The association between glycemic, lipids and blood pressure control among Israeli diabetic patients

A. ELIS\textsuperscript{1,2}, L. ROSENMANN\textsuperscript{3}, G. CHODICK\textsuperscript{2,3}, A.D. HEYMANN\textsuperscript{2,3}, E. KOKIA\textsuperscript{3} and V. SHALEV\textsuperscript{3}

From the \textsuperscript{1}Department of Medicine, Meir Medical Center, Kfar Saba, \textsuperscript{2}Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv and \textsuperscript{3}Maccabi Healthcare Services, Tel-Aviv, Israel

Received 3 July 2007 and in revised form 29 October 2007

Summary

Background: It is recommended that in diabetes mellitus patients all risk factors for cardiovascular disease should be controlled.

Aim: To evaluate the rate of reaching all glycemic, lipids and blood pressure target levels among diabetic patients in Israel and to analyze demographic and clinical parameters associated with it.

Design: A cross-sectional study.

Methods: The study was conducted in Maccabi Healthcare Services, Israel’s second largest health maintenance organization. All patients ($n = 41,936$), older than 20 years, who were listed on Maccabi Healthcare Service’s diabetes mellitus computerized database and had all three study parameters ($\text{HbA1c, LDL-C and blood pressure levels during 2005}$) were eligible for the study. The rate of reaching $\text{HbA1c <7.0\%, LDL-C <100 mg/dl and blood pressure <130/85 mmHg}$, as well as its association with various demographic and clinical parameters were analyzed.

Results: Only 13\% of all study patients achieved all three target levels. The parameters which were significantly associated with goal achievement were compliance to medical treatment for all three parameters (OR 1.56, 95\% CI 1.44–1.69, $P = 0.0001$), male gender (OR 1.42, 95\% CI 1.31–1.54, $P = 0.0001$), comorbidity with ischemic heart disease (OR 1.23, 95\% CI 1.13–1.34, $P = 0.0001$), and $>12$ visits per year to family physician (OR 1.10, 95\% CI 1.02–1.19, $P = 0.012$).

Conclusion: Non-compliance with treatment and sub-optimal follow-up by family physicians are associated with increased risk of failure to control major risk factor among diabetic patients.

Introduction

It has been shown that adherence to clinical guidelines can improve the quality of health care while increasing the efficiency of health services and constraining expenditures.\textsuperscript{1,2} These advantages have been specifically demonstrated for the care of diabetes mellitus (DM) which imposes a huge burden of morbidity and mortality, due to micro- and macro-vascular complications.\textsuperscript{3}

The American Diabetes Association’s (ADA’s) guidelines for treatment of DM emphasize the importance of controlling all risk factors for cardiovascular disease (CVD), e.g. blood pressure (BP) be reduced to $<130/85$ mmHg, LDL-C level to $<100$ mg/dl and HbA1c level to $<7.0\%$.\textsuperscript{4,5} Nevertheless, based on previous studies, these guidelines are usually not fulfilled and only about 3\% of the patients achieve the goal levels of all three parameters.\textsuperscript{6–8} These studies comprised of small study groups and did not correlate their findings with demographic and clinical parameters.

The aim of the study was to evaluate the rate of achievement of the combined target levels of...
HbA1c, LDL-C and BP among DM patients in Israel and to analyze demographic and clinical parameters associated with it.

Methods

Settings

This is a cross-sectional study undertaken by Maccabi Healthcare Services (MHS), the second largest Health Maintenance Organization (HMO) in Israel serving a population of 1.6 million, ~24% of the total population. According to the National Health Act in Israel—1994, MHS may not bar applicants on any ground, including age or state of health. Thus, all Israeli population sectors are represented in MHS. Since 1997 diagnoses of MHS members are downloaded daily to a central computer, and the database is automatically updated with all hospitalizations, visits to outpatient clinics, primary and secondary care physicians, and prescribed medication purchases. In addition MHS has developed and validated computerized registries of its patients suffering from ischemic heart disease, diabetes and oncology diseases.

