optimal effect, insulin need to be stored under refrigerated conditions, between 2 and 8°C as maintained below the freezer or in the butter compartment of most fridges, and be protected from light when vials or pens are unopened [47]. However, in India, up to 80% patients lack a good storage facility at home, while even in places where refrigerators are available, electrical supply may be erratic [47, 48]. The insulin pen in use (insulin cartridge inside) can be stored at room temperature (15–25°C) for 30 days [49]. However, the room temperature in many parts of India exceeds 25°C especially during summer season.

A survey in India showed approximately 75% of insulin to be stored at cool places, while cool places were not defined [8]. Additionally, the median time gap between taking out insulin vials from refrigerator and insulin injection was reported to be only 5 min, which is considered likely to cause pain at the injection sites [8].

In another study performed in Puducherry, India, it was reported that storage of regular and biphasic insulin at 32°C and 37°C decreased the potency of insulin by 14 to 18% [50], emphasizing a need for patient education about the temperature and duration of storage of insulin vials to maintain adequate glycaemic control [47]. Nonetheless, improvised practical methods of insulin storage being implemented in rural India with limited facilities are as follows (Figure 7) [47].

- Storing insulin in a small bowl of water protected from exposure to direct sunlight and wetting of the label using a water-proof tape.
- Using a small clay pot or earthenware pitcher to reduce an exposure to external temperature variations with insulin vial cap is not submerged, and the labels with insulin name, date of opening, and date of expiry are preserved.
- Using thermo cool boxes, with ice packs inside them (replaced by frozen ones on weekly basis), as effective refrigeration devices for insulin that would keep the temperature within acceptable limits for many days.
- Using a good insulated extra vaccination boxes that can keep insulin stable for many days.
- Keeping a cool wet cloth around insulin to preserve insulin potency.

In fact, resource-poor mountainous areas such as Himalayas also pose significant challenges to insulin supply, storage and disposal where keeping insulin warm enough is an issue with temperature extremes range from 30°C in summer to –20°C in winter as well as high indoor temperature during winter since members of the family stay together in a single room warmed by an iron-framed oven [51]. Hence persons living with diabetes on insulin therapy report insulin storage to be a major challenge during winter, since they are unable to store their insulin vial and pens in living rooms, because of extreme heat, and cannot use adjoining rooms, as night-time temperatures routinely fall below freezing point [51]. Accordingly, patients are advised by HCPs to store insulin vials and pens by wrapping them in two to three layers of warm woollen cloths, made of sheep wool, in wooden or steel cupboards, as the local method of storing foodstuffs [51].

Manufacturer instructions on storage of insulins are provided in Table 6.

Consensus statement on storage of insulin

The expert panel recommends storage of injectable medicines in accordance with the manufacturer's instructions. Insulin should be discarded if it is past the expiry date, is open for more than a month, is discoloured or become cloudy. Insulin should be stored at refrigeration temperature (2–8°C) until use, and at room temperature once in use, while it should never be frozen or exposed to extreme heat (> 30°C) for prolonged periods.

Consensus statement 5. Storage of insulin

- Injectable medicines should be stored according to the manufacturer's instructions
- Insulin should be discarded if it is past the expiry date on the bottle or if the vial has been open for more than a month
- If insulin is discoloured, lumps or flakes are seen, or clear insulin has turned cloudy, it must be discarded
- Insulin should be stored at refrigeration temperature (2–8°C). Once in use, insulin may be stored at room temperature
- Insulin should never be frozen or exposed to extreme heat (> 30°C) for prolonged periods as this will affect insulin potency and alter its action

Safety precautions, disposal and complications

Safety precautions and sharp disposal practice

Insulin pens are only approved for single-patient use and even though the needles were changed between uses, the patients were at risk due to possible biological contamination in the pen cartridges [52, 53]. In accordance with widespread concern about disease transmission due to repeated instances of misuse of insulin pens, FDA, Institute for Safe Medication Practices (ISMP), and Centres for Disease Control (CDC) issues similar warnings against using the same insulin pen to administer insulin to multiple patients [53–55].

