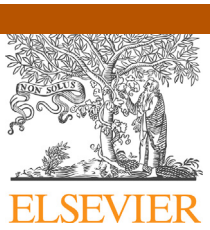
PRIMARY CARE DIABETES XXX (2014) XXX–XXX





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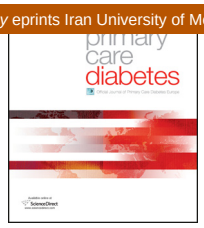

Original research

# Insulin adherence in patients with diabetes: Risk factors for injection omission

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ARTICLE INFO

*Article history:*
Received 8 July 2013
Received in revised form
9 March 2014
Accepted 13 March 2014
Available online xxx

*Keywords:*
Adherence
Diabetes mellitus
Insulin
Barrier

ABSTRACT

*Aims:* The purpose of this study was to evaluate adherence to insulin therapy in patients with diabetes. The underlying factors affecting insulin injection omission among patients with type 1 or 2 diabetes were also investigated.
*Methods:* This cross-sectional study has been conducted on 507 patients with diabetes. Adherence to insulin therapy was measured by the 8-Item Moriskey Medication Adherence Scale (MMS) and the autocompliance method. Furthermore, socio-demographic, disease and injection-related barriers to insulin injection were assessed.
*Results:* Based on the Morisky Green test, 14.3% and 28.8% of patients with type 1 and 2 diabetes respectively had low adherence to insulin therapy. However, almost all patients were adherent according to the autocompliance method. Different factors showed a significant association with insulin compliance in both groups.
*Conclusions:* The current study suggests acceptable adherence to insulin therapy among patients with type 1, and poor adherence in patients with type 2, diabetes. Our findings regarding barriers with significant effect on insulin adherence may be useful to identify patients at risk for low compliance, and to guide the design of proper strategies to improve adherence and the consequential clinical outcomes.



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http://dx.doi.org/10.1016/j.pcd.2014.03.001
1751-9918/

## 1. Introduction

The increasing number of patients with diabetes is costly and has a large economic burden on society, so the care and management of patients with insulin treatment has seen a rapid evolution, contributing to improved metabolic control and delayed progression of microvascular complications in these patients [1–4]. Also, clinical outcomes support benefits associated with early initiation and intensification of insulin therapy in patients with type 2 diabetes [5].

However, medications are effective only when they have been taken according to the recommendations of health care providers and unfortunately poor adherence among patients with diabetes remains a common problem [6,7].

The centers for disease control and prevention (CDC) estimates that more than 25% of patients with diabetes take insulin. In spite of the crucial role of adherence to insulin for achieving therapeutic goals, few studies have evaluated adherence to insulin and its associated factors.

In a study using an internet survey of 502 U.S. adults with type 1 or type 2 diabetes, more than half of them reported intentional insulin omission [8]. Another study revealed that 77% of the prescribed insulin dose was taken by patients [9]. A systematic review in 2004 disclosed that only one-third of the prescribed insulin dose was used by young patients and estimated adherence was 62–64% among patients with type 2 diabetes.

Low insulin adherence reported in previous studies may be the culprit for the unstable and generally poor glycemic control [10]. Therefore, identification of the underlying factors which predispose patients to poor adherence is necessary for better glycemic control.

Several studies have been conducted to detect factors associated with insulin adherence, but there is lack of evidence regarding the influence of these factors on adherence to insulin [8,11,12]. In addition there is scarce information about the rate of poor adherence to insulin therapy and related risk factors in developing countries which play a fundamental role in achievement and maintenance of adequate glycemic control [11,13,14].

Therefore, the present study was designed to evaluate adherence to insulin therapy in patients with diabetes. The secondary goal of the study was to investigate the underlying factors that may predispose patients to low insulin adherence.

## 2. Methods

In this cross-sectional study 507 patient with type 1 ($n = 251$) or type 2 ($n = 256$) diabetes were selected using the convenience sampling method from Endocrinology and Metabolism Research Center (EMRC) outpatient diabetes clinic, affiliated to Tehran University of Medical Sciences (TUMS).

Participants had to be on a stable dose of insulin prior to the study and willing to participate in the study. Patients who had cognitive impairment or a severe health condition, who could not participate in the study, were excluded.

A questionnaire was designed to collect information about socio-demographic characteristics (age, sex, BMI, level of education), type and duration of diabetes and insulin injection, adherence to insulin and barriers to patient compliance.

Adherence to insulin was measured by the 8-Item Moriskey Medication Adherence Scale (MMAS) reported by Sakthong et al. According to 8-Item MMAS, a patient was considered a low adherent if s/he received scores of less than 6.0, while scores between 6.0 to <8.0 and 8.0 were categorized as medium and high adherence respectively [1].

Furthermore, compliance with insulin was also measured by the autocompliance method. The autocompliance test estimates the number of skipped insulin injections during the previous month, following the methodology of Haynes et al. [15]. It measures according to patient self reporting of difficulty in taking the medication by asking two open questions: (1) "Did you have any difficulties in insulin injection?" and (2) "How many times did you skip insulin injection in the last month?"

Autocompliance was calculated by using the following formula:

$$\frac{\text{Total number of insulin injections}}{\text{Total number of prescribed insulin injection}} \times 100$$

Patients who affirmed taking more than 80% of the total number of prescribed insulin injections were considered as compliers with insulin [16].

Barriers to insulin injection were assessed in the last section of the questionnaire which covered patient and medication factors.

Validity and reliability of the questionnaire was determined in a pilot study.

A pharmacist assessed adherence to insulin and its associated factors via telephone interview, using the final questionnaire.

The TUMS ethic committee approved the study protocol and verbal informed consent was obtained from participants prior to the interview.

### 2.1. *Statistical analysis*

The distribution of continuous variables was assessed by the Kolmogrov–Smirnov test. Continuous variables are expressed as mean ± SD and categorical data are expressed as a percentage. The chi square test was used to analyze categorical data. The association between level of adherence and continuous variables was assessed by independent sample *T*-test for parametric variables and Mann–Whitney *U*-test for non-parametric variables. A *P*-value less than 0.05 was considered as statistically significant. Analysis was done with SPSS version 11.5 software.

## 3. Results

Almost half of the studied population (49.4%, $n = 251$) were patients with type 1 diabetes. Demographic variables and diabetes characteristics of the participants are shown in Table 1.

Cronbach's alpha coefficient was 0.82, confirming the reliability of the questionnaire.

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**Table 1 – Demographic variables and diabetes characteristics of participants.**

| | Total ($n=508$) | Type 1 ($n=251$) | Type 2 ($n=257$) |
|---|---|---|---|
| **Socio-demographic characteristics** | | | |
| Age, years[a] | 38.2 (2.0) | 20.6 (9.9) | 55.3 (11.5) |
| Educational status[b] | | | |
| Student | 136 (26.9) | 136 (54.8) | 0 (0.0) |
| Illiterate | 55 (10.9) | 0 (0.0) | 55 (21.4) |
| Under diploma | 154 (30.5) | 26 (10.5) | 128 (49.8) |
| Diploma | 102 (20.2) | 47 (19.0) | 55 (21.4) |
| University | 58 (11.5) | 39 (15.7) | 19 (7.4) |
| Sex, male[b] | 217 (42.7) | 128 (51.0) | 89 (34.6) |
| BMI, kg/m$^2$ [a] | 24.7 (5.7) | 21.5 (4.5) | 27.9 (4.8) |
| **Diabetes characteristics** | | | |
| Duration of diabetes, years[a] | 11.2 (8.2) | 8.3 (7.3) | 14.0 (8.1) |
| Duration of insulin injection, years[a] | 6.1 (6.3) | 8.1 (7.2) | 4.2 (4.6) |
| Insulin daily dose, unit[a] | 48.5 (26.6) | 44.7 (24.5) | 52.3 (28.0) |
| Number of daily injections[b] | | | |
| 1 | 41 (8.0) | 13 (5.2) | 28 (10.9) |
| 2 | 330 (65.0) | 149 (59.4) | 181 (70.4) |
| ≥3 | 137 (27.0) | 89 (35.5) | 48 (18.7) |
| Injection device[b] | | | |
| Syringe | 462 (90.9) | 228 (90.8) | 234 (91.1) |
| Pen | 46 (9.1) | 23 (9.2) | 23 (8.9) |

[a] Continuous variables are expressed as mean (SD).
[b] Categorical variables are expressed as *n* (%).