Study population

All MHS members, older than 20 years, who were diagnosed as suffering from DM before 1 January 2005 were eligible for the study. The diagnosis of DM was based upon one of the following criteria: HbA1c >7.25%; serum glucose level >200 mg/dl on at least two occasions within a period of at least 30 days; purchasing insulin or oral hypoglycemic medications at least twice in a period of 3 months. Patients who died or left MHS during 2005 or lacked at least one of the study parameters (BP, LDL-C or HbA1c) were excluded from the study.

Data collection

The study period was 1 January 2005 to 31 December 2005. For each patient the following data were collected: demographic variables [age, gender, date of immigration to Israel (new immigrant was defined as one who immigrated to Israel after 1999)]; most recent values of LDL-C and HbA1c levels—last values in 2005; for BP—mean of the last two measures during 2005 or the last if only one was found; kidney function tests according to mean serum creatinine during 2005 (renal failure was defined as mean serum creatinine level >1.5 mg/dl); coexistence of ischemic heart disease (IHD) (based on the MHS computerized cardiology register); treatments for diabetes (insulin/oral hypoglycemics), for hypertension (ACE inhibitors/A2 antagonists/calcium channel blockers/beta blockers/alpha blockers/diuretics) and for dyslipidemia (statins/ fibrates/ezetemibe) according to purchases in MHS pharmacies; follow-up by a dietician; the number of family physician visits and hospitalizations.

Compliance with drug treatment was defined as the purchase of at least 80% of the amount of their recommended medications from 1 January 2005 or from the date of the first prescription in 2005.

The levels of each study parameter were categorized as follows: For HbA1c: <7.0% (optimal); 7–8% (suboptimal); 8–9% (poor); >9.0% (very poor). For LDL-C <100 mg/dl (optimal): 100–130 mg/dl (suboptimal); 130–160 mg/dl (poor); >160 mg/dl (very poor). For systolic BP (SBP): <130 mmHg (optimal); 130–140 mmHg (suboptimal); 145–160 mmHg (poor); >160 mmHg (very poor). For diastolic BP (DBP): <85 mmHg (optimal); 85–100 mmHg (suboptimal); >100 mmHg (poor).

Outcome variables

The study outcome variable was defined as the proportion of MHS’ DM patients with optimal management of cholesterol (LDL<100 mg/dl) glycemic control (HbA1c <7.0%), and blood pressure (<130/85 mmHg) during 2005.

The study was approved by the MHS institutional review board.

Statistical analysis

The data was analyzed by using descriptive statistical procedures for calculating frequencies and percentages, along with cross-tabulation chi-squared tests for categorical variables. Logistic regression model was used to estimate the factors which influenced the probability to reach the combined target level. All analyses were conducted by using SPSS 14.0 (SPSS, Chicago, Ill).

Results

There were 69 553 diabetic patients in MHS on 1 January 2005. Patients who died or left MHS during 2005 (n=2160, 3%) and those who lacked at least one of the study parameters (BP, LDL-C, HbA1c) (n=25 457, 37%) were excluded. The rest, 41 936 patients (60%), older than 20 years, had all three study variables in the computerized files available and were included in the study. The study group included 21 607 men and
20,329 women. Their mean age was $61 \pm 12$ and $63 \pm 12$ years, respectively.

### Study parameters

Figure 1 describes the percentage of patients within the different levels of each study parameter. Diabetes control (HbA1c <7.0%) was achieved by 59% of the patients. Fifty-one percent of the patients had systolic blood pressure (SBP) of <130 mmHg, and 82% of them had diastolic blood pressure (DBP) of <85 mmHg. Hypercholesterolemia was the least controlled parameter with 40% of the patients at LDL-C level <100 mg/dl.

Furthermore, about one-fifth of the patients were poorly controlled in at least one parameter. Twenty percent of the study group had HbA1c $>8.0$, 27% had LDL-C levels $>130$ mg/dl, while 19% had systolic BP $>145$ mmHg (Figure 1).

### Reaching the combined target levels

Thirteen percent ($n = 5392$) of the patients reached all 3 target levels, e.g. HbA1c $<7.0$, LDL-C $<100$ mg/dl and BP $<130/85$ mmHg. Thirty percent ($n = 12,794$) were at optimum levels for HbA1c and BP, 25% ($n = 10,332$) were at optimum levels for HbA1c and LDL-C, 20% ($n = 8,529$) were at optimum levels for BP and LDL-C.