Improper sharp disposal practices among diabetes patients have been considered to be as high as 80–90% [56, 57].

ITQ 2014–2015 Study revealed a very large number of used diabetes sharps to still end up in the general community trash with use of a container specially made for used sharps by only 20.7% of patients and lack of a past training on proper disposal of sharps in 30% of patients [10]. Indian arm of ITQ 2014–2015 study revealed that almost 65% of patients were never trained on proper disposal of sharps [36].

Nearly 3 billion injections (83% for curative purposes, 63% in an unsafe manner) is estimated to be administered annually in India [58], whereas the proper way of disposing sharps is one of the important, but often neglected component of proper injection techniques [58–60].

Accordingly, in a KAP study on disposal of sharp waste in India, 84.1% of diabetic patients were reported to discard the sharps directly into their household waste bins [61]. Authors also reported that 71% patients disposed at least 7 needles/week, 89% patients disposed at least 7 lancets/week, whereas only 14.1% diabetes patients received education from their HCP regarding proper sharp disposal [61].

This seems notable given the higher likelihood of improper sharp disposal practice with lack of counselling from HCPs [60], along with a wide gap between

Table 6. Manufacturer instructions on storage of insulins

Insulin	Before first use	After opening	Shelf life
Novorapid (vial & penfill)	2°C–8°C up to ED	Do not refrigerate, below 30°C for 4 weeks	30 months
Novomix 30 penfill	2°C–8°C up to ED	Do not refrigerate, below 30°C for 4 weeks	24 months
Novomix 50 penfill	2°C–8°C up to ED	Do not refrigerate, below 30°C for 4 weeks	24 months
Tresiba Flextouch	2°C–8°C up to ED	Do not refrigerate, below 30°C for 8 weeks	30 months
Ryzodeg Flextouch & penfill	2°C–8°C up to ED	Do not refrigerate, below 30°C for 4 weeks	30 months
Levemir Flexpen	2°C–8°C up to ED	Do not refrigerate, below 30°C for 6 weeks	30 months
Xultophy prefilled pen	2°C–8°C up to ED	Do not refrigerate, below 30°C for 21 days	24 months
Insulatard	2°C–8°C up to ED	Do not refrigerate, below 25°C for 4 weeks	
Actrapid 40 IU (vial & flexpen)	2°C–8°C up to ED	Do not refrigerate, below 25°C for 4 weeks Flexpen below 30°C for 6 weeks	
Mixtard 40 IU (vial & flexpen)	2°C–8°C up to ED	Do not refrigerate, below 25°C for 6 weeks Flexpen below 30°C for 6 weeks	
Lantus	2°C–8°C up to ED	Refrigerated or RT for 4 weeks	36 months
(vial & cartridge)	At RT for 4 weeks	Within pen device at RT for 4 weeks	
Humalog	2°C–8°C up to ED	Refrigerated or RT for 4 weeks (vial)	36 months
(vial & cartridge)	At RT for 4 weeks	Cartridge at RT	
Humalog Mix25,	2°C–8°C up to ED	Refrigerated or RT (below 25°C) for 4 weeks (vial)	36 months
Mix50	At RT for 4 weeks (vial)	Pen at RT (below 25°C) for 10 days	
(vial & prefilled pen)	Pen at RT for 10 days		
Basalog	2°C–8 °C up to ED	Refill at RT (below 25°C) up to 4 weeks	24 months
Apidra	2°C–8°C up to ED	Refrigerated or RT (below 25°C) for 4 weeks	
	At RT for 4 weeks	Within pen device at RT (below 25°C) for 4 weeks	
Basaglar	2°C–8°C up to ED	Do not refrigerate, below 30°C for 4 weeks	
	At RT for 4 weeks		
Insugen 50/50	2°C–8°C up to ED	Do not refrigerate, below 25°C for 42 days	36 months
	At RT (< 25°C) for 6 weeks		
Eglucent	2°C–8°C up to ED	Within pen device at RT (below 30°C) for 4 weeks	36 months
Lupisulin	2°C–8°C up to ED	RT (between 15°C–25°C) for 2 weeks	
Insuman	2°C–8°C up to ED	Vails can be refrigerated or RT (below 25°C) for 4 weeks	24 months
(vials & cartridge)		Within pen device at RT (below 25°C) for 4 weeks	

ED — expiry date; RT — room temperature

translation of research findings and their implementation in practice and poor adherence to established guidelines for sharp disposal practice in India [60, 62].