### 3.1. *Adherence to insulin injection*

Based on the Morisky Green test, 22.3% of patients with type 1 diabetes had high adherence, while 63.4% and 14.3% of them had medium and low adherence respectively. In patients with type 2 diabetes, 24.9% were highly adherent to insulin injections whereas, 46.3% and 28.8% of them were considered to have medium and low adherence to insulin therapy. There was a significant difference regarding patients with low compliance in these two study groups ($P<0.01$).

According to the autocompliance method, almost all patients (99.4%) of the studied population were compliant with insulin injections and only two patients were non-compliant.

### 3.2. *Barriers to insulin injection*

Possible factors influencing patient's adherence to insulin injection are illustrated in Table 2.

In patients with type 1 diabetes, insulin injection by the patient's care giver was more common than patients with type 2 diabetes ($P=0.03$). Furthermore the number of daily insulin injections in this group was significantly higher than patients with type 2 diabetes ($P<0.01$).

In patients with type 1 diabetes, older patients ($23.9\pm9.4$ years old) injected insulin themselves compared to younger patients ($13.5\pm6.9$ years old) who needed care givers for insulin injections ($P=0.03$). However, caregivers of older adults ($62.5\pm11.5$ years old) with type 2 diabetes injected insulin for them in comparison with younger patients ($53.2\pm10.6$ years old) who could inject insulin themselves ($P=0.25$).

Patient complaints regarding interference of insulin injection with physical and daily activities and meal plans was significantly more common in patients with type 2 diabetes ($P\leq0.01$). There was more frequent complaint of injection site reactions in patients with type 2 diabetes than type 1 ($P=0.03$), but on the other hand patients with type 1 diabetes experienced more embarrassment with insulin injections ($P<0.01$). Patients with type 2 diabetes more commonly forget about insulin injections than patients with type 1 diabetes ($P<0.01$), and also a greater number of type 2 patients believed that insulin injection have a negative effect on their overall health than patients with type 1 diabetes ($P<0.01$). More patients with type 2 diabetes reported insulin omission because of illness than type 1 patients ($P<0.01$). Taking multiple daily medications was another factor contributing to skipped insulin injections with higher frequency in patients with type 2 diabetes ($P<0.01$). In addition, patients with type 2 diabetes were more concerned about weight gain than patients with type 1 diabetes ($P=0.04$).

### 3.3. *Association between patients' adherence to insulin injection and independent factors*

Association between adherence to insulin injection based on the MMAS method in patients with type 1 and 2 diabetes and potential barriers are shown in Tables 3 and 4.

Factors that showed a significant association with insulin compliance in both groups were: being a time consuming process; embarrassment; feeling worse after injections; forgetfulness; sick days; experience of hypoglycemia; medication cost; weight gain; insulin shortage; and difficulties in preparing injection.

In patients with type 1 diabetes there was a significant inverse correlation between insulin compliance and BMI while a significant correlation with lack of enough injection instructions or injection site pain was only noted in patients with type 2 diabetes.

