Diabetes Mellitus and Impaired Glucose Tolerance among Coronary Heart Disease Patients.

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Diabetes mellitus (DM) and impaired glucose tolerance (IGT) are associated with increased cardiovascular disease (CVD) morbidity and mortality. DM and IGT prevalence and their relation to other risk factors were investigated among coronary heart disease (CHD) patients. 250 In- and outpatients with CHD visited or/and admitted to the Emergency Cardiology Center in Tbilisi, Georgia were enrolled in the study. Information on medical and surgical histories, CVD risk factors and current medical condition was obtained via interviews, medical record abstraction, physical examinations and laboratory studies. Fasting blood glucose and 2-hour post load glucose concentration were determined for each patient.Overall 40.8% (46% among males and 12.9 among females) of patients were diagnosed with DM, and 13% were diagnosed with IGT. Of the DM cases, more than half were previously undiagnosed. IGT and DM were highly associated with a dyslipidemic profiles and elevated inflammatory marker concentrations in this population. Undiagnosed DM cases shared similar CVD risk factors as previously diagnosed DM cases including dyslipidemia, other metabolic syndrome components and inflammation.Both DM (diagnosed and undiagnosed) and IGT are prevalent; and are associated with other important CVD risk factors among CHD patients. Future studies assessing associations of DM and IGT with CVD morbidity and mortality in this population, as well as studies that assess prevalence of DM and IGT and their relation with CVD in the general population are needed.

Key words: diabetes mellitus, cardiovascular disease, dyslipidemia

Actuality

Cardiovascular diseases (CVD) are leading causes of morbidity and mortality in developed countries (1, 2). Their importance is increasing in developing countries like Georgia (1, 3). This increase in morbidity and mortality may be related to an increasing prevalence of risk factors. Both diabetes mellitus (DM) and impaired glucose tolerance (IGT) have been shown to worsen CVD associated morbidity and mortality (4, 5, 6, 7). While these relationships have been well documented, the prevalence of DM and IGT, especially the prevalence of previously undiagnosed DM or IGT, which is highly population-dependent, has not been well researched among CHD patients in Emergency Cardiology Center.

Studies conducted among geographically diverse populations have reported previously undiagnosed DM frequencies that range from 30-605 (8, 9, and 10). A recent multi-center study conducted among participants recruited from 44 countries reported a 36.5% impaired fasting glucose prevalence among patients who were not known to have DM previously (11).

We investigated the prevalence of clinically diagnosed DM, previously undiagnosed DM and IGT among patients attending the Emergency Cardiology Center. We also examined the extent to which putative CVD risk factors (e.g. dyslipidemia and chronic inflammation) are associated with DM and IGT in this population.

Material and methods

Study population and study setting: This study was conducted among attendants of the Emergency cardiology Centre in Tbilisi, Georgia. Eligible patients, ages 30-79, who attended the hospital for conservative/surgical treatment, were approached by center physicians and invited to participate in the study. A total of in- and out CHD patients were enrolled in the study. All participants provided informed consent. Institutional review boards of the Emergency Cardiology Center approved the study protocol.
Data collection: Information on medical and surgical histories, potential risk factors and current medical condition was obtained via in-person interviews, medical record abstraction, physical examination and laboratory studies. Body mass index (BMI) was defined as weight in kilograms divided height in meters squared. Metabolic syndrome was diagnosed using the revised National Cholesterol Program (ATP III) criterion as the presence of the following three or more characteristics: hypertension (BP≥130/85mm.Hg), elevated triglycerides (TG)(≥ 150mg/dl), low high-density lipoprotein (HDL) cholesterol(< 40 and 50 mg/dl for males and females respectively), elevated fasting glucose (≥ 110mg/dl) and abdominal obesity (waist circumference > 102 an 88 centimetres among males and females respectively) (12). DM history was determined during interviews and review of medical record. Current glucose tolerance status included classifications according to the WHO criteria (13). Patients were classified to have DM if they had previous DM diagnosis history or if their fasting blood glucose was ≥110mg/dl or if their 2-hr post glucose load was ≥200 mg/dl. Patients were classified to have IGT if they had no history of DM, if their fasting glucose was <110mg/dl and if their 2-hr post glucose load was between 140 and 200 mg/dl. Patients were classified to have IFG if their fasting glucose was between 100 and 110 mg/dl and if their 2-hr post load glucose was < 140 mg/dl. Patients with acute myocardial infarction with hyperglycaemia were excluded from the study if they were not diagnosed DM previously. Other exclusion criteria were C-reactive protein (CRP) level > 10mg/dl and TG levels ≥400mg/dl as low density lipoproteins (LDL) cholesterol was measured by Friedwald formula.

Laboratory analysis: Fasting glucose and 2-hour post load glucose (75mg) concentrations were measured on capillary blood using Finetest™ (Infopia Co. Ltd, Korea). Total cholesretol, HDL-C and TG were measured enzymatically using standardized assays (Humana Kits, Germany). LDL cholesterol was calculated using the Friedwald equation. High-sensitive CRP - an inflammatory marker, was measured using an enzyme linked immunosorbent assay (ELISA) kit (IBL, Germany).

Data analysis: Socio-demographic and physical characteristics of study participants were described. Continuous variables were expressed as mean (standard deviation, SD) while categorical variables were expressed as number (percentages). All continuous variables were assessed for skewness and skewed variables (i.e. CRP) were transformed to obtain an approximate normal distribution. Significant differences in continuous variables among group were assessed using Students t-test. Regression models were fit to assess associations of plasma lipids and CRP concentrations with glucose tolerance status after age adjustment. Liner test for trend evaluated incremental associations of glucose tolerance status with plasma lipids and CRP concentrations. All analyses were stratified by gender. All confidence intervals were calculated as the 95% alpha-level. Statistical analysis was conducted using STATA version 8.2 (College Station, TX).

Results and discussion

Study participant characteristics are presented in Table 1. Mean age of patients was 54.7 years. Among participants 60 %(n=149) were male. Overall, male participants tended to be married, currently employed and to have a history of smoking, compared with their female counterparts. Parental history of hypertension or diabetes and personal history of hypertension were common risk factors among participants (about 70% and 90% respectively). Overall, 40.8% of patients were diagnosed with DM, and 13% were diagnosed with IGT. The prevalence of DM was higher among males than females (46% vs. 33%). Notably, 57% of male DM cases and 25% of female DM cases had not been previously diagnosed. Plasma lipids and CRP concentrations according to glucose tolerance status are presented in Table 2. Male patients with IGT had significantly higher total cholesterol and LDL cholesterol concentrations when compared with normoglycemic patients (means: 246.1 vs. 216.3 and 173.0 vs. 144.4mg/dl respectively; both p-values <0.05). Similar associations were observed among females although the differences were not statistically significant. Higher total cholesterol and LDL cholesterol concentrations were observed among female patients with DM when compared with participants who were not normoglycemic. No similar trends were evident among males. HDL cholesterol concentrations were not different between the groups among males. Among females however, those participants with IGT had significantly higher HDL cholesterol concentrations as compared with normoglycemic participants. Glucose tolerance showed consistently linear relationships with TG (p-value for trend<0.05 among males and females) and CRP concentrations (p-value for trend <0.05 among males).

Table 1 General characteristic of study participants by gender status

Characteristics	Male		Female		Total	
	N=149	% (SD)	N=101	% (SD)	N=250	% (SD)
Age (years)*	55.3	10.7	53.9	14.3	54.7	12.3
Education (≥secondary)	102	68.4	80	79.2	182	72.8
Married/living together	137	92.0	61	60.4	198	79.2
Currently employed	90	60.4	32	31.7	122	48.8
Ever smoker	119	80.4	17	17.0	136	55.1
Hypertensive	107	71.8	72	71.3	179	71.6
Glucose tolerance status						
Normal	60	40.3	55	54.5	115	46.0
IGT	20	13.4	13	12.9	33	13.2
DM	69	46.3	33	32.7	102	40.8
Undiagnosed DM	39	56.5	17	51.5	56	54.9
Metabolic syndrome (ATP III)	60	42.0	43	43.9	103	42.7
Parental history of hypertension/diabetes	118	88.7	84	92.3	202	90.2
Body Mass Index (kg/m^2)*	30.0	5.8	28.7	6.8	29.4	6.2
Waist-hip ratio*	1.6	2.1	1.3	1.8	1.5	2.0

*** Mean (standard deviation, SD)**
Abbreviations: IGT=Impaired glucose tolerance, DM=Diabetes mellitus, ATP III=Adult Treatment Panel III.

Table 2 Glucose tolerance and plasma lipid and CRP concentrations

Characteristics	Male		Female	
	Mean (SD)	Coefficients (95%CI)*	Mean (SD)	Coefficients (95%CI)*
Total Cholesterol (mg/dl)				
Normoglycemic	216.3(55.1)	referent	220.5(46.9)	referent
IGT	246.1(54.7)	29.1(0.8, 57.5)	258.0(43.7)	29.1(-4.6, 62.8)
DM	225.3(55.7)	8.3(-11.3, 27.9)	256.9(58.8)	31.5 (8.7, 54.2)
	p-value for trend**	0.434		0.006
LDL Cholesterol (mg/dl)				
Normoglycemic	144.4(53.8)	referent	140.7(43.9)	referent
IGT	173(49.1)	27.4(1.3, 53.5)	155.3(53.3)	6.3(-25.5, 38.0)
DM	144.5(19.6)	-1.1(-19.4, 17.1)	163.3(47.8)	16.1(-5.6, 37.7)
	p-value for trend			
HDL Cholesterol (mg/dl)				
Normoglycemic	44.6(9.3)	referent	54.5(10.8)	referent
IGT	42.0(12.0)	-2.7(-7.8, 2.4)	66.8(48.3)	13.0(0.0, 25.9)
DM	41.7(9.8)	-2.9(-6.4, 0.6)	50.8(12.2)	-3.3 (-12.1, 5.4)
	p-value for trend	0.107		0.543
Triglycerides (mg/dl)				
Normoglycemic	131.9(54.4)	referent	132.3(64.5)	referent
IGT	181.4(88.0)	51.9(21.1, 101.6)	186.0(96.9)	52.5(-5.3, 110.3)
DM	222.9(126.6)	93.3(58.8, 127.8)	228.5(109.9)	95.5(56.5,134.5)
	p-value for trend	0.000		0.000
Log (CRP)				
Normoglycemic	1.5(1.5)	referent	1.0(1.4)	referent
IGT	1.9(1.0)	0.4(-0.3, 1.1)	1.6(1.9)	0.2(-0.6, 1.1)
DM	1.2(1.2)	0.5(0.1, 1.0)	1.8(1.2)	0.6(-0.0, 1.2)
	p-value for trend	0.026		0.056

*** Regression coefficients and their 95% confidence intervals of models comparing participants with IGT and DM with participants who were normoglycemic after age adjustment.**
Abbreviations: IGT=Impaired glucose tolerance, DM=Diabetes mellitus.

In general, normoglycemic patients were younger, had a significant smoking history and were non-hypertensive when compared with either previously undiagnosed or diagnosed DM patients (Table 3). Participants with either previously undiagnosed or diagnosed DM were more likely to have metabolic syndrome (approximate 7-fold among males and 4-fold among females), and to have higher BMI compared with normoglycemic participants. Plasma lipid profiles and CRP concentrations were similar for previously undiagnosed and diagnosed DM patients with the exception of HDL cholesterol concentration among males. Among females, those with IGT and DM had higher total cholesterol, LDL cholesterol, TG and CRP concentrations and lower HDL cholesterol levels when compared to their normoglycemic counterparts. Males with IGT and DM had significantly higher TG concentrations when compared with their normoglycemic counterparts. Generally, considerable similarity was observed in distributions of known CVD risk factors between participants with previously diagnosed and undiagnosed DM that was different (statistically significant differences in most cases) when compared with normoglycemic participants.

In the current study we showed that abnormal glucose tolerance is prevalent among cardiology patients (IGT 13% and DM 40%). Of these, more than half were previously undiagnosed. IGT and DM were highly associated with dyslipidemic profiles and elevated inflammatory marker concentrations in this population. Undiagnosed DM cases shared similar CVD risk factors as previously diagnosed DM cases including dyslipidemia, other metabolic syndrome components and inflammation.

Previous studies conducted among CVD patients have reported similar high prevalence of abnormal glucose metabolism (IGT and DM). Among a prospective cohort of acute coronary syndrome patients, Conaway et al reported a rate of 57% (8), 66% of these patients met criteria for new DM previously undiagnosed (8). Among Korean acute myocardial infarction patients, Choi et al reported 40% and 37% IGT prevalence at discharge and at three months with corresponding new DM diagnosis of 33% and 30% (9). In a recent large-scale study involving 67,888 atherothrombotic patients from 44 countries, the prevalence of DM was 44.3%, with rates as high as 64.4% in Eastern Europe (11). In that particular study, rates for fasting hyperglycemia and impaired fasting glucose were 4.9% and 36.5% respectively among those not known to be diabetic (11). Although, generally, the prevalence of DM and IGT was high among CVD patients, significant differences were observed in prevalence among different population. Lankisch reported a rate of 40.4% and 22.7% for impaired glucose regulation (IGR) and undiagnosed DM among Australian patients admitted for elective coronary angiography (14). Similar rates for undiagnosed DM were 17.9% and 16% among CHD patients in Germany and Poland (15, 16).

Table 3 Cardiovascular disease risk factors among study participants by DM status

Characteristics	Male			Female		
	Normoglycemic (N=79)	UnDx DM (N=39)	Dx DM (N=30)	Normoglycemic (N=68)	UnDx DM (N=17)	Dx DM (N=16)
Age (years)	54.7(11.8)	54.7(9.4)	57.6(9.2)	52.3(15.2)	56.3(12.1)	58.0(11.7)
Smoking (>5pack/life time)*	65(83.3)	31(79.5)	23(76.7)	13(19.4)	2(11.8)	2(12.5)
Hypertension*	40(50.0)	26(66.7)	16(53.3)	36(52.9)	14(82.4) §	12(75.0)
Metabolic syndrome *	9(11.7)	30(81.1)§	21(72.4)‡	15(22.7)	15(93.8) §	13(81.3)‡
BMI (kg/m^2)	28.9(5.3)	31.2(5.8) §	31.3(6.6)	1.1(1.4)	31.9(6.8) §	29.5(8.8)
Waist Hip Ratio	1.8(2.5)	1.4(1.6)	1.3(1.4)		1.8(2.4)	1.5(2.4)
Plasma lipids (mg/dl)						
Total Cholesterol	223.9(56.2)	221.8(53.7)	230.0(58.9)	226.8(48.2)	253.7(52.4)	260.3(66.7)‡
LDL	151.6(53.8)	143.3(47.8)	146.3(53.0)	143.0(45.3)	160.6(47.7)	166.3(49.6)
HDL	44.0(10.1)	44.1(9.2)¥	38.5(9.8)‡	56.5(21.8)	51.6(11.9)	49.9(12.9)
TG	144.5(67.5)	209.4(72.8)§	241.2(175.3)‡	141.3(72.8)	212.8(104.6) §	245.3(116.5)‡
Log (CRP)	1.6(1.4)	2.1(1.2)	2.0(1.2)	1.1(1.5)	1.7(1.2)	1.9(1.2)

Abbreviations: UnDx DM= undiagnosed DM: Diabetes mellitus diagnosed at the current visit using fasting glucose and 2-hr post load glucose. Diagnosed DM: Diabetes mellitus diagnosed previously per medical history and medical records.

*** number (%) otherwise mean (SD)**

§ p-value statistically significant (<0.05) comparing previously undiagnosed DM to normoglycemic patients.

¥ p-value statistically significant (<0.05) comparing previously undiagnosed DM to previously diagnosed DM patients.

‡ p-value statistically significant (<0.05) comparing previously diagnosed DM to normoglycemic patients.