India is home to a huge diabetic population and concerns over sharp disposal practices in diabetes self-management are therefore important and should not be neglected given the likelihood of outbreaks of blood-borne infections and related adverse health and economic outcomes [60].

Current guidelines on safety precautions and disposal consider training of HCPs, caregivers and patients based on local regulations to be essential. The main recommendations include avoiding recapping, bending, or breaking a needle as well as disposing in household or public disposal system and using needle clipping device and puncture-resistant container (Table 7) [5, 22, 23, 25, 26].

Consensus statement on safety precautions and sharp disposal practice

The expert panel recommends single person use of syringes and pen needles, patient's education about the safe disposal of their used sharps with reinforcement during subsequent visits, following local regulations regarding sharps disposal, avoiding disposal of sharps material into the public rubbish or household garbage.

Consensus statement 6. Safety precautions and sharp disposal practice

- Syringes and pen needles are for single person use only
- Pen devices and cartridges or vials are for single person use only, and must never be shared due to the risk of cross contamination even if the needle is changed
- Any HCP who is required to use a lifted skin fold must exhibit caution to avoid needle stick injury

Table 7. Guidelines on safety precautions and sharp disposal practice

Guideline	Recommendation
Canadian FIT Recommendations for Best Practice in Injection Technique (2012) [22]	• Training essential — based on local regulations • Where available, a needle-clipping device can be used • Needles should never be re-sheathed
UK FIT Recommendations for Best Practice in Injection Technique (2015) [23]	• Training of HCPs, caregivers and patients with reinforcement • Based on local regulations • Use needle clipping device • Never dispose in household or public disposal system • Pen devices without needle — can be disposed in house hold rubbish
American Association of Diabetes Educators (AADE) Strategies for Insulin Injection Therapy in Diabetes Self-Management (2011) [24]	None
American Diabetes Association (ADA) Insulin Administration Guidelines (2004) [25]	• Avoid recapping, bending, or breaking a needle • Dispose according to local regulations • Used sharps — puncture-resistant container
Australian Diabetes Educators Association (ADEA) Clinical Guiding Principles for Subcutaneous Injection Technique (2015) [26]	• Education extremely essential on disposal and safety • Occupational safety • Follow local regulations
Indian FIT Recommendations for Best Practice in Injection Technique (2017) [5]	• Adequate training on safety and disposal — patients and caregivers • Sharps containers in every ICU, ward and nursing station • Used needles or syringes — puncture proof box/safety box/strong cardboard/ /glass container • Label the box as biohazard and handover to health-care facility • NACO guidelines — gives safe disposal methods

- People with diabetes are taught about the safe disposal of their used sharps with reinforcement during subsequent visits
- Local regulations regarding sharps disposal must be followed
- Sharps material must not be disposed of into the public rubbish or household garbage
- Empty pen devices can be disposed of in the normal household refuse when the needle is removed

Complications of insulin injections

ITQ 2014–2015 Study revealed higher rates of unexplained hypoglycaemia and glucose variability in those with LH, injecting into LH, incorrect rotation of sites and needle reuse [10].

According to ITQ 2014–2015 data, LH was highly prevalent (30.8%), while associated with consumption of 10.1 IU more insulin daily, 0.55% higher HbA_{1c} levels, higher rates of unexplained hypoglycaemia and glycaemic variability as well as with incorrect rotation of injection sites, use of smaller injection zones and reuse of pen needles [38].

Indian ITQ revealed 21.9% of Indian patients had nurse-confirmed LH with almost equivalent risk across sites (8.7–10.1%) except buttocks (0.0%) [36]. Injecting into LH was consistently reported to be associated with delayed or erratic insulin absorption, potentially worsening the diabetes management [63, 64]. In this regard, it should be noted that Indian patients with LH were found not to inject into LH lesions as frequently as in ROW (35.0% *vs.* 56.0%), while 53% were unaware of the reasons underlying this practice with convenience and pain less frequently cited by Indian patients compared to ROW (17.0 *vs.* 38.0%) [36].

Although none is evidence-based, several approaches have been recommended in treatment of LH such as changing the insulin formulation (e.g., aspart to lispro, or lispro to glulisine, etc.), changing injection sites, or shifting to CSII and possibly cortisone injection [36].

ITQ 2014–2015 data revealed that 60.2% of patients experience bleeding and bruising (never: 50.8%, sometimes: 41.5%, often: 7.3%) [38]. In Indian ITQ, 41.4% of Indian patients reported bleeding or bruising from their injection sites (never: 37.7%, sometimes: 53.6%, often: 7.8%) [36].

Injection using a 4 mm needle at 90° is considered to deliver insulin into subcutaneous tissue for > 99.5% of times with minimal risk of intradermal (ID) injections. Majority of injections at four commonly-used sites with

Table 8. IM injection risk according to needle length and injection angle at injection sites [32]

Needle length, injection angle		Risk of IM injection (%)			
		Thigh	Arm	Abdomen	Buttock
4 mm	90°	1.6	1.0	0.3	0.1
	45°	NA	NA	NA	NA
5 mm	90°	4.7	3.1	1.1	0.5
	45°	NA	NA	NA	NA
6 mm	90°	10.0	7.0	2.8	1.3
	45°	2.2	1.3	0.4	0.2
8 mm	90°	25.0	19.5	9.7	5.5
	45°	8.0	5.5	2.1	1.0
12.7 mm	90°	63.0	55.0	38.0	26.9
	45°	34.0	27.0	14.6	8.8

a 4–5 mm needle at 90° would be delivered into the subcutaneous tissue with < 2% risk of intramuscular (IM) injections [30, 32].

When inserted 90° without pinch-up, the most commonly used needle worldwide (8 mm) has estimated IM risks of 25% and 9.7%, respectively, in the thigh and abdomen, *versus* 1.6% and 0.1%, respectively, with a 4 mm needle. A 45° insertion reduces, but does not eliminate, IM risk with longer needles [32].

Risk of IM injection in considered to be higher in arm and thigh injections and further increase with increasing needle size, from 1% (4 mm) to 55% (12.7 mm, 27% for 45°) in the arm and from 1.6% (4 mm) to 63% (12.7 mm, 34% for 45°) in the thigh (Table 8) [32].

ITQ 2014–2015 data revealed that pain was associated with larger needle size and needle reuse and increase as a function of the number of times the needle is reused [38]. Pain was commonly associated with bleeding, injecting through clothes, injecting insulin while it is still cold, LH, injecting into LH, incorrect site rotation, higher HbA_{1c} levels, lower BMI, younger age, and higher total daily dose of insulin [38].

Indian ITQ revealed that 50% of Indian injectors had pain on injection [36], while authors also emphasized that patient awareness of injection discomfort depends on several factors such as needle length, needle diameter, injection context and apprehension of HCPs [36, 65, 66].

Past studies addressing injection pain reported no impact of injection speed (150, 300, and 450 μl/s; equivalent to 15–45 IU/s of U100 insulin) on pain [67], whereas more pain with higher injection volume (≥ 1200 μl or 120 IU of U100 insulin) [67–69] and selection of thigh compared to abdomen as an injection site [67]. Nonetheless, it was concluded that injection pain is mild enough to be acceptable to most of patients particularly with today's very thin, short needles [36, 67].

Current guidelines recommend regular inspection and palpation of sites, rotation of sites and avoiding needle reuse and injecting in LH to prevent LH; recommend reassurance for avoid occasional bleeding and bruising and review of technique for frequent bleeding and bruising, use shorter needles and avoid IM injection to prevent bleeding and bruising, recommend avoiding injection through clothes to prevent intradermal injection, avoiding 12.7 mm needles and injecting at 45 degree and using lifted skin fold or injecting abdomen in slim patients to prevent IM injection; and recommend injecting at room temperature, using distraction methods, using needles of shorter length and smaller diameter and a new needle at each injection, allowing topical alcohol (if used) to evaporate before injection, inserting needle in a quick smooth movement and injecting slowly and removing at same angle with not changing the direction of needle during insertion and withdrawal to prevent pain (Table 9) [5, 22–26].

Consensus statement on complications of insulin injections

For LH, the expert panel recommends patient education about examining injection sites to detect LH and avoiding injection into the hypertrophic and atrophic areas. HCP inspection and palpation of injection sites at each visit, use of site rotation and non-reuse of needles are also recommended to prevent LH which should be ruled out as a cause of poor glycaemic control, hypoglycaemia and high glycaemic variability. For bleeding and bruising the expert panel recommends reassuring patients about no significant impact of occasional bruising or bleeding at site on insulin action, whereas a review of injection technique for frequent

Table 9. Guideline recommendations about complications of insulin injections

Guideline	Recommendation
Canadian FIT Recommendations for Best Practice in Injection Technique (2012) [22]	**Lipohypertrophy** • Avoid injection in LH, hair roots, scars, moles and other skin abnormalities • Use needles of shorter length and smaller diameter • To prevent LH — site rotation, use larger injection zones, new needle • Inspect and palpate site at each visit, patient education • Dose reduction — if site changed from LH site to normal tissue **Bleeding and bruising** • Frequent bleeding and bruising — review injection technique • Occasional bleeding and bruising — reassurance that won't affect insulin action **Intradermal injection** • Avoid injection through clothes to avoid intradermal injection **IM injection** • 12.7 mm needles not recommended — risk of IM injection • Slim patients — inject at 45° to avoid IM injection **Pain** • Inject at room temperature — to avoid pain, relax apprehensive patient
UK FIT Recommendations for Best Practice in Injection Technique (2015) [23]	**Lipohypertrophy** • Patient education, inspect site at each visit • To prevent LH — site rotation, avoid reuse of needles • Reduce dose — if shifting from LH to normal tissue **Bleeding and bruising** • To avoid bleeding — avoid IM injection • Occasional bleeding and bruising — reassurance • Frequent bleeding and bruising — review technique **Pain** • Keep injectable at room temperature • Use needles of shorter length and smaller diameter • Use a new needle at each injection • Insert needle in a quick smooth movement • Inject slowly and ensure plunger or thumb button is fully depressed • Remove at same angle and keep hand steady **IM injection** • Use lifted skin fold in slim limbs and abdomen
American Association of Diabetes Educators (AADE) Strategies for Insulin Injection Therapy in Diabetes Self-Management (2011) [24]	**Lipohypertrophy** • Patient education, inspect site at each visit • To prevent LH — site rotation **Pain** • Inject at room temperature • Allow topical alcohol (if used) to evaporate before injection • Relax muscles at the site • Using distraction methods • Quickly penetrate the skin • Don't change direction of needle during insertion or withdrawal • Don't reuse needles • Use injection device that puts pressure on skin around the site • Apply pressure for 5–8 seconds after injection, without rubbing, if really painful **IM injection** • Use smaller size needles

→

Table 9 (cont.). Guideline recommendations about complications of insulin injections