Although patients who were considered adherent according to MMS had a better compliance to physical activities, the difference was only significant in patients with type 1 diabetes

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**Table 2 – Distribution of possible barriers to insulin adherence in patients with type 1 and type 2 diabetes.**

| Barrier | Total ($n=508$) | Type 1 ($n=251$) | Type 2 ($n=257$) | P-value |
|---|---|---|---|---|
| **Injection device** | | | | 1.00 |
| Syringe | 462 (90.9) | 228 (90.8) | 234 (91.1) | |
| Pen | 46 (9.1) | 23 (9.2) | 23 (8.9) | |
| Incapability for self injection | 138 (27.2) | 79 (31.5) | 59 (23.0) | 0.03 |
| **Number of daily injections** | | | | |
| 1 | 41 (8.0) | 13 (5.2) | 28 (10.9) | <0.01 |
| 2 | 330 (65.0) | 149 (59.4) | 181 (70.4) | |
| ≥3 | 137 (27.0) | 89 (35.4) | 48 (18.7) | |
| **Interference with** | | | | |
| Usual daily activities | 99 (19.5) | 38 (15.1) | 61 (23.7) | 0.01 |
| Meal planning | 136 (26.8) | 53 (21.1) | 83 (32.2) | <0.01 |
| Physical activities | 313 (61.6) | 120 (47.8) | 200 (78.1) | <0.01 |
| Being time consuming | 321 (63.2) | 233 (92.8) | 224 (87.5) | 0.12 |
| Difficult to inject | 187 (36.8) | 228 (90.8) | 215 (84.0) | 0.06 |
| Injection site pain | 100 (19.7) | 176 (70.1) | 188 (73.4) | 0.69 |
| Injection site reactions | 458 (90.2) | 120 (47.8) | 148 (57.8) | 0.03 |
| Weight gain | 12 (2.4) | 2 (0.8) | 10 (3.9) | 0.04 |
| Embarrassment | 137 (27.0) | 122 (48.6) | 68 (26.5) | <0.01 |
| Fear of hypoglycemia | 444 (87.4) | 198 (78.9) | 224 (87.2) | 0.53 |
| Forgetfulness | 53 (10.4) | 17 (6.8) | 36 (14.0) | <0.01 |
| Belief in negative effects of insulin on overall health | 129 (25.4) | 46 (18.3) | 83 (32.3) | <0.01 |
| Lack of enough injection instructions | 306 (59.6) | 152 (60.6) | 154 (59.9) | 0.89 |
| Feeling worse after insulin injection | 24 (4.7) | 6 (2.4) | 18 (7) | 0.02 |
| Polypharmacy | 31 (6.1) | 7 (2.8) | 24 (9.3) | <0.01 |
| Sick days | 61 (12.0) | 18 (7.2) | 43 (16.7) | <0.01 |
| Cost | 13 (2.6) | 6 (2.4) | 7 (2.7) | 1.00 |
| Insulin shortage | 15 (3.0) | 4 (1.6) | 11 (4.3) | 0.11 |

Variables are expressed as *n* (%).

($P=0.02$). On the other hand, patients adherent to insulin therapy also had a better compliance to medical nutrition therapy and this difference was only significant among patients with type 2 diabetes ($P=0.02$). Moreover, persistence with insulin therapy was more common among adherent patients with both type 1 and type 2 diabetes ($P=0.02$ and $P<0.01$ respectively).

## 4. Discussion

In spite of the importance of adherence to insulin for achieving therapeutic goals, there is lack of evidence about the rate of adherence to insulin therapy and associated risk factors.

Current study revealed that according to the Morisky Green test, 85.7% of patients with type 1 diabetes and 71.2% of patients with type 2 diabetes had intermediate to high adherence. Higher adherence in patients with type 1 diabetes may be related to the understanding of these patients about the more crucial role of insulin injection for glycemic control and a higher possibility of life threatening events as a result of insulin omission compared to patients with type 2 diabetes who have residual insulin secretions.

Unexpectedly, based on the autocompliance method almost all patients were adherent. In this study there was a great discordance between results of the two study methods which might be partly due to overestimated medication adherence by the autocompliance method. Although self-reporting methods are considered as a convenient and cheap way to assess medication adherence, review of prescription records may lead to more accurate results, but such a database was not available for our population which may indicate that patients over-report their adherence when using direct questions for measuring compliance.

In comparison to other studies, Morris et al. found evidence of poor adherence to insulin therapy among young patients with type 1 diabetes. They noted that 28% of patients obtained less insulin compared with their prescribed dose according to pharmacy record data [10]. Similarly, results of another study revealed that nearly one-third of prescribed insulin doses were prepared by young patients with type 2 diabetes, and estimated adherence was 62–64% among patients with type 2 diabetes [16]. In 2007, Donnelly et al. reported poor adherence in 1099 patients with type 2 diabetes. Seven years pharmacy record data revealed a $70.6\% \pm 17.7\%$ mean adherence to insulin among these patients. Patients with advanced age, an older age at diagnosis, a lower BMI or who were more socially active, had higher adherence [6]. Whereas, Cramer et al. measured adherence using pharmacy records during the 2 year study period, results revealed good intentions to follow the prescribed insulin regimen as patients used, on average, 77% of prescribed doses [9].

Findings of the current study are in line with those of Donnelly et al. and indicate that participants with type 2 diabetes have poor adherence. In contrast participants with type 1 diabetes had acceptable compliance.

Please cite this article in press as: S. Farsaei, et al., Insulin adherence in patients with diabetes: Risk factors for injection omission, Prim. Care Diab. (2014), http://dx.doi.org/10.1016/j.pcd.2014.03.001

**Table 3 – Association between potential barriers and insulin adherence in patients with type 1 diabetes.**

| Barrier | Low adherence ($n = 36$) | Intermediate to high adherence ($n = 215$) | P-value |
|---|---|---|---|
| Sex, male[b] | 18 (50) | 110 (51.2) | 0.90 |
| Age, years[a] | 21.4 (9.6) | 20.5 (10.0) | 0.61 |
| BMI[a] | 23.3 (5.5) | 21.2 (4.3) | 0.01 |
| Duration of diabetes, years[a] | 6.7 (5.6) | 8.5 (7.5) | 0.24 |
| Duration of insulin injection, years[a] | 6.5 (5.6) | 8.3 (7.4) | 0.22 |
| **Educational status**[b] | | | |
| Student | 17 (47.2) | 119 (56.1) | 0.05 |
| Under diploma | 8 (22.2) | 18 (8.5) | |
| Diploma | 8 (22.2) | 39 (18.4) | |
| University | 3 (8.4) | 36 (17.0) | |
| Insulin daily dose, unit[a] | 50.7 (27.4) | 43.7 (23.9) | 0.11 |
| **Injection device**[b] | | | |
| Insulin pen | 3 (8.3) | 20 (9.3) | 0.85 |
| Syringe | 33 (91.7) | 195 (90.7) | |
| Incapability for self injection[b] | 11 (30.6) | 68 (31.6) | 0.90 |
| Number of daily injections[b] | | | 0.37 |
| 1 | 2 (5.5) | 11 (5.1) | 0.47 |
| 2 | 28 (77.8) | 121 (56.3) | |
| ≥3 | 6 (16.7) | 83 (38.6) | |
| **Interference with**[b] | | | |
| Physical activities | 13 (36.1) | 81 (37.7) | 0.90 |
| Meal planning | 10 (27.8) | 43 (20.0) | 0.29 |
| Usual daily activities | 9 (25.0) | 29 (13.5) | 0.08 |
| Time consuming[b] | 7 (19.4) | 11 (5.1) | <0.01 |
| Difficulties with injection[b] | 5 (13.9) | 18 (8.4) | 0.30 |
| Injection site pain[b] | 8 (22.2) | 67 (31.2) | 0.28 |
| Embarrassment[b] | 3 (8.3) | 1 (0.5) | <0.01 |
| Injection site reactions[b] | 16 (44.4) | 104 (48.4) | 0.66 |
| Fear of hypoglycemia[b] | 29 (80.6) | 169 (78.6) | 0.80 |
| Belief in negative effects of insulin on overall health[b] | 9 (25.0) | 37 (17.2) | 0.26 |
| Feeling worse after insulin injection[b] | 5 (13.9) | 1 (0.5) | <0.01 |
| Forgetfulness[b] | 7 (19.5) | 10 (4.7) | <0.01 |
| Lack of enough injection instructions[b] | 3 (8.3) | 10 (4.7) | 0.36 |
| Sick days[b] | 9 (25) | 9 (4.2) | <0.01 |
| Polypharmacy[b] | 1 (2.8) | 6 (2.8) | 0.99 |
| Hypoglycemia episodes[b] | 17 (47.2) | 39 (18.1) | <0.01 |
| Cost[b] | 3 (8.3) | 3 (1.4) | 0.01 |
| Weight gain[b] | 2 (5.6) | 0 (0.0) | <0.01 |
| Insulin shortage[b] | 3 (8.3) | 1 (0.5) | <0.01 |
| Difficulties in preparing injection[b] | 2 (5.6) | 0 (0.0) | <0.01 |

[a] Continuous variables are expressed as mean (SD).
[b] Categorical variables are expressed as *n* (%).

Demographic and disease characteristics of patients may have association with insulin omissions [8]. Results of this work indicate that the pattern might be different in patients with type 1 and type 2 diabetes. Patients with type 1 diabetes are more dependent on their care givers for insulin injections and also they were more embarrassed regarding insulin injections, these were barriers that were more frequently reported by patients with type 1 diabetes than type 2. However in this study, there was a significant relationship between compliance and embarrassment in both studied groups.

The emotional burden of injection may interfere with psychological well-being. In a review of psychological barriers to initiation and persistence with insulin therapy, different strategies to decrease psychological insulin resistance have been introduced [17]. Furthermore, interventions to improve the relationship between health care providers and patients seem to be beneficial for overcoming psychological insulin barriers [18] which need to be implemented in our health care services.

Moreover, there are several device based strategies to reduce embarrassment including insulin pens, which could be considered to overcome this barrier to insulin injections.

Because patients with type 1 diabetes are more commonly on intensive insulin injections, the number of daily insulin injections was higher compared with patients with type 2 diabetes. Peyrot et al. showed more frequent insulin omission among patients taking more injections [8]. This could indicate that the more complex regimens are associated with lower levels of adherence. However, the number of daily injections was not significantly related to adherence in our studied population.

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**Table 4 – Association between potential barriers and insulin adherence in patients with type 2 diabetes.**

| Barrier | Low adherence ($n=74$) | Intermediate to high adherence ($n=183$) | $P$-value |
|---|---|---|---|
| Sex, Male[b] | 25 | 64 | 0.86 |
| Age, years | 55.9 (10.1) | 55.1 (12.0) | 0.60 |
| BMI[b] | 28.8 (4.8) | 27.5 (4.8) | 0.06 |
| Duration of diabetes, years[a] | 13.9 (7.8) | 14.1 (8.3) | 0.90 |
| Duration of insulin injection, years[a] | 4.0 (4.1) | 4.2 (4.8) | 0.92 |
| Educational status[b] | | | 0.47 |
| Illiterate | 16 (21.6) | 39 (21.3) | |
| Under diploma | 41 (55.4) | 87 (47.5) | |
| Diploma | 14 (18.9) | 41 (22.4) | |
| University | 3 (4.1) | 16 (8.7) | |
| Insulin daily dose. unit[a] | 51.8 (26.7) | 52.5 (28.6) | 0.86 |
| Injection device[b] | | | 0.21 |
| Insulin Pen | 4 (5.4) | 12 (6.6) | |
| Syringe | 70 (94.6) | 164 (89.6) | |
| Incapability for self injection[b] | 16 (21.6) | 43 (23.5) | 0.75 |
| Number of daily injections[b] | | | 0.60 |
| 1 | 6 (16.7) | 22 (12.0) | |
| 2 | 55 (74.3) | 126 (68.9) | |
| ≥3 | 13 (36.1) | 35 (19.1) | |
| Interference with[b] | | | |
| Physical activities | 30 (40.5) | 62 (33.9) | 0.31 |
| Meal Planning | 24 (33.8) | 59 (32.2) | 0.98 |
| Usual daily activities | 15 (20.3) | 46 (25.1) | 0.41 |
| Time consuming[b] | 15 (20.3) | 17 (9.3) | 0.02 |
| Difficulties with injection[b] | 16 (21.6) | 25 (13.7) | 0.12 |
| Injection site pain[b] | 13 (17.6) | 55 (30.1) | 0.04 |
| Embarrassment[b] | 9 (12.2) | 1 (0.5) | <0.01 |
| Injection site reactions[b] | 48 (64.9) | 100 (54.6) | 0.13 |
| Fear of hypoglycemia[b] | 60 (81.1) | 132 (72.1) | 0.14 |
| Belief in negative effects of insulin on overall health[b] | 30 (40.5) | 53 (29.0) | 0.07 |
| Feeling worse after insulin injection[b] | 14 (18.9) | 4 (2.2) | <0.01 |
| Forgetfulness[b] | 30 (40.5) | 6 (3.3) | <0.01 |
| Lack of enough injection instructions[b] | 6 (8.1) | 4 (2.2) | 0.03 |
| Sick days[b] | 22 (29.7) | 21 (11.5) | <0.01 |
| Polypharmacy[b] | 9 (12.2) | 15 (8.2) | 0.32 |
| Hypoglycemia episodes[b] | 42 (56.8) | 31 (16.9) | <0.01 |
| Cost [b] | 5 (6.8) | 2 (1.1) | 0.01 |
| Weight gain[b] | 8 (10.8) | 2 (1.1) | <0.01 |
| Insulin shortage [b] | 9 (12.2) | 2 (1.1) | <0.01 |
| Difficulties in preparing injection[b] | 4 (5.4) | 1 (0.5) | 0.01 |

