SUMMARY

In numerous studies, asymptomatic hyperglycemia has been shown to be a risk factor for cardiovascular and coronary disease, with a higher risk of dying from coronary disease. Hyperglycemia may develop during severe diseases (e.g., acute myocardial infarction) in people who have not previously suffered from diabetes. The aim of the study was to determine the number of patients with acute myocardial infarction (AMI) in whom hyperglycemia was detected for the first time during AMI. The study included 412 nondiabetic patients treated for AMI at the Department for Medicine, Cantonal Hospital in Zenica, during 1991, 1993 and 1996. The 1993 European standards were used to make the diagnosis of hyperglycemia. Out of 412 nondiabetics with AMI, 113 (27.43%) had hyperglycemia during their hospital stay. According to year of treatment, there were 29 (22.83%), 50 (34.97%) and 34 (23.94%) patients in 1991, 1993 and 1996, respectively. According to year of hospitalization, a statistically significantly higher percentage of nondiabetics with first-ever detected hyperglycemia during AMI were recorded in the war year 1993 as compared with 1991 and 1996 (p<0.05). At the time of discharge, hyperglycemia normalized in 102 (90.27%) patients, which was statistically significant in comparison with 11 (9.73%) patients in whom hyperglycemia failed to normalize until their discharge from the hospital (p<0.001). During their hospital stay, hyperglycemia was found in 27.43% of AMI patients without previously confirmed diabetes, and had normalized in 90.27% of these patients by discharge.

INTRODUCTION

In numerous studies, asymptomatic hyperglycemia has been found to be a risk factor for cardiovascular disease and coronary disease, with a consequently higher risk of dying from coronary disease. Hyperglycemia may occur during severe diseases such as acute myocardial infarction (AMI) in people who did not suffer from diabetes prior to the current disease. The majority of people with a disorder of glycemia regulation in whom impaired glucose tolerance (IGT) or diabetes (based on oral glucose tolerance test (oGTT)) is diagnosed never develop fasting hyperglycemia or symptomatic diabetes when followed longitudinally. For example, during the follow-up of more than 300,000 people in Cleveland (Ohio) who exhibited 2-h glycemia of ≥10 mM/L on 75-g glucose load, only 31% developed diabetes 5 years later (1). Whether a prediabetic state or IGT can be considered risk factors for AMI and other cardiovascular diseases is a controversial question (2). Whether a high risk of cardiovascular diseases like that present in manifest diabetes exists in asymptomatic hