Original Article

Pattern of anti-diabetic treatment and its relation with glycaemic control among diabetic patients in a tertiary care hospital of Bangladesh

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ABSTRACT

Background: *The main determinants of diabetes management, therapeutic habits and glycaemic control are likely to differ between populations. The pharmacological armamentarium to treat hyperglycaemia in type 2 diabetes mellitus (T2DM) has changed substantially over the past few years with the development of new therapeutic agents. This study evaluated relationships between pattern of pharmacological treatment and glycaemic control in patients with T2DM.*

Methods: *This cross-sectional study was carried out among 486 T2DM patients attending the endocrinology outpatient clinic of MARKS Medical College & Hospital, Dhaka, Bangladesh during the period between July 2018 and June 2019. After obtaining written informed consent, both the treatment pattern and the degree of glycaemic control were estimated from T2DM patients. Glycosylated hemoglobin A1C (HbA1c) was determined by liquid chromatography. Glycaermic control categorized as fair control (HbA1c <7.0%), poor control (HbA1c ≥7.0%- <9.0%) and very poor control (HbA1c ≥9.0%).*

Results: *Out of 486 participants, 65.8% were females. A total 68.1% of the patients were treated with oral anti-diabetic drugs (OADs) and 31.9% were treated with both insulin and oral agents. Metformin (92.4%) was the most commonly used OAD; [p=0.01]. Over one fifth (22.1%) were taking combinations of sulfonylurea and metformin [p<0.05] and 19.5% were taking combination of sulfonylurea, metformin and dipeptidyl peptidase-IV inhibitors (DPP4i); [p=0.87]. More than one fourth (25.7%) were treated with two OADs along with insulin; [p=0.05]. In this context, familiar dual OADs combination (14.2%) was metformin and DPP4 inhibitors [p=0.86]. Premixed insulin (17.1%) was the frequently used regimen among different regimen of insulin used in both OADs and insulin group [p=0.22]. More than 50% of the subjects attained fair glycaemic target of HbA1c. But 46.3% accomplished poor and very poor glycaemic control [p=0.08].*

Conclusion: *The study shows that the proportion of patients treated with only oral diabetic agent was high. In most instances, they were treated with two or three drus combination therapies. The proportion of patients with fair glycaemic control was higher than reports from many countries.*

Keywords: *anti-diabetic treatment, glycaemic control, type 2 diabetes mellitus.*

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INTRODUCTION

Diabetes mellitus is a chronic disease with a high prevalence and a growing concern worldwide. As per World Health Organization (WHO), the total number of people with diabetes is projected to rise to 366 million in 2030[1], but International Diabetes Federation (IDF) estimated that the situation is much worse as the burden would increase from 417 million (2030) to 486 million (2045). The IDF estimated[1] 8.4 million people with diabetes in Bangladesh and 4.7 million people with

undetected diabetes. This number is estimated to double by 2045. There is no cure for this disease and it requires continuing medical care and education to prevent acute complications and to reduce the risk of long-term complications.[2,3]

Glycemic control, however, is not an easy task for many patients. It is well known that even in clinical trials and routinely in clinical practice, the majority of patients fail to achieve good glycemic control.[4] Although diet and lifestyle changes are initially effective, most patients will need an oral glucose-lowering agent to control blood glucose levels and most will eventually need multiple therapies as the disease progresses.[5] The pharmacological armamentarium to treat hyperglycaemia in type 2 diabetes mellitus (T2DM) has changed substantially over the past 20 years with the development of new therapeutic agents, such as insulin secretagogues (glinides), thiazolidinediones, incretins (glucagon like peptide-1 receptor agonists [GLP-1RA] and dipeptidyl peptidase-IV inhibitors ([DPP4i]), sodium-glucose transporter-2 inhibitors (SGLT2i), fixed dose combinations and also with the advent of insulin analogues.[6] This, together with changing treatment recommendations advocating for an intense glycaemic control in early stages of the disease,[7] makes drug choice increasingly challenging and it has driven substantial changes in current prescribing practices with wide variations between countries depending on each therapeutic class.[8-10] Key factor for long-term success of pharmacotherapy in T2DM is the dependence on patients continuing to take their medications as prescribed.[11,12] Suboptimal persistence can lead to compromised health outcomes.[13]

Providing information based on real-world data may be a useful way to explore the dynamics of anti-diabetic therapy within a specific context and to optimize the use of resources for a better management of the disease. General practice databases are a reliable and rich source of information from the general population and therefore a valuable tool to study medical practice in the community.[14] The present study aimed to examine prescribing patterns for anti-diabetic medications and how this pattern impacted the degree of attained glycaemic control in patients with T2DM.