[a] Continuous variables are expressed as mean (SD).
[b] Categorical variables are expressed as $n$ (%).

Patients with type 2 diabetes had more complaints regarding interference of insulin injections with their activities and meal planning which might be related to more social engagements and less flexible lifestyle according to their age group. Although these factors did not affect adherence significantly another study showed that interference with eating and exercise played roles as barriers to insulin therapy [8].

Replacement of short acting regular insulin with rapid acting insulin analogs is advisable in these patients and may ameliorate their problem.

Use of multiple medications was another factor more frequently reported by type 2 patients as influencing insulin omission than type 1 in our study. Multidrug regimens providing medical care to patients with type 2 diabetes may have negative impact on adherence [19]. Polypharmacy is more required in type 2 than type 1 patients to control other metabolic risk factors such as hyperlipidemia and hypertension in addition to hyperglycemia [20] and may partly be related to advanced age. However, in contrast to other reports, polypharmacy was not significantly associated with lower adherence in our study.

Forgetfulness was raised more by patients with type 2 diabetes, which could be frequent problems for their age group. These patients were more concerned regarding insulin induced weight gain than the type 1 group, which may be due to higher prevalence of obesity in this patient population. This work also indicate that patients with type 2 diabetes are more prone to stop insulin injections during illness than patients

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with type 1 diabetes, which may be related to an underestimation of the role of insulin by patients with type 2 diabetes and poor patient knowledge. These factors were associated with lower level of adherence.

In this study more patients with type 2 diabetes declared that insulin injection had negative impact on their overall health than type 1 diabetes, which needs to be managed by addressing the common misconceptions and negative attitudes regarding insulin therapy in educational programs and incorporating patient-centered treatment alliance in practice, which may improve health belief and attitude toward insulin injection.

Despite ease of administration and dosing accuracy of insulin pens, in the studied population, minority of patients (9.1%) were using insulin pens which may be due to the great difference in medication cost compared to syringes. At the time of the study, insulin pens were 15–20 times more expensive than insulin vials and pen devices were not under medication insurance coverage, which had resulted in 45–60 times more out of pocket expenses.

There are piles of evidence which support the advantages of pen devices over syringes for improving insulin adherence, which in most cases simultaneous reduction in healthcare utilization and overall treatment costs has been reported [21].

