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Characteristics and Treatment Pattern of Diabetic Patients with ACS: A Saudi Perspective from the MIDAS Registry

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Background: The Multicenter International Diabetes – Acute coronary Syndromes (MIDAS) study aimed to monitor the adherence to evidence-based therapy among diabetic patients (DM) with unstable angina or non-ST-segment elevation myocardial infarction (ACS) and to describe the in-hospital outcomes of DM in the setting of ACS. We present the data of the Kingdom of Saudi Arabia (KSA) based on the risk profile of the patients in comparison to the international registry. Design: Data of DM patients with ACS who presented at the time of admission to the emergency/coronary care units in 5 hospitals in KSA were extracted from the registry. A total of 3624 patients were enrolled in several countries in Europe, the Middle East, and India. The following variables were extracted: ST deviation ≥0.5 mm, positive troponin, and TIMI risk score. The Z test for 2 proportions was used to compare the KSA values with the international figures. Analysis was done using stata 10. Level of significance was set at 5 %. Results: "Type-2:type-1 DM ratio" in KSA was comparable to the international ratio (93.65 vs 93.83). The high risk factors were significantly less prevalent in KSA in comparison to the international figures (17 % showed significant ST deviation ≥0.5 mm vs 46 % [p = 0.005], 40 % showed positive troponin vs 70 % [p < 0.0001], and 32 % showed a TIMI risk score > 3 in comparison to 62 % [p < 0.0001]). Utilization of GPIIb/IIIa was 18.3 % in KSA vs 37.4 % internationally (p = 0.046). On the contrary, the utilization of clopidogrel/ticlopidine was 96.8 % in KSA vs 74.7 % internationally (p < 0.0001). The percentage of early coronary angiography was 38.9 % in KSA vs 46.1 % internationally (p = 0.292). Among patients who had early coronary angiography, 34.9 % had revascularization (PCI and/or CABG) in KSA in comparison to 54.8 % in the international samples (p = 0.199). Conclusions: Saudi DM patients with ACS had similar demographic data compared to international patients. There was a satisfactory use of evidence-based medicine in the treatment in such a group. ***J Clin Basic Cardiol 2013; 16 (online): 6–9.***

Key words: *diabetics, NSTEMI, ACS, Saudi, GPIIb/IIIa, MIDAS*

The tremendous surge in socioeconomic growth in developing countries like KSA has considerably influenced the lifestyle of the people. Epidemiological studies conducted in KSA have shown a high prevalence of DM with an overall prevalence of NIDDM of 28.82 % and 24.92 % in males and females, respectively, in those over the age of 60 years [1, 2]. On the other hand, in a recent Saudi registry, DM was the most prevalent risk factor for coronary artery disease, present in 56 % of patients, of which 3 % were diagnosed after hospital admission [3].

It is noteworthy that DM was found to be an independent predictor of mortality in the setting of non-ST-segment elevation ACS (NSTEMI-ACS) [4]. Moreover, DM has been associated with worse outcomes following both percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) [5–7].

Despite the preferential benefit observed among high-risk diabetic individuals, previous registry data have shown that these patients are less likely to undergo early invasive strategy and to receive GPIIb/IIIa receptor inhibitors in the setting of ACS [8, 9].

Nevertheless, none of the risk scores has focused on the DM-ACS population, although it may account for 20–30 % of all ACS patients. For instance, the TIMI and GRACE risk scores that allow for prediction of mortality or major morbidity in the setting of ACS remain to be validated in the DM population [10, 11]. This is a crucial step in estimating patient prognosis and optimizing treatment. In addition, it remains to be fully elucidated what is the impact on prognosis of DM-specific parameters such as glucose level, HbA_{1c}, or microalbuminuria in the setting of ACS. These parameters might be a part of future studies.

The MIDAS-ACS study aimed to monitor the adherence to evidence-based antiplatelet therapy among DM with ACS and to assess the impact of DM-specific parameters on early morbidity and mortality in the current era of early invasive strategy and aggressive antiplatelet therapy [12, 13]. In this paper, we present the data of KSA based on the risk profile of the patients in comparison to the international registry.

