

Glycemic Control and Accompanying Risk Factors: 4-Year Primary Care Study

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Abstract

Objective: This study is to assess the glycemic control and the other risk factors like LDL, blood pressure readings and body mass index for type 2 diabetes mellitus (T2DM) in 8 primary care centers over 4 years of time.

Methods: An observational, retrospective cohort, multicenter study which was conducted in 8 National Guard primary health care centers. Four of the centers were located in Riyadh; while the others are from different regions in Saudi Arabia. A stratified random sampling method was used according to number of diabetic patients at each center

The main study outcomes were to measure the mean HbA1c, LDL levels, blood pressure and BMI readings and the percentage of diabetic patients who reached the ADA goal of HbA1c, LDL, and blood pressure and how it changed during 4 years of time. Also the percentage of adults with diabetes who have HbA1c<0.07 and the changes of controlled patients within the study period.

Results: Total number of type-2 diabetic patients of this study was 778, with mean age of 55.03 ± 11.4, 62.7% of them were females. The mean of the HbA1c was 8.7 on 2006 and reduced to 8.6 within four years, 16.6% of diabetic patients had their last HbA1c reading reached the HbA1c goal (≤7%). The LDL and diastolic blood pressure decreased also within the follow up years insignificantly (-0.299 and -1.37). While the systolic blood pressure and BMI increased over 4 years of time (+0.58 and +0.27). HbA1c level shows a significant relation with the education levels in 2007 and 2008. HbA1c also prove a significant relation with LDL for three years in sequence. Age and BMI had a significant relation with the systolic blood pressure.

Conclusion: Poor glycemic control has serious impact not only on patients but on the society. The primary health care setting and structure were not well-prepared to properly manage diabetes and its related comorbidities.

Keywords: Diabetes mellitus; HbA1c; Glycemic control; Quality of care; Risk factors; Hypertension; Obesity; Dyslipidemia; High lipid

Introduction

Diabetes is a chronic disease with complex causes, manifestations, complication, and management. It is a chronic disease which is considered a major cause of death, illness and reduce quality of life [1]. Diabetes is gradually becoming a global health issue. The disease imposes huge public health and economic burdens that affect the society before the individuals. As estimated by International Diabetes Federation, there were 366 million people suffering from diabetes worldwide in 2011, and most probably by 2030 this figure will rise to 552 million. Diabetes also caused 4.6 million deaths and at least 465 billion US dollars in healthcare expenditures [2]. Moreover, the prevalence of type 2 diabetes is also increasing dramatically in the Middle East and North Africa region [3].

Type 2 diabetes is known to be a disease of disordered lipid metabolism as well as a disease of abnormal glucose metabolism [4]. Hemoglobin A1c (HbA1c) is a standard measure of glycemia over 2–3 months [5]. Nowadays, there is a contemporary tendency to focus on HaemoglobinA1c (HbA1c) rather than Fasting Plasma Glucose (FPG) or oral glucose tolerance test (OGTT) in the diagnosis of diabetes [6].

It was proved that patients with HbA1c ≥ 6.5% have more critical cardiovascular and metabolic risks than those with HbA1c<6.5%, especially in OGTT-negative population. This is clinically important because it indicates that patients with HbA1c ≥ 6.5% and normal OGTT may not be at low hazard as previously thought, and more intensive management should be preceded. Also an increase of 1% in HbA1c is associated with an approximately 40% increased risk of coronary heart disease and 30% increased risk of all-cause mortality after adjusting for

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other risk factors [7]. There are many factors causing the poor control of diabetes related to patients, healthcare professionals and health care system [8].

HbA1c testing should be performed routinely in all patients with diabetes; first, to document the degree of glycemic control at initial assessment, and second, as part of continuing care. The HbA1c level for patients to maintain in general is to be of <7%. Lowering HbA1c has been associated with a reduction of many microvascular and neuropathic complications of diabetes [9-12]. But there is a deficiency treating the diabetic patients especially in the developing countries.

This study aimed to assess glycemic control and changes in glycemic control and other risk factors over 4 years in patients with type 2 diabetes mellitus (T2DM) treated at primary health setting.

Literature Review

Type-2 Diabetes mellitus presents an epidemic proportions in Saudi Arabia, throughout the country with exceedingly high rates concentrated in urban areas [13]. A national survey indicates that the overall prevalence of DM is 23.7%. [14,15] and despite the readily available access to healthcare facilities, a large number of diabetics, 27.9%, were unaware of having DM [16]. A recent national study found that diabetes mellitus affects 1,745,532 persons with prevalence of 13.45%, 16.6% of them were adequately controlled (HbA1c of \leq 7%) [17].

The majority of diabetic patients are not receiving recommended levels of healthcare [18-20] and there is large variation in how often people with diabetes receive these recommendations. There are 20-90% of diabetics who receive an HbA1c test annually, those who have HbA1c levels <7% are 12- 40% [21-23], nearly one-third do not have a retinal examination; foot examinations were not documented for 33-94% of patients. Additionally, many patients had elevated and untreated hypertension and lipid abnormalities [24].

There is accumulated evidence from well conducted studies confirming the relationship between proper glycemic control and reduction or prevention of diabetic complications. UKPDS showed that patients receiving intensive treatment over 10 years had 11% decrease HbA1c and 10% reduction in any diabetes-related complication [9,11,25-27].

However, the percentage of patients who reached the glycemic goal vary between studies, but generally it is unexpectedly low. It ranges between 15-50% [17].

Materials and Methods

Study design

An observational, retrospective cohort study conducted between 1st January 2006 and 31st December 2009.

Study setting

The study was conducted on medical records collected from 8 primary health care centers belonging to National Guard Health Affairs-Saudi Arabia. Four of the targeted centers were located in the capital of Riyadh and the other 4 are in Qassim, Arar, Rafha, and Najran.

Study subjects

The study included only charts of patients who were 18 years old or older and are known to have type II diabetes mellitus, who received

any type of anti-diabetic treatment. Records lacking follow up notes of 12 months or more between 2006 and 2009 were excluded from the study. Also, records that indicate patient refusal to accept treatment or discontinuation of management against medical advice during this period were excluded from the study.

Sampling method and sample size calculation

Records of diabetic subjects in the primary care centers represented the sampling frame. Stratified sampling method was used. Each of the 8 targeted primary care centers was considered a stratum and sampled using simple random sampling method. After calculating the total sample size required, the number of records obtained from each center was calculated in proportion to the total number of diabetics served by that center.

The total number of diabetics in all the clinics was estimated to be 200,000 based on 20.22% prevalence of adult diabetes mellitus in Saudi Arabia (IDF country records). The sample size was calculated based on the percent of diabetic patients with optimum HbA1c of 7.0 or less. We assumed that 50% of diabetics in our clinics have well controlled diabetes. Using a 95% confidence interval, margin of error of 4% and 1.5 design effect (this will increase the sample size by 50% to account for imperfections in the sampling method) the sample size was calculated using open-Epi online epidemiologic calculator. The calculator used can be accessed online at: <http://www.openepi.com/SampleSize/SSPropor.html>

The total number of records required for the study was 898 of which 120 were excluded due to incomplete data. The total number of records included in the analysis was 778.

HbA1c, LDL, HDL determination

Measurement of HbA1c is key in monitoring and long-term management of patients with diabetes, thus its measurement should be optimally accurate and precise. Recent developments in medical technology allow clinicians to determine HbA1c test results during a patient's office visit. Several manufacturers offer an assay that can be done by trained medical staff and yield HbA1C results in minutes. The National Glycohemoglobin Standardization Program (NGSP) certifies methods annually at the manufacturer level. Every laboratories should use only HbA1c assay methods that are certified by the (NGSP).

The guideline shows that, the desirable specifications for Hb A1C measurement are an intralaboratory coefficient of variation (CV) should be less than 2% and an interlaboratory (CV) should be less than 3.5%.

LDL: Our laboratory is using the MULTIGENT Direct LDL assay; it is a homogeneous method for directly measuring LDL levels in serum or plasma, without the need for off-line pretreatment or centrifugation steps. This detergent solubilizes only the non-LDL particles. The cholesterol released is consumed by cholesterol esterase and cholesterol oxidase in a non-color-forming reaction. A second detergent solubilizes the remaining LDL particles and a chromogenic coupler allows for color formation. The enzyme reaction with LDL in the presence of the coupler produces color that is proportional to the amount of LDL cholesterol present in the sample.

HDL: Our laboratory is using the Ultra HDL assay; it is a homogeneous method for directly measuring HDL cholesterol concentrations in serum or plasma without the need for off-line

pretreatment or centrifugation steps. The method uses a two-reagent format and depends on the properties of a unique detergent.

Data collection

Data were collected using data collection form created by the authors of the study. The form included non-identifying patient demographics, patient lab records (biomarkers) and associated comorbidities. Data collection staff received special training to be able to use the form and record the data in a standardized manner. Data collection was conducted between March 2010 and May 2011.

Data management

IBM Statistical Package for Social Science (SPSS) version 20 was used for data entry and analysis. Data were entered into a unified SPSS database by trained data entry clerks.

Data analysis

Categorical variables were summarized using simple frequency and percentage. Continuous variables summarized using arithmetic mean and standard deviation.

Comparing proportions was performed principally using Chi square test. Fisher exact test was used when the assumptions for Chi square were violated.

Comparing two means was carried out using independent group student t-test. ANOVA was used to compare more than two means when needed. When significant differences detected by ANOVA, Post Hoc analysis was carried out using Bonferroni test.

All statistical tests were bidirectional. Statistical significance was set to 0.05 or less for all statistical tests.

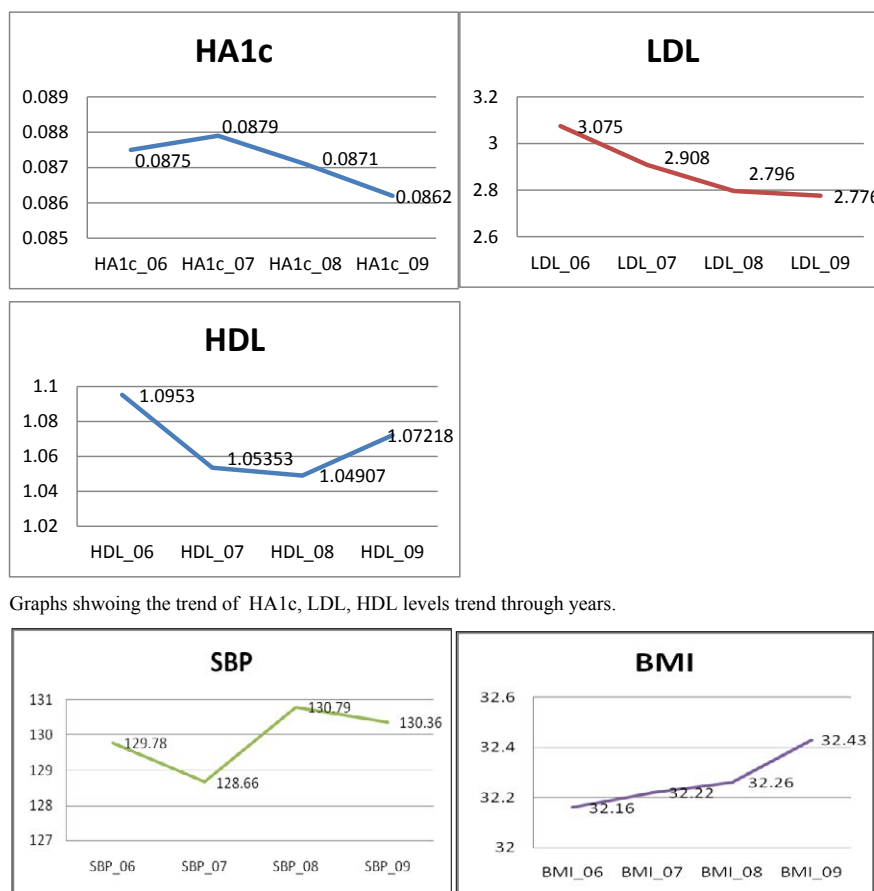
Results

Socio-demographic characteristics

The study included 778 patients from 8 primary care centers inside Saudi Arabia. The mean age of patients was 55.03 ± 11.4 ; the highest percentage of age group is 51-64 (41.51%), then 31-50 (36.81%). Elderly people >65 years old is 20.7%, and female patient is predominant 62.7%. Most study subjects were married 89.4%, illiterate 55.6%, and housewives 39.2%.

HbA1c

The mean HbA1c reduced from 8.75 (2006) to 8.63 (2009) with no significant difference (P value of T-test = 0.147). Diabetic patients who reached the HbA1c goal increased from 12.6% in 2006 to 16.6% in 2009 with P value<0.00, while the poorly controlled (HbA1c>0.09) reduced from 63.8% in 2006 to 46.9% in 2009 with P value<0.001 (chi square test), reduction is consistent through the 4 years follow-up (Figure 1).



Graphs showing the trend of HA1c, LDL, HDL levels trend through years.

Graphs showing the trend of SBP, DBP, BMI levels trend through years.

Figure 1: Four Year's Trend for 6 important variables.

LDL

The mean LDL was 3.08 (2006) reduced to 2.8 (2009). Those who reached the LDL goal ($LDL \leq 2.6$) was around 53% over the 4 years with a significant difference between groups in the beginning to the end of the study with P value of $\chi^2 < 0.00$.

SBP and DBP

The mean SBP was $129.8 \pm SD 19.2$ (2006) increased to 130.4 ± 17.50 (2009).

Diabetic patients who were uncontrolled ($SBP \geq 130$) were increased over the 4 years of follow-up, from 28.9% (2006) to 39.6 (2009). Uncontrolled Systolic Blood Pleasure increased too from 17.4 of the sample in (2006) to 19.9 (2009). While the mean DBP in general was 77.29 (2006) reduced to 76.42 (2009), both variables differences between 2006 and 2009 are significantly different with P value of < 0.00 .

BMI

The mean BMI was 32.16 ± 5.9 (2006) which increased to $32.43 \pm$

SD 5.7 (2009). The percentage of obesity increased during the years of follow-up from 40.2% (2006) to 48.4% (2009). The difference gave a significant difference P value of $\chi^2 < 0.00$.

HbA1c relationships

HbA1c 2006 and 2009 had no significant relationships with sex, age, education or BMI levels. While in 2007 and 2008, it is showing a significant relationship with education level with P value of $\chi^2 < 0.01$. HbA1c had significant relationship with LDL in 2006, 2007 and 2008 excluding 2009 with P value of $\chi^2 < 0.001$.

SBP has significant relationship with age groups in 2006 to 2009 with a P value of One way Anova < 0.001 , also with BMI in 2006 and 2007 P value $\chi^2 < 0.005 - 0.020$ and HbA1c in 2008 P value (0.032). These results were also presented in linear graph (Figure 1). Number of diabetic patient who had annual eye and foot examination increased from 30% (2006) to almost 50% (2009) presented in Figure 2.

Figure 3 shows that the oral hypoglycemic drugs were highly used

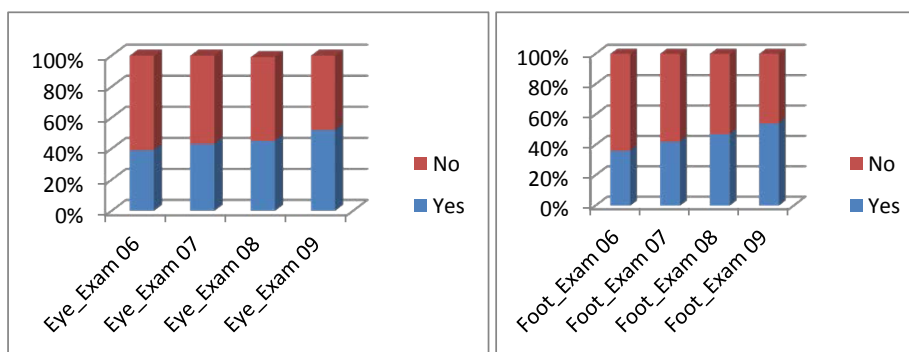
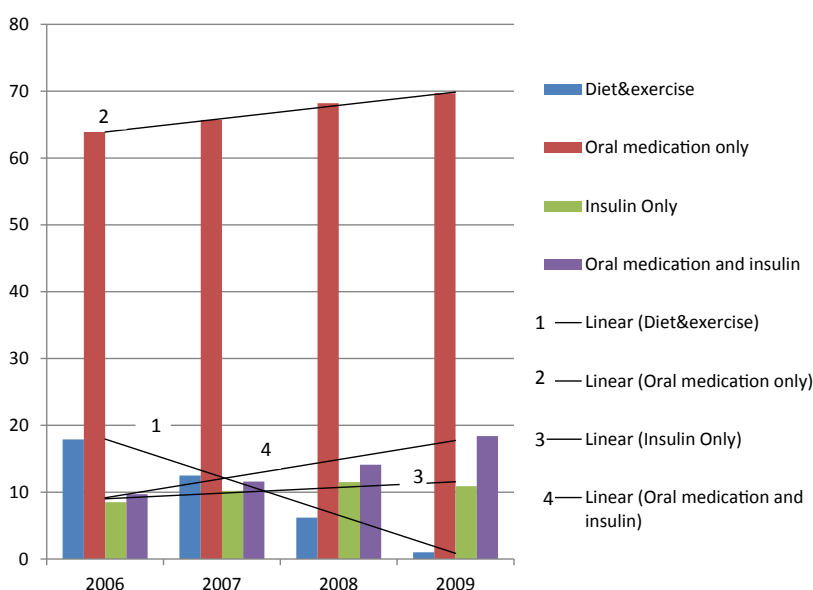