METHODS

Study design and patient population

This cross-sectional study was carried out among 486 T2DM patients attending the outpatient department of the endocrinology outpatient clinic of MARKS Medical College & Hospital in Dhaka, Bangladesh from July 2018 to June 2019.

Eligibility criteria

All the patients that had these characteristics were included in the study:

i) Patients diagnosed with T2DM for one year or more;

ii) Patients who had received at least one prescription of anti-diabetic drug (AD) or insulin during the study period;

iii) Patients receiving the current ADs for a period of at least three months or more.

Patients without any record of ADs prescription in one year preceding the index date and receiving only one prescription (spot users) were excluded from the analysis.

Upon screening, patients were given an information sheet which explained the purpose of the study. Participation was voluntary and they were able to refuse participation in or withdraw from the study. Only the patients who met the inclusion criteria and signed consent form were recruited in this study.

Data collection

Data including demographic features were collected using a semi-structured questionnaire through face to face interview of patients and review of respective prescription of ADs. The questionnaire also covered the respondent's demographic and clinical information which included: age, sex, having education on diabetes, regular physical exercise, dietary plan and biochemical parameter of glycaemic status. The ethical permission was obtained from the respective authority of the hospital.

Anthropometric and laboratory measures

Anthropometric measurements of height and weight were measured by a reliable height scale and weighing scale, respectively.[15] Body mass index (weight in kilograms/square of height in meters (kg/m^2) was calculated. Blood pressure was measured by a manual sphygmomanometer in standard conditions (measured 2 times after a 5-min rest between each measurement). Waist circumference was measured in a horizontal plane, midway between the inferior margin of the ribs and the superior border of the iliac crest using a reliable measuring inch tape.[16]

Serum samples were used for glucose analysis (fasting and post prandial) on a glucose analyzer (Beckman

Coulter, Auto Analyzer). Glycosylated hemoglobin A1c (HbA1c) was determined by liquid chromatography. Glycaermic control was categorized as: fair control (HbA1c < 7.0 %), Poor control (HbA1c ≥7.0 %- < 9.0%) and very poor control (HbA1c ≥9.0%).

Patterns of utilization of anti-diabetic medication

Users of ADs were stratified in different categories according to their latest prescription (persistence for ≥3 months) during the study period: metformin, sulfonylurea, DPP-4i, SGLT2i, thiazolidinediones, alpha-glucosidase inhibitors, glucagon-like peptide-1 receptor agonists (GLP- 1RAs) etc.

Patients were on different combinations of oral blood glucose-lowering drugs were classified as mono, dual and triple anti-diabetic drugs therapy categories.

For patients, who were on concomitant ADs and insulin, were categorized as combination group of anti-diabetic drugs and insulin. The patients who were on insulin were stratified into different insulin regimen groups: premixed, basal and basal plus or bolus group.

Statistical analysis

Continuous variables were reported as means and standard deviations (SD). Categorical data were reported as counts and percentages. For continuous variables, the two-sample t-test was carried out. While for categorical variables, the chi-square test was applied. Analysis was carried out using statistical package for social science (SPSS) software version 16. All statistical tests were two-sided and a p-value less than 0.05 was considered statistically significant, unless specified otherwise. If a p-value was less than 0.001, it was reported as <0.001.

RESULTS

Baseline characteristics

Out of 486 participants, 65.8% were females and 34.2% were males. The mean age of the study subjects was 46.23 ± 9.54(±SD) years. Average BMI (kg/m^2) was 26.08 ± 3.78 (±SD). Mean waist circumference (cm) was 87.08 ± 7.05 (±SD) (Table I).

Glycaemic status of the patients

Blood glucose pattern is shown in Table II. There was significant difference of mean HbA1c between male and female subjects [p=0.01] (Table II).