Guideline	Recommendation
American Diabetes Association (ADA) Insulin Administration Guidelines (2004) [25]	**Lipohypertrophy** • To prevent LH — site rotation, avoid reuse of needles **Bleeding and bruising** • Frequent bleeding and bruising — review technique • Apply pressure for 5–8 seconds without rubbing • Frequent glucose monitoring **Pain** • Injecting insulin at room temperature • Making sure no air bubbles remain in the syringe before injection • Wait for topical alcohol (if used) to evaporate • Keep muscles in the injection area relaxed • Penetrating the skin quickly • Don't change direction of needle during insertion or withdrawal • Don't reuse needles **IM injection** • Use short needles specially in slim patients and children • Inject at 45° (especially in thigh)
Australian Diabetes Educators Association (ADEA) Clinical Guiding Principles for Subcutaneous Injection Technique (2015) [26]	**Lipohypertrophy** • Inspect and palpate injection sites for nodules, multiple pricks over small area • Ask about the frequency and method of site rotation and needle reuse • Longer diabetes duration and insulin use, frequency of injecting — higher risk of LH • Document location and size of LH • Rotate injection sites, use new needle **Intradermal injection** • Injection at 90° with 4 mm needle **IM injection** • Inject into the abdomen or buttocks • Avoid sites with little SC tissue such as arms and thighs • Use shorter needle lengths, lift skin fold, Insertion needle at 45° angle **Pain** • Injecting insulin at room temperature rather than when cold • If using alcohol to clean the skin, injecting only after this has dried • Use a new needle, shorter length and smaller diameter • Penetrate skin quickly with needle and inject slowly • Don't change direction of needle during insertion and withdrawal
Indian FIT Recommendations for Best Practice in Injection Technique (2017) [5]	**Lipohypertrophy** • Regular inspection and palpation of sites • Rotation of sites, no needle reuse • Use larger injection surface areas • Do not inject into LH sites • Reduce dose of insulin in habitual LH site injections if shifting to normal SC tissue • Rule out LH — poor glycaemic control, hypoglycaemia, and high glycaemic variability **Bleeding and bruising** • Frequent bleeding and bruising — review injection technique • Use shorter needles **IM injection** • Use 6 mm needles • Avoid syringe needles in < 6 years old children and exceptionally thin adults (BMI < 19 kg/m^2) **Pain** • Inject at room temperature, use new needles, concentrated insulin if large dose • Neutral pH insulin if pain with acidic insulin • Penetrate skin quickly, don't move needle after insertion

bruising or bleeding, and use of shorter needles for less frequent bleeding and bruising and consideration of the likelihood of IM injection for frequent bleeding and bruising with glycaemic variability. The expert panel recommends injecting into the abdomen or buttocks and use of shorter needle lengths, lifted skin fold and insertion of the needle at 45° to prevent IM injection and avoiding injection through clothing to prevent intradermal injection. For pain, the expert panel recommends considering all factors contributing to the perception of pain such as individual perception, needle length and diameter, injection technique and IM injection and recommends use of short and narrow-gauge (4–5-mm × 32G) insulin pen needles, injecting at room temperature and allowing topical alcohol (if used) to evaporate before injection, relaxing muscles at the site when injecting, using distraction methods, not reusing needles and penetrating skin quickly without changing needle direction during insertion or withdrawal to prevent pain.

Consensus statement 7. Complications of insulin injections

Lipohypertrophy

- Individuals should be taught to examine their own injection sites and how to detect lipohypertrophy
- Best current preventative and therapeutic strategies for lipohypertrophy — site rotation and non-reuse of needles
- HCP should inspect and palpate sites at each visit ideally in a standing position
- Avoid injection into the hypertrophic and atrophic areas
- When switching injection from areas of LH to normal tissue, insulin dose reduction may be required (guided by glucose measurement)
- Rule out LH as a cause of poor glycaemic control, hypoglycaemia and high glycaemic variability

Bleeding and bruising

- Reassure patients — insulin action is not affected by occasional bruising or bleeding at site
- Frequent bruising or bleeding — warrants a review of injection technique
- Less frequent bleeding and bruising — with use of shorter needles
- Frequent bleeding and bruising with glycaemic variability may point towards IM injection