In this study medication cost had a significant relationship with low compliance, which is in line with other reports in patients with diabetes [22–24]. Although at time of the present study insurance companies covered 70% of the cost of insulin vials, still medication cost was considered as a barrier to insulin injections. In order to address this barrier, pressure of financial barriers should be buffered by changing the insurance schemes to reduce patient co-payments [25]. Moreover, some studies indicate that addressing non-cost barriers to adherence may also decrease the tendency to medication underuse while encountering cost related problems [26,27].

In the current study patients with type 1 and type 2 diabetes with lower adherence had experienced more hypoglycemic episodes and were more concerned about weight gain.

We noted that almost all patients periodically missed doses as they were concerned about the possibility of insulin induced hypoglycemia. This was associated with an overall lower adherence and has been reported previously by Peyrot et al. [28]. Other studies also reported that patients with diabetes on insulin therapy who experienced hypoglycemia had lower adherence because they had experienced an unpleasant or dangerous situation that had changed their behaviors [29].

Moreover, specific risk factors for the development of hypoglycemia should be addressed in individuals. Hypoglycemia awareness and management should be considered as part of educational programs for patients and caregivers. In corroboration, some studies have indicated that educational programs can significantly reduce the risk of severe hypoglycemia [30,31]. Additionally, behavioral interventions that focus on habituation may be beneficial adjuncts to educational strategies to prevent hypoglycemia. Besides, changing to insulin analogs may also reduce hypoglycemia risk. Since insulin analogs in our country are exclusively available as pen devices, results of the present study indicate under usage of these insulins in our population, which could be mainly due to the high cost of insulin analogs.

To manage weight gain problem, some patients intentionally omit their insulin injections as a weight management plan [32]. A well-integrated health system is needed to incorporate a customized program of medical nutrition therapy and physical activity in therapeutic strategies.

Forgetfulness and insulin omission during sick days were more common in patients with low compliance.

This may reflect that future interventions should also focus on family support, reminder systems and telemedicine. Increasing awareness through patient education and family engagement in implementation of specific measures to target insulin injection barriers may be associated with higher adherence among patients with diabetes.

In one study, pain and embarrassment associated with insulin injection resulted in insulin omission but skin bruising, dissatisfaction with time needed for injection, and ease of insulin use did not affect insulin therapy [8]. This study suggests that dissatisfaction with time needed for injection, embarrassment, and difficulties in preparing injections was associated with lower adherence in patients with both type 1 and type 2 diabetes, which could all be mitigated by changing to insulin pens.

Injection site pain and lack of enough injection instructions had a statistically significant relationship with lower adherence exclusively in patients with type 2 diabetes. This might reflect the requirement for reinforced injection instructions in patients with type 2 diabetes probably due to their age group.

On the other hand, moderate to high adherent patients with type 1 diabetes had higher educational attainment compared to low adherence patients. It shows that planning strategies to improve adherence should be intensified for patients educated to a lower level.

In the current study, insulin persistence was more common in adherent patients which may indicate that barriers are common to both practices.

Considering factors influencing skipping insulin doses could be helpful to plan proper strategies to improve adherence among patients with diabetes.

A large sample of patients with diabetes mellitus was recruited in this study, however, more adherent patients might have been more interested to be involved in this study and therefore we may have overestimated adherence. In this study objective methods for measurement of insulin use such as refill data were not used. Therefore, patients might have perceived themselves more adherent compared to other studies measuring adherence by refill data. Moreover, we did not evaluate the correlation between adherence and HbA1c and health outcome.

In conclusion, there is no single solution to overcome compliance barriers in our studied population, but results indicate that changing to insulin pens might alleviate most of detected barriers and significantly improve patient compliance.

Recently insulin pens have become under the coverage of insurance companies in our country and authors of the present study are assessing its effect on patients' compliance.

## Conflict of interest

The authors state that they have no conflict of interest.

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## Acknowledgement

This study was supported by Tehran University of Medical Sciences (TUMS); Grant No: 10736-33-02-89.

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