Table I Comparison of demographic, anthropometric and clinical parameters in between male and female subjects (N=486)

Variable		Male	Female	Total
Age (yrs)	(Mean ±SD)	48.45±1.00	45.07±9.04	46.23±9.54
Height (m)	(Mean ±SD)	1.62±0.07	1.53±0.09	1.56±0.09
Weight (kg)	(Mean ±SD)	66.66±1.03	62.05±9.34	63.62±9.92
BMI (kg/m^2)	(Mean ±SD)	25.39±3.66	26.43±3.80	26.08±3.78
WC (cm)	(Mean ±SD)	86.59±5.56	87.34±7.71	87.08±7.05
SBP (mm Hg)	(Mean ±SD)	124.73±14.93	122.19±15.76	123.06±15.51
DBP (mm Hg)	(Mean ±SD)	81.71±7.21	81.12±9.19	81.34±8.56
Duration of DM (yrs)	(Mean ±SD)	4.63±3.77	4.62±3.76	4.62±3.76
Do regular exercise	N (%)	139 (28.6)	236 (48.6)	375 (77.2)
Follow diet plan	N (%)	121 (24.9)	205 (42.2)	326 (67.1)

BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; DM: diabetes mellitus

Table II Comparison of glycaemic status in between male and female subjects (N=486)

Variables	Male (Mean ±SD)	Female (Mean ±SD)	Total (Mean ±SD)	p value
FBS (mmol/L)	8.30±2.35	8.96±7.18	8.73±5.99	0.249
PPBG (mmol/L)	12.52±3.70	12.56±5.30	12.55±4.81	0.927
HbA1C (%)	7.87±1.09	7.64±0.90	7.72±0.97	0.014

FBS: fasting blood glucose; PPBG: post prandial blood glucose.

Prescribing pattern of anti-diabetic medication

Among 486 diabetic patients, 68.1% were treated with only oral anti-diabetic drugs (OADs) and 31.9% were treated with both insulin and oral agent [p=0.29]. Among oral anti-diabetic drugs, most common one (92.4%) was the metformin [p=0.01] (Table III & IV).

In most instances (37.7%), patients were treated with dual combination of OADs [p=0.65]. Most familiar dual combination were sulfonylurea and metformin (22.2%) [p<0.05] and triple combination were sulfonylurea, metformin and DPP4 inhibitors in OADs alone treatment group (19.5%) [p=0.87].

Commonly, insulin was used along with dual OADs combination (25.7%) [p=0.05]. In this context, familiar dual OADs combination (14.2%) was metformin and DPP4 inhibitors [p=0.86]. Premixed insulin (17.1 %) was the frequently used regimen among different regimen of insulin used in both OADs & insulin group [p=0.22] (Table IV &V).

Table III Distribution of different types of anti-diabetic medication among subjects (N=486)

Types of ADs medication	Male [N (%)]	Female [N (%)]	Total [N (%)]	p value
SU	112 (23.0)	249 (51.2)	361 (74.3)	0.013
Metformin	160 (32.9)	289 (59.5)	449 (92.4)	0.011
DPP4i Inhibitors	72 (14.8)	123 (25.3)	195 (40.1)	0.207
SGLT2	27 (5.6)	73 (15.0)	100 (20.6)	0.096
GLP-1 Ra	6 (1.2)	5 (1.0)	11 (2.3)	0.198
Others	0 (0.0)	0 (0.0)	0 (0.0)	

ADs: anti- diabetic drugs; SU: sulfonylurea; DPP4i inhibitors: inhibitors of dipeptidyl peptidase 4; SGLT2 inhibitors: sodium-glucose co- transporter- 2 inhibitors; GLP-1 Ra: glucagon-like peptide-1 receptor agonists; Others: thiazolidinediones, repaglinide, alpha-glucosidase inhibitors etc.

Table IV Prescribing pattern of anti-diabetic medication among diabetic subjects (N=486)

Prescribing pattern of anti-diabetic medication		Male [N (%)]	Female [N (%)]	Total [N (%)]	p value
Treatment type	OAD only	108 (22.2)	223 (45.9)	331 (68.1)	0.299
	Both OAD& insulin	58 (11.9)	97 (20.0)	155 (31.9)	
Number of OADs used in	Mono	2 (0.4)	7 (1.4)	9 (1.9)	0.657
OADs alone group	Dual	59 (12.1)	124 (25.5)	183 (37.7)	
	Triple	47 (9.7)	92 (18.9)	139 (28.6)	
Number of OADs used in both	Mono	8 (1.6)	4 (0.8)	12 (2.5)	0.057
OADs & insulin group	Dual	46 (9.5)	79 (16.3)	125 (25.7)	
	Triple	4 (0.8)	14 (2.9)	18 (3.7)	
Types of different regimen of	Premixed	36 (7.4)	47 (9.7)	83 (17.1)	0.229
insulin used in both OADs &	Basal	22 (4.5)	49 (10.1)	71(14.6)	
insulin group	Basal Plus/Bolus	0 (0.0)	1 (0.2)	1(0.2)	

OAD: Oral anti- diabetic drugs

Table V Distribution of different combination of OADs among different treatment group (N=486)

Different treatment groups		Male [N (%)]	Female [N (%)]	Total [N (%)]	p value
OADs only group					
Combination of dual OADs	SU+ Met	33 (6.8)	75 (15.4)	108 (22.2)	0.005
	Met+DPP4i	16 (3.3)	10 (2.1)	26 (5.3)	
	Met+SGLT2	5 (1.0)	11 (2.3)	16 (3.3)	
	SU+SGLT2	5 (1.0)	28 (5.8)	33 (6.8)	
Combination of triple OADs	SU+Met+DPP4i	31 (6.4)	64 (13.2)	95 (19.5)	0.879
	SU+Met+SGLT2	17 (3.5)	29 (6.0)	46 (9.5)	
Both OADs & insulin group					
Combination of dual OADs	SU+ Met	17 (3.5)	38 (7.8)	55 (11.3)	0.864
	Met+DPP4i	24 (4.9)	45 (9.3)	69 (14.2)	
Combination of triple OADs	SU+Met+DPP4i	5 (1.0)	15 (3.1)	20 (4.1)	0.378

OADs: oral anti- diabetic drugs; SU: sulfonylurea; Met: metformin; DPP4 inhibitors: inhibitors of dipeptidyl peptidase 4; SGLT2 inhibitors: sodium-glucose co- transporter- 2 inhibitors.

Evaluation of glycaemic control and its association with pattern of anti-diabetic medication

More than 50% of the subjects attained fair glycaemic target of HbA1c. But 46.3% accomplished poor and very poor glycaemic control [p=0.08] (Figure 1).

A total 38.7% of the patients treated with only OADs and 15.0% of the both insulin and oral agent treated group achieved fair glycaemic control [p=0.12]. Among OADs only group, 12.8% of patients treated with dual combination of sulfonylurea and metformin attained fair glycaemic control [p=0.03]. In contrast, 9.7% of the triple combination of OADs treated group (sulfonylurea, metformin and DPP4 inhibitors) acquired fair glycaemic control [p=0.29]. Among different insulin regimen in both OADS and insulin treated group, premixed group (7.8%) earned good glycaemic control [p=0.21] (Table VI).

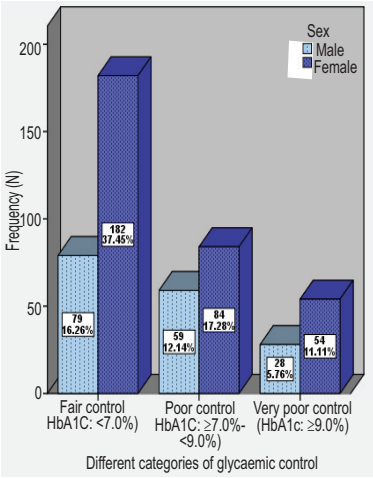

Figure 1 Types of glycaemic control according to HbA1C among study subjects (N=486)

DISCUSSION

An increase in the use of combinations of oral anti-diabetic drugs (OADs) has been consistently observed in several studies from different countries,[8,9,17] but the trends in its use as monotherapy vary among reports, with some describing an overall increase over time[18] and others a progressive decrease.[8,17] DPP4i is the class of newly developed OADs with the greatest increase in use, which is in agreement with other reports conducted worldwide.[17-19] This rapid adoption, mainly as an alternative to sulfonylurea, may respond to the lower risk of hypoglycaemia, its neutral effects on body weight and also the greater convenience of an oral treatment instead of the need of injections for GLP-1Ra or insulin.[20] Metformin was the most frequently used OAD in this study, as recommended by international guidelines.[21] In the current study, most familiar combination of dual OADs were sulfonylurea and metformin [p<0.05] and triple OADs combination were sulfonylurea, metformin and DPP4 inhibitors [p=0.87].