IM injection

- Inject into the abdomen or buttocks
- Avoid sites with thin subcutaneous tissue such as arms and thighs
- Consider different techniques according to sites chosen: shorter needle lengths, lifted skin fold and insertion of the needle at 45° angle

Pain

- Factors contributing to pain — perceptual sensitivity, needle length and diameter, injection technique, and intramuscular injection
- Less pain with short and narrow-gauge (4–5-mm × 32G) insulin pen needles
- Inject at room temperature and allow topical alcohol (if used) to evaporate before injection
- Relax muscles at the site when injecting, and using distraction methods
- Penetrate skin quickly and don't change needle direction during insertion or withdrawal
- Don't reuse needles, and use pressure applying injection device around the injection site

Intradermal injections

- Intra-dermal injection — appearance of white area when withdrawing needle indicates insulin has not been injected deeply enough
- Avoid injection through clothing to prevent intradermal injection

Conclusion

This expert panel based consensus statement provides a simple and easily implementable practical educational guideline for HCPs and patients to optimize insulin injection practices (preparation and selection of injection sites, site rotation, selection of device, storage of insulins, safety precautions, sharp disposal practice and complications) in accordance with recent advances in device manufacturing, newer research findings, and updated international guidelines as well as widespread concerns about neglected safety precautions such as single-patient use of pens and appropriate sharp disposal practices. This seems important given the overall findings from ITQ studies that highlight the need of easy to use practical guidance to optimize insulin injection practices as well as findings specific to Indian cohort such as suboptimal rates for patient training on injection practice and routine check of injection sites by HCPs at every visit.

Accordingly, the expert panel recommendations regarding insulin injection practices provided in this consensus statement emphasize:

— injecting into a clean site after inspection and palpation and with use of soap and water for cleaning rather than disinfecting the skin;

— selection of abdomen (offering the most consistent/fastest absorption) as followed by thighs and buttocks as the appropriate injection sites for adults, whereas potential of thigh and buttocks to be more appropriate for NPH due to slowest

absorption from these sites along with no site-specific alterations in absorption rate of basal insulin analogues;

- teaching an easy-to-follow and structured site rotation scheme to patients from the onset of injection therapy and checking injection sites routinely at each visit;
- preferring use of insulin pens (particularly Novo Pen® 4 and Flex Touch® for dose accuracy) over syringes for the convenience, ease of use, reduced fear of injections, greater treatment adherence and greater social acceptance;
- storing injectable medicines in accordance with the manufacturer's instructions, with storing insulin at refrigeration temperature (2–8°C) until use, and at room temperature once in use by preventing exposure to extreme cold or heat;
- adhering to single person use of syringes and pen needles and providing patient education on safe sharp disposal practices per local regulations with avoiding disposal of sharps material into the public rubbish or household garbage and reinforcement during subsequent visits;
- inspection and palpation of injection sites by HCPs at each visit to identify LH which should be ruled out as a cause of poor glycaemic control, hypoglycaemia and high glycaemic variability, and use of site rotation, non-reuse of needles, providing patient education about examining injection sites to detect LH and to avoid injecting into the hypertrophic and atrophic areas to prevent LH; reassuring patients about no significant effect of occasional bruising or bleeding at site on insulin action, whereas a review of injection technique, encouraging use of shorter needles and considering the likelihood of intramuscular injection and consequent glycaemic variability for frequent bruising or bleeding; injecting into the abdomen or buttocks and use of shorter needle lengths, lifted skin fold and insertion of the needle at 45° to prevent intramuscular injection and avoiding injection through clothing to prevent intradermal injection; considering all factors contributing to the perception of pain such as individual sensitivity, needle length and diameter, injection technique and intramuscular injection, use of short and narrow-gauge (4–5-mm × 32G) insulin pen needles, injecting at room temperature and allowing topical alcohol (if used) to evaporate before injection, using distraction methods, not reusing needles and penetrating skin quickly without changing needle direction during insertion or withdrawal to prevent pain.

Declaration of interest

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