When using sub-optimal target levels: LDL-C $<110$ mg/dl, HbA1c $<7.5$, BP $<140/90$ mmHg, the rate of patients who reached the combined target levels increased to 26%.

### Association between reaching the combined target levels and demographic and clinical parameters

#### Gender

More males than females achieved all three target levels (14.7% vs. 10.9%, $P < 0.0001$).

#### Age

The differences in the rates of reaching the combined target level by age were statistically significant, although the clinical significance of these differences is doubtful (20–40 years: 14.5%; 40–60 years: 12%; 60–80 years: 13.5%; >80 years: 12.5%; $P = 0.0001$). The same trend was found when age analysis was stratified according to gender.

#### Recent immigration to Israel

There was a statistically significant difference in achieving ADA’s recommendations between the 3147 (7.5%) new immigrants and all other patients (11% vs. 12%, $P = 0.041$). Again, the clinical significance of this slight difference is questionable.

#### Renal failure and ischemic heart disease

Six percent ($n = 2520$) of the study group had renal failure. There was a borderline statistical significance of reaching the combined target level between those with and without renal failure (13.7% vs. 12.7%, $P = 0.081$).
Twenty-two percent (9372 patients) had IHD. Seventeen percent of the IHD patients achieved all three target levels, while only 12% of those without IHD achieved it ($P < 0.0001$).

Follow-up by dietician
During 2005, 9337 (22%) of the patients were followed by a dietician. There was a statistical trend for reaching the combined target levels (13.3% of the patients who were followed by a dietician vs. 12.7% of those who were not followed reached the combined target levels, $P = 0.06$, respectively).

Family physician visits
The study group patients’ median number of family physicians’ visits during 2005 was 12. When comparing the subjects who had >12 visits to those who had <12 visits, more patients in the first group achieved the combined target levels (13.6% vs. 12.1%, $P < 0.001$).

Hospitalizations
Seventeen percent (7296) of the patients were hospitalized during 2005. There was no significant association between hospitalization and reaching the combined target levels (12.8% of the hospitalized patients vs. 13.1% of those who were not hospitalized, $P > 0.05$).

Medications and compliance
Medications to control all three parameters were prescribed to half of the study group patients. Nevertheless, it did not predict reaching the combined target levels. Only 50% of the patients who reached the combined target level used medications to control all three parameters, whereas 87% of the patients who used these medications did not reach the combined target levels.

Compliance with medications to control all three parameters predicted the achievement of the combined target level. Fourteen percent of the compliant patients reached the combined target level as compared to 9% of the non-compliant ($P = 0.0001$). Furthermore, 67% of the patients who received medications for all three risk factors and reached the combined target level, were medications compliant, while only 33% of the non-compliant patients achieved the target goals ($P = 0.0001$).

Multivariable model
Logistic regression model was used to estimate the factors which influenced the probability of the patients to reach the combined target level. The results showed that compliance with medications to all three risk factors increased the probability of reaching the combined target by 1.56 times (95% CI 1.44–1.69, $P = 0.0001$); males were 1.42 times more likely to have the combined target (95% CI 1.31–1.54, $P < 0.001$). Also, comorbidity with IHD and more than 12 visits to the family physician during the year increased the probability of reaching the combined target by 1.23 and 1.1, respectively (95% CI 1.13–1.34, <0.001, and 95% CI 1.02–1.19, $P = 0.012$, respectively) (Table 1).

Discussion
We found that in 13% of our patients with diabetes all three main CVD risk factors, namely: DM, hypertension and hypercholesterolemia were within the recommended target levels. The parameters which were significantly associated with the achievement of this goal were: compliance to medical treatment for all three risk factors, male gender, comorbidity with IHD and >12 visits per year to family physician. The LDL-C level was the least well controlled parameter.

Our study group included 41936 patients. However, one third of the registered diabetic patients were excluded because they lacked, and may not have been evaluated for at least one of the study parameters. Previous similar studies included small local populations, ranging from a few

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exp (B)$^a$</th>
<th>95% CI Exp (B)$^a$</th>
<th>Significance$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication compliance for all three targets</td>
<td>1.56</td>
<td>1.441–1.693</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male gender</td>
<td>1.42</td>
<td>1.315–1.540</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Comorbidity with IHD</td>
<td>1.23</td>
<td>1.130–1.340</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>More than 12 visits to family physician</td>
<td>1.10</td>
<td>1.022–1.193</td>
<td>0.012</td>
</tr>
<tr>
<td>Older age</td>
<td>1.006</td>
<td>1.001–1.008</td>
<td>0.006</td>
</tr>
</tbody>
</table>

$^a$Exp (B) – [by SPSS] – odds ratio.
$^b$The overall model is significant at the 0.01 level according to the Model Chi-square statistic.
hundreds to several thousands patients. These studies reported lower rates (about 3%) of patients who reached the combined target level. Recently, two studies based on Spanish and Swedish national data reported that the majority of type 2 DM subjects do not achieve the current target levels for HbA1c, BP and blood lipids. According to the Spanish data ($n = 1907$), 50.6% had HbA1c levels of $<$7.0%, only 7.8% have achieved the target of BP $<$130/85 mmHg and only 5.9% of the patients achieved the target of LDL-C $<$100. The European treatment targets of HbA1C $\leq$6.1%, BP $<$130/80 mmHg and total cholesterol $<$174 mg/dl were attained by 16, 13 and 28% of 57119 type 2 DM registered swedish patients. Although those studies did not report the rate of reaching the combined target level, it should also be very low.

In contrast to these studies, our study was designed to evaluate the correlation between achievement of the combined goal and demographic as well as clinical parameters. Males achieved the combined target levels more often. Similar findings were reported by McFarlane et al. They concluded that the control of BP and LDL-C levels as well as the rates of screening for retinopathy and nephropathy were especially sub-optimal among diabetic women. These findings may represent the lack of awareness among women and their health care providers regarding risk factors’ control as well as less aggressive management of them as compared with men.

Comorbidity with IHD predicted reaching the combined goal. This may reflect the fact that patients with symptomatic atherosclerotic disease are treated more aggressively by their family physician and/or cardiologist, along with their own high adherence to medical treatment. On the other hand, coexistence of renal disease predicted only tendency towards achieving the goals. It may be secondary to the low rate (6%) of renal failure among the study group, but also to the hesitation of many physicians of using combination of medications at high doses in these patients.

The main result of the demographic and medical data analysis was that adherence to medical treatment for all three risk factors as well as more than 12 visits to the family physician per year predicted the achievement of the combined target goal. These findings reflect both the patients’ responsibility for their health control and the physician’s attitude by the frequent visits for evaluation and medications’ dose modifications.

When using less aggressive target levels, the rate of patients who reached the combined goals significantly increased. It implies that many patients reach levels which are close to target. Keeping adherence to medications in combination with medication modification will bring most of them to the goals.

Among the three parameters more attention should be paid to control the hypercholesterolemia by using higher doses of statins and/or by adding ezetimibe. Most of the uncontrolled BP levels were the systolic ones, whereas 82% of the patients had DBP $<$85 mmHg. This result may reflect the facts that isolated systolic hypertension is the predominant type of hypertension in the elderly because more than half of our study group are older than 60 years.

Recently, revised recommendations for primary prevention of CVD in diabetic patients had been published by the ADA. The systolic BP should be $<$130 mmHg and a diastolic BP $<$80 mmHg; the LDL-C goal is $<$100 mg/dl; and the HbA1C general goal is $<$7.0%. These levels are very similar to the ones we used.

Our study summarizes the every day reality of a large diabetic patients’ cohort. However, it has several limitations. The study group was heterogeneous and included severely ill patients with target organ damage who needed aggressive and comprehensive medical treatment as well as newly diagnosed and uncomplicated patients who could be easily treated and controlled. Because of this limitation any analysis concerning medications and dosages could not be done.

In conclusion, the control of hyperglycemia, BP and hypercholesterolemia among diabetic patients should be improved. It should include efforts to increase patients’ adherence to medical therapy as well as closer follow-up by the family physicians.

Conflict of interest: None declared.

References