A regulatory warning of cardiovascular risk associated with rosiglitazone[22] and risk of bladder cancer with pioglitazone in 2011[23] alerted clinicians to prescribe

Table VI Comparison of glycaemic control in different pattern of treatment groups (N=486)

Different treatment groups	Glycaemic control(According to HbA1C)			
	Fair control[N (%)]	Poor control[N (%)]	Very poor control[N (%)]	pvalue
OADs only	188(38.7)	92 (18.9)	51 (10.5)	0.128
Both OADs & insulin	73 (15.0)	51 (10.5)	31 (6.4)	
OADs only group				
Combination of dual OADs				
SU+ Met	62(12.8)	34 (7.0)	12(2.5)	0.031
Met+DPP4i	18 (3.7)	4 (0.8)	4 (0.8)	
Met+SGLT2	10(2.1)	1 (0.2)	5 (1.0)	
SU+SGLT2	17 (3.5)	6 (1.2)	10 (2.1)	
Combination of triple OADs				
Su+Met+DPP4i	47(9.7)	36 (7.4)	12(2.5)	0.297
SU+ Met +SGLT2	27(5.6)	11(2.3)	8(1.6)	
Different regimen of insulin in combination of OADS & insulin group				
Pre mixed	38(7.8)	25 (5.1)	20(4.1)	0.210
Basal	35 (7.2)	25 (5.1)	11(2.3)	
Basal plus/bolus	0(0.0)	1 (0.2)	0(0.0)	

OAD: oral anti- diabetic drugs; SU: sulfonylurea; Met: metformin; DPP4 inhibitors: inhibitors of dipeptidyl peptidase 4; SGLT2 inhibitors: sodium-glucose co- transporter- 2 inhibitors.

Fair control- HbA1C: <7.0%; Poor control- HbA1C: ≥7.0%- <9.0%; Very poor control- HbA1C:≥9.0%

these drugs. Though both side effects have been recently ruled out,[23,24] but the influence of these alarms has omitted its use. This inclination is also noted in our study. Least use of GLP-1Ra in our study is similar to that of a recent study conducted in the UK[25] showed the marginal use of GLP-1Ra.

Moreover, while the number of prescriptions of insulin in combination with an OAD has been shown to increase with time[8,9,18] the use of insulin alone has been reported to remain stable[19] to decrease[8] or even to increase.[18] We believe that insulin therapy is underutilized among our study population. In this study, only 31.9 % of patients were treated with insulin in combination with OADs.

When we imposed the attained glycaemic control based on the treatment pattern, we found that there were no remarkable differences among patients on OADs alone or in combination with insulin regimen. This is in line with the results of several studies showing a delay in treatment intensification in patients already on combination therapies whose control of blood glucose remained or became inadequate.[26] Moreover, we found that about half of the patients had HbA1c levels <7% as recommended by clinical guidelines[21], which is higher than reports from many countries.[27] But the proportion of patients with poor glycemic control was still high [p=0.08].

Conclusion

This study showed that the proportion of patients treated with only oral diabetic agent was high. In most instances, they were treated with dual or triple combination therapies. Insulin therapy in our study population is underutilized. Most often, patient was treated with insulin along with dual combination of oral diabetic agents. The proportion of patients with fair glycaemic control is higher than reports from many countries. But the proportion of patients with poor glycemic control deserves attention. There is a need to address the issue of the importance of maintaining good glycemic control by all means through utilizing different treatment modalities in order to prevent or retard diabetes complications at the national and individual levels.

Author's contribution: Concept & design, Data analysis & interpretation, Drafting & preparation of final manuscript.

Conflicts of interest: Nothing to declare.