CVD and DM share a number of risk factors including obesity, hormonal changes such as low adiponectin and inflammation (9). Further, the presence of DM or IGT has been shown to increase both short term and long term morbidity and mortality from CVD (9, 17, 18, and 19). In a meta analysis of five prospective cohort studies conducted among Asians, the overall hazard ratio for CVD mortality associated with screen-detected DM was 3.42 (95% CI: 2.23 – 5.23) (4). This risk was especially increased in the presence of other CVD risk factors. For example, participants with co-morbidities of hypertension and hypercholesterolemia comprised 78% of CVD deaths among screen-detected DM (4). Anderson et al have also shown that IFG and undiagnosed DM were as equally important as diagnosed DM in increasing mortality after percutaneous coronary interventions in CHD patients (20).

The importance of undiagnosed DM and IGT are best seen in light of reports of studies that document improvement in CVD morbidity and mortality in association with medical and lifestyle treatment for abnormal glucose metabolism. Insulin infusion in patients with acute myocardial infarction has been shown to reduce long-term mortality by 30-50% in both diabetic and non-diabetic patients (9, 21). Investigators have also suggested that optimal glucose control will significantly decrease CVD morbidity and mortality at the secondary prevention level (14, 22). Besides under diagnosed of DM and IGT, lack of optimal management contributes to increased CVD morbidity and mortality (14). Bhatt et al in their world-wide study have observed that only a minority of patients undergoing treatment were at target goals for blood pressure, glucose, cholesterol, body weight and nonuser of tobacco (11). This observation is in agreement with out findings.

Several limitations of our study deserve mention. A one time measurement of fasting and 2-hour post load glucose, especially during times of stress (as in visits to clinics for treatment) may not adequately represent basal glucose metabolism. However, other follow-up studies on similar patients with incident DM have shown increased glucose concentrations after 3 months of initial diagnosis (8,23). Finally, unmeasured factors (such as lifestyle and conservative/surgical treatment interventions) that were not taken into account in the current study may confound observed associations.

DM and IGT are prevalent and are associated with other important CVD risk factors among cardiology patients in Emergency Cardiology Center. Future prospective studies that assess associations DM and IGT with CVD morbidity and mortality in this population will provide new insights of disease burden.

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შაქრიანი დიაბეტი და გლუკოზის მიმართ ტოლერანტობის დარღვევა გულის კორონარული დაავადების მქონე ავადმყოფებში.

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აკად. გ.ჩაფიძის სახელობის გადაუდებელი კარდიოლოგიის ცენტრი. თბილისი. საქართველო.

კვლევაში მონაწილეობდა 250 ამბულატორიული და სტაციონარული პაციენტი გულის კორონარული დაავადებით. შაქრიანი დიაბეტი აღმოაჩნდა 40,8%, ხოლო გლუკოზის მიმართ ტოლერანტობის დარღვევა 13%. შაქრიანი დიაბეტი ფარულად მიმდინარეობდა ნახევარზე მეტ შემთხვევაში და ადრე დიაგნოსტირებული არ იყო. შაქრიანი დიაბეტი და გლუკოზის მიმართ ტოლერანტობის დარღვევა მჭიდროდ იყო დაკავშირებული სისხლის ლიპიდური სპექტრის პარამეტრების ცვლილებებთან, განსაკუთრებით კი ჰიპერტრიგლიცერიდემიასთან. დადასტურდა კავშირი C-რეაქტიული ცილის კონცენტრაციის მომატებასთან სისხლში. შაქრიანი დიაბეტი და გლუკოზის მიმართ ტოლერანტობის დარღვევა აუარესებს კარდიოვასკულური დაავადებების კლინიკურ გამოსავალს და დაკავშირებულია სიკვდილობისა და რეკურენტული შემთხვევების სიხშირის მომატებასთან. შაქრიანი დიაბეტი ერთად-ერთი რისკის ფაქტორია, რომელიც გულის კორონარული დაავადების ექვივალენტად არის აღიარებული. მის დროულ დიაგნოზს და მკურნალობას დიდი მნიშვნელობა აქვს კორონარული ათეროსკლეროზის პროგრესირების პრევენციის მიზნით.