Figure 2: Percentage of Diabetic Patients who performed Annual Eye and Foot Exam.



Cluster bar chart showing trends in different DM treatment modalities.

Figure 3: 4 years trend of antidiabetic medications.

among the participants with 60% in 2006 to 70% in 2009, while insulin use over the 4 years was only around 10%.

Discussion

Our study showed that 16.6% of diabetic patients were adequately controlled (last HbA1c reading at 2009 of $\leq 7.0\%$), while the mean in the 4 years follow-up is 13.55%. This is similar to the results of a recent national study in Saudi Arabia which showed that 16.6% were adequately controlled (HbA1c of $\leq 7\%$) [17]. These findings were far less than RECAP-DM study findings were 27% of diabetic patients in 7 European countries have HbA1c of $<6.5\%$, (RECAP study) and 31% in CODE study and 33.5% in US study [28,29]. Other study showed even better HbA1c readings which reached up to 47% [30,31].

Although the overall percentage of adequately controlled patients was low (16.6% last reading at 2009) compared to other studies, the percentage of poorly controlled diabetic patients (HbA1c $>9.0\%$) was reduced over the follow up period of the study from 63.8% (2006) to 46.9% (2009), a reduction of -16.7% in 4 years duration. However, the mean HbA1c was almost similar during the study period (8.75 at 2006 to 8.63 at 2009), [32] found that the mean HbA1c of 7.6 ± 1.6 . This was lower than our study's findings.

The barriers behind the poor control of diabetes in our setting were many, but they can be grouped into health professional factors, patient's factors, health system factors and disease factors.

Diabetes is a progressive disease due to gradual decline in mass and function of B-cells in the pancreas, which requires PHC physicians to intensify the medication prescribed to their patients from OHD to insulin therapy.

Primary care physicians are at the frontline for providing the best care to diabetic patients because they encounter and manage more diabetic patients than the diabetologists. However, there are many factors affecting this role [33,34], early insulin initiation in the course of diabetic management of poorly controlled cases has been proven to reduce and prevent the long-term diabetes complications [35-37]. However, there was delay and underuse in insulin therapy, as 83% of study participants were uncontrolled, however 10% only were on insulin therapy (Tables 1-3). Studies showed that insulin initiation was delayed for two to five years after trials and failures of oral hypoglycemic medications [26,38]. One substantial factor is the Psychological Insulin Resistance (PIR), defined as psychological resistance towards insulin therapy, among patients and healthcare providers [8,39].

Diabetes is a silent disease, patients need to be monitored and reinforced on a regular basis and enrolled in a structured diabetic care program at PHC settings. The program includes periodic assessment and a regular complication screening by a diabetes team and enforcing diabetic self-care program. Such programs reduced HbA1c from 8.4 to 6.9 and increased the adequately controlled HbA1c from 30% to 63% in one year duration [27,40,41].

The mean LDL was reduced from 3.1 mmol/dl (2006) to 2.8 mmol/dl (2009), a change of only -0.3 mmol/dl and almost half (52.5%) of diabetic patients had their LDL reached the goal (LDL <2.6 mmol/dl) in 2006. This percentage was almost maintained during the follow-up period. Studies showed wide variation of the percentage of those who reached the LDL goal (15% to 87%) [30,31]. The problem in our study in addition to the modest control of LDL was that our PHC providers failed to make significant change in the number of controlled patients, dislike the findings of Ackermann study who reported the positive change of 20.5% [42].

Variable	No	%
Age		
30 and less	8	1
31-50	286	36.8
51-64	323	41.5
65 and more	161	20.7
Sex		
Male	293	37.3
Female	493	62.7
Marital Status		
Single	15	1.9
Married	707	89.4
Divorced	8	1
Widow	61	7.7
Education Level		
Illiterate	429	55.6
Primary	223	28.9
Intermediate	45	5.8
Secondary	47	6.1
University graduate	27	3.5
Occupation		
Teacher	10	1.3
Military	141	17.8
Unemployed	311	39.2
Retired	114	14.4
Others	217	27.4

Table 1: Patient's socio-demographic characteristics.

Unfortunately, there was deterioration of the percentage of diabetic patients who had their systolic BP controlled (from 71.1% in 2006 to 60.4% in 2009), this was in contrast to the findings of one study which reported that 6.4% had positive change [42]. Diabetics who had ideal systolic BP varies between 29% to 73% [30,31,43].

Obesity is progressively worsened among diabetic patients which may be due to insulin therapy and other medication, poor glycemic control and diabetic complications [44,45].

When associated with diabetes, obesity may cause insulin resistance, hypertension, increased risk of cardiovascular diseases and other complications of obesity [46].

On the other hand, weight reduction improves diabetes and the need for anti-diabetic medication [47]. Obesity and overweight were progressively increased among our patients in the expense of normal weight patients. Obesity increased from 40.5% (2006) to 48.4% (2009), this finding was much higher than other studies [47,48].

Conclusion

Diabetes affects the community in two ways. First, its prevalence increases, and second, its severity increases and become more aggressive during the course of the disease. It is evident that proper controlling of diabetes, obesity, LDL and hypertension reduce diabetic complications. The current primary health care centers' structure to properly manage diabetes and the other related risk factors is suboptimal.

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Variable	2006		2007		2008		2009		*P value
	No.	%	No.	%	No.	%	No.	%	
HA1c									
Target =< 0.07	100	12.6	91	11.5	107	13.5	132	16.6	0.000
Optimal (controlled) =< 0.08	98	12.4	124	15.6	138	17.4	164	20.7	
Uncontrolled >0.08 - < 0.09	89	11.2	101	12.7	120	15.1	125	15.8	
Poorly controlled > 0.09	505	63.8	477	60.2	428	54.0	372	46.9	
LDL									
Controlled =< 2.6	416	52.5	433	54.6	434	54.7	420	53.0	0.000
Uncontrolled > 2.6	377	47.5	460	45.4	359	45.3	373	47.0	
SBP									
Controlled =< 130	564	71.1	565	71.2	500	63.1	479	60.4	0.000
Uncontrolled > 130	229	28.9	228	28.8	293	36.9	314	39.6	
DBP									
Controlled =< 85	655	82.6	656	82.7	644	81.2	635	80.1	0.000
Uncontrolled > 85	138	17.4	137	17.3	149	18.8	158	19.9	
BMI									
Normal	260	36.6	223	32	199	29.3	166	24.7	0.000
Overweight	163	22.9	163	23.4	171	25.1	180	26.8	
Obese1	164	23.1	177	25.4	175	25.7	180	26.8	
Obese2	75	10.5	79	11.3	79	11.6	89	13.3	
Morbid Obesity	49	6.9	55	7.9	56	8.2	56	8.3	

*P value of chi-square comparison of 2006 and 2009 within variables

Table 2: Percentage per year of important variables' categories for 4 years.

	2006		2007		2008		2009		*P value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
HA1c	.08750	.019081	.08799	.018759	.08710	.018627	.08628	.019376	0.147
LDL	3.07523	.949100	2.90858	.922470	2.79688	.827124	2.77625	.888498	0.000
SBP (last reading)	129.78	19.175	128.66	18.676	130.79	18.030	130.36	17.502	0.867
DBP (last reading)	77.79	8.899	76.87	9.052	76.73	9.371	76.42	9.241	0.000
BMI	32.16	5.907	32.22	5.894	32.26	5.856	32.43	5.793	0.002
BUN	5.080	1.4800	5.115	2.2203	4.962	1.7366	5.158	2.3898	0.118
Creatinin	83.5316	51.79371	80.7730	19.12130	79.6151	49.83476	76.0155	45.65241	0.034

*P value of T-test comparison of mean between 2006 and 2009 variables.

Table 3: Mean and standard deviation per year of important variables' categories for 4 years.

financially gain or lose from publishing this study. Moreover, there are no patents relating to the content of the manuscript.

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