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REFERENCES

1. IDF Diabetes Atlas, 9th edn. Brussels, Belgium: 2019. Available at:https://www.diabetesatlas.org
2. Mooradian A. Cardiovascular disease in type II diabetes mellitus: current management guidelines. Arch Intern Med 2003; 163: 33–40.
3. IDF (2012) Diabetes atlas, 5th ed. via http://www.idf.org/diabetesatlas/5e/the-global burden: Accessed 2012 November 20.
4. Akbar D, Al-Gamdi A .Common causes of admission in diabetics. Saudi Med J 2000; 21: 539–42.
5. Turner RC, Cull CA, Frighi V, Holman RR. Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49).UK Prospective Diabetes Study (UKPDS) Group. JAMA1999; 281:2005–12.
6. Bailey CJ. The current drug treatment landscape for diabetes and perspectives for the future. Clin Pharmacol Ther 2015; 98:170–84.
7. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA.10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med2008;359:1577–89.
8. Baviera M, Monesi L, Marzona I, Avanzini F, Monesi G, Nobili A. Trends in drug prescriptions to diabetic patients from 2000 to 2008 in Italy's Lombardy region: a large population-based study. Diabetes Res ClinPract 2011;93:123–30.
9. Chang CH, Jiang YD, Chung CH, Ssu-Wei C, Yu Ko. National trends in anti-diabetic treatment in Taiwan, 2000–2009. J Formos Med Assoc2012;111:617–24.
10. Leal I, Romio SA, Schuemie M, Dídac M. Prescribing pattern of glucose lowering drugs in the United Kingdom in the last decade: a focus on the effects of safety warnings about rosiglitazone. Br J Clin Pharmacol 2013;75:861–8.
11. Lamberts EJ, Nijpels G, Welschen L M, Hugtenburg J G, Souverein P C, Bouvy M L. Long term patterns of use after initiation of oral antidiabetic drug therapy. Pharmacoepidemiol Drug Saf 2011;20, 351–8.
12. Orlando V, Guerriero F, Putignano D, Monetti V M, Tari D U, Farina G, et al. Prescription patterns of antidiabetic treatment in the elderly. Results from southern Italy. Curr Diabetes Rev 2015;12 (2):1–7.
13. Rascati K L, Worley K, Meah Y, Everhart D. Adherence, persistence, and health care costs for patients receiving dipeptidyl peptidase-4 inhibitors. J Manag Care Spec Pharm 2017;23 (3): 299–306.
14. Lawrenson R, Williams T, Farmer R. Clinical information for research; the use of general practice databases. J Public Health Med 1999;21:299–304.
15. Glumer C, Jorgensen T, Borch-Johnsen K. Targeted screening for undiagnosed diabetes reduces the number of diagnostic tests. Inter Diabet Med 2004; 21: 874–80.
16. Smith Liz. New AHA recommendations for blood pressure measurement: American Heart Association Practice Guide-lines. Am Fam Physician 2005; 72(7): 1391–8.
17. Turner LW, Nartey D, Stafford RS, Singh S, Alexander GC. Ambulatory treatment of type2 diabetes in the U S, 1997–2012. Diabetes Care2014;37:985–92.
18. Oishi M, Yamazaki K, Okuguchi F, Sugimoto H, Kanatsuka A, Kashiwagi A, et.al. Changes in oral antidiabetic prescriptions and improved glycemic control during the years 2002–2011 in Japan (JDDM32). J Diabetes Investig 2014;5:581–7.
19. Kohro T, Yamazaki T, Sato H, Harada K, Ohe K, Komuro I, Nagai R. Trends in antidiabetic prescription patterns in Japan from 2005 to 2011. Int Heart J 2013;54:93–7.
20. Karagiannis T, Paschos P, Paletas K, Matthews DR, Tsapas A. Dipeptidyl peptidase-4 inhibitors for treatment of type 2 diabetes mellitus in the clinical setting: systematic review and meta-analysis. BMJ 2012;344:e1369.
21. American Diabetes Association. Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes-2018. Diabetes Care 2018;41(Suppl 1):S73–S85.
22. Nissen SE, Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. N Engl J Med2007;356:2457–71.
23. Swinnen SG, Hoekstra JB, DeVries JH. Insulin therapy for type 2diabetes.Diabetes Care 2009;32(Suppl 2):S253–9
24. Lewis JD, Ferrara A, Peng T, Hedderson M, Bilker WB, Quesenberry CP, et al. Risk of bladder cancer among diabetic patients treated with pioglitazone: interim report of a longitudinal cohort study. Diabetes Care 2011;34: 916–22.
25. Sharma M, Nazareth I, Petersen I. Trends in incidence, prevalence and prescribing in type 2 diabetes mellitus between 2000 and 2013in primary care: a retrospective cohort study. BMJ Open 2016;6:e010210.
26. Mata-Cases M, Benito-Badorrey B, Roura-Olmeda P, Franch-Nadal J, Pepió-Vilaubí JM, Saez M, et al. Clinical inertia in the treatment of hyperglycemia in type 2 diabetes patients in primary care. Curr Med Res Opin 2013;29:1495–502.
27. Angamo MT, Melese BH, Ayen WY. Determinants of Glycemic Control among Insulin Treated Diabetic Patients in Southwest Ethiopia: Hospital Based Cross Sectional Study. PLoS ONE 2013;8(4): e61759.