Design

Data of 142 DM patients presenting with NSTE-ACS at the time of admission to the emergency/coronary care units in 5 hospitals in KSA were extracted from the registry. Unstable angina is defined as ischemic chest pain occurring either at rest (or with minimal exertion) in a crescendo pattern or severely and of new onset. If these symptoms are accompanied by a release of cardiac biomarkers of necrosis (ie, creatine-kinase-MB or troponin), then an NSTEMI has occurred.

Target enrolment was 4000 with a total of 3624 patients finally enrolled. Several countries in Europe (Belgium, Italy, Netherlands, Norway, Spain, and Switzerland) and the Middle East (Israel, Jordan, and KSA) plus India were involved. Primary clinical outcome measure was in-hospital death or ST elevation myocardial infarction (STEMI). The following variables were extracted: utilization of GPIIb/IIIa inhibitors, utilization of clopidogrel/ticlopidine, percentage of early coronary angiography, percentage of PCI procedures, and percentage of patients who had CABG. The Z test for 2 proportions was used to compare the KSA values with the international figures. Analysis was done by stata 10. Level of significance was set at 5 %.

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Results

Baseline characteristics were typical for diabetics presenting with ACS, with a mean age of 67 ± 15 years. Males constituted 36 % of the patients and 94 % of patients were type-2 diabetics.

Evidence of end-organ damage was present in a relatively small percentage (11 % retinopathy, 16 % nephropathy, and 8 % neuropathy). The predominant symptom at presentation was chest pain (occurring in 78 %). 75 % were in class-I Killip classification. 18 % had normal ECG while 47 % had ST depression, 10 % had transient ST elevation, and 17 % had T-wave inversion.

Random glucose at the time of presentation was 203 ± 85 mg/dl, fasting glucose was 155 ± 61 mg/dl, HbA_{1c} was 7.5 ± 1.6 (available for 53 % of patients), and creatinine was 1.3 ± 0.9 mg/dl.

Primary clinical outcome measure was in-hospital death in 3.1 % and STEMI in 4.6 %.

DM medications were mostly applied orally, predominantly metformin and sulfonylureas, while about 1/3 were receiving insulin. "Type-2:type-1 DM ratio" in KSA was comparable to the international ratio (94:6).

The high risk factors were less prevalent in KSA in comparison to the international data: ST ≥ 0.5 mm (17 % vs 46 %; p = 0.005), troponin + ve (40 % vs 70 %; p < 0.0001), TIMI > 3 (32 % vs 62 %; p < 0.0001; Figure 1). The utilization of GPIIb/IIIa inhibitors in the international data of MIDAS was 37.4 %, which was significantly higher than in KSA (18.3 %; p = 0.046; Figure 2).

On the contrary, the utilization of clopidogrel/ticlopidine was higher in KSA (96.8 %, as recommended by the ACC/AHA guidelines), exceeding the international 74.7 % (p < 0.0001; Figure 3).

The overall percentage of early coronary angiography in Saudi Arabia (38.9 %) was lower than in the international samples (46.1 %; p = 0.292; Figure 4).

The percentage of PCI procedures was lower in KSA (24.6 %) in comparison to the international 46.0 % (p = 0.001; Figure 5), while the percentage of patients who had CABG was higher in KSA (10.3 %) in comparison to the international percentage (9 %; p = 0.864; Figure 6). However, the overall percentage of patients who had revascularization (PCI and/or CABG) was lower in KSA (34.9 %) in comparison to the international 54.8 % (p = 0.005; Figure 7).

Discussion

The main goal of the MIDAS registry was to improve the awareness of this potentially deadly combination of DM and ACS and to monitor the application of evidence-based guidelines in this condition. This goal is of great importance since a significant number of patients presenting with NSTE-ACS are diabetic and this number is expected to increase as a result of the global DM epidemic. More importantly, diabetic patients who present with ACS are at high risk for developing subsequent cardiovascular events. At the same time, diabetic patients derive greater benefit than non-diabetic counterparts from aggressive antithrombotic therapy, early coronary angiography, and percutaneous coronary intervention [6].

Despite the evidence of a prothrombotic diabetic state, the exact mechanisms linking DM to the initiation and progression of the atherosclerotic process remain elusive. An angioscopic study performed in ACS patients revealed that plaque ulceration and intracoronary thrombus were more frequent among diabetic patients than among non-diabetics [14]. Similarly, the incidence of thrombus was found to be higher in atherectomy specimens from patients with DM [15]. Moreover, increased levels of procoagulant agents and decreased concentrations of endogenous anticoagulants have been documented in DM [16]. In addition, diabetic individuals have increased platelet activation and aggregation to shear stress and platelet agonists [17] and, more importantly, platelets of diabetic individuals are larger and have an in-

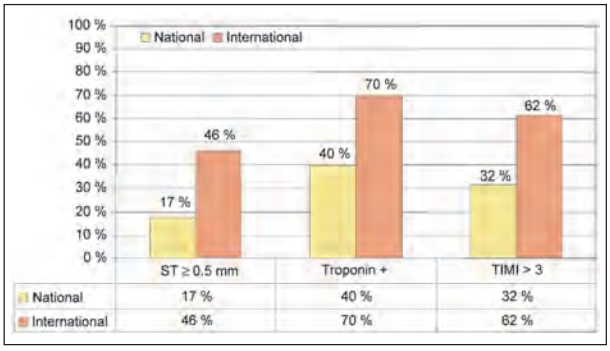

Figure 1. Distribution of risk factor prevalence (%).

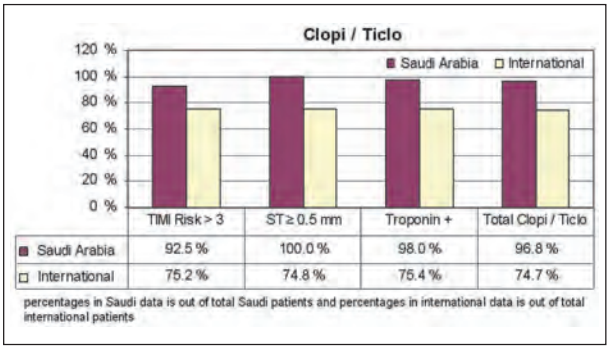

Figure 3. Clopidogrel utilization based on risk factors.

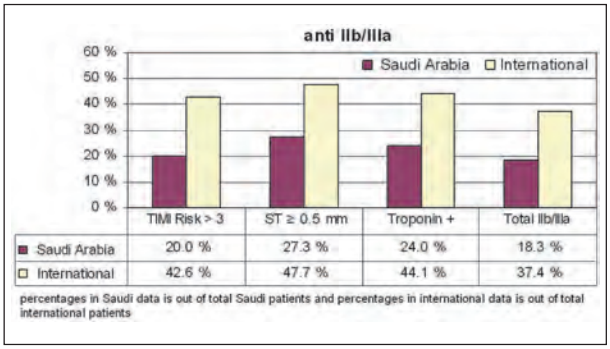

Figure 2. GPIIb/IIIa utilization based on risk factors.

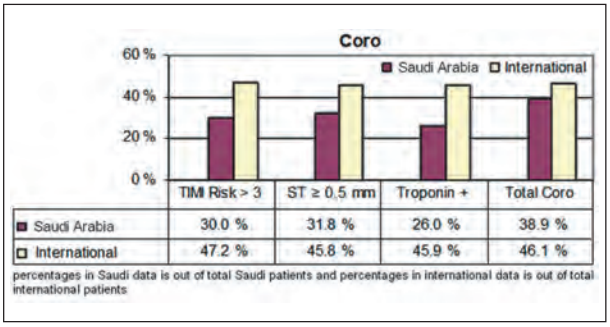

Figure 4. Percentage of early coronary angiography approaches based on risk factors.

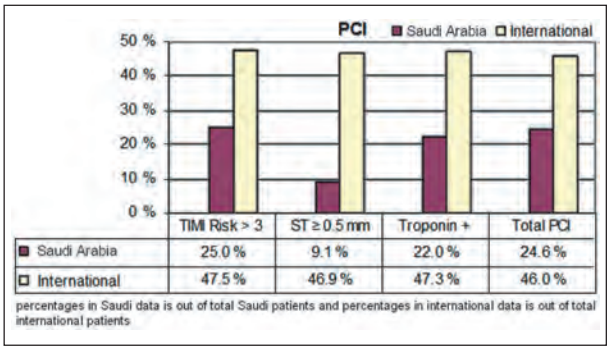

Figure 5. Percentage of PCI based on risk factors.

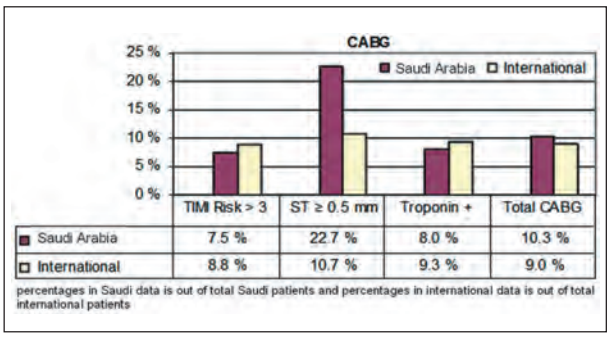

Figure 6. Percentage of CABG based on risk factors.

creased number of glycoprotein (GP) IIb/IIIa receptors per platelet [18].

Data from MIDAS showed, in general, a satisfactory use of evidence-based medicine and acceptable rates of in-hospital death or MI in DM patients who present with ACS. However, there was a marked underutilization of GPIIb/IIIa inhibitors despite recommendations for their use in diabetic patients presenting with ACS. Reviewing the data from KSA, we can easily notice that utilization of GPIIb/IIIa inhibitors, particularly in the elderly population, was significantly less frequent than in the international samples. Seemingly, this is related to concerns about bleeding complications of intensive antiplatelet strategy.

It is also noteworthy that some of the recent reports and guidelines showed more concern about the increased risk of bleeding in this setting, particularly upon using double or triple antiplatelet therapy in combination with heparin [19].

On the contrary, the utilization of clopidogrel/ticlopidine was higher in KSA in comparison to the international figures. This observation was difficult to interpret; however, it might be related to financial issues or the greater interest in use of clopidogrel in patients who are not receiving GPIIb/IIIa inhibitors.

In general, indications for coronary angiography in most cases of the MIDAS registry were predominant because it was a routine strategy at the admitting institution (72 %).

The overall percentage of early coronary angiography in KSA was lower than the international figure. This might be related to the lower number of centers that had catheterization laboratories in the MIDAS registry.

Moreover, the overall percentage of patients who had revascularization (PCI and/or CABG) was lower in KSA in comparison to the international figures, showing a relative tendency towards conservative management in our region. Again, this is probably related to concerns about complications of intervention and a lower number of centers that had catheterization laboratories.

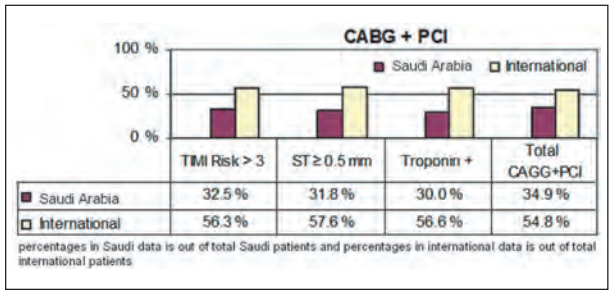

Figure 7. Percentage of CABG + PCI based on risk factors.

However, in another Saudi registry, coronary angiography was performed in 260 of the 435 patients in the entire cohort (60 %); of these, 39 % had percutaneous coronary intervention and coronary artery bypass graft surgery was performed in 9 % of the patients [3].

MIDAS is a registry and accordingly it has some limitations that are common to most registries where no additional diagnostic, monitoring, or therapeutic procedures are applied to the patients. Thorough screening for diabetes mellitus (including glucose tolerance test) was not part of the study and this could have underestimated the real number of patients with diabetes in the study population. Patients were classified into diabetic and non-diabetic according to the local practice.

Conclusions

MIDAS aimed to increase the awareness of the use of evidence-based treatment in the potentially lethal combination of DM and ACS. There was a satisfactory use of evidence-based medicine in KSA in such a patient group. Further studies and clinical trials are required to identify the clinical significance of the differences in the Saudi practice in comparison to the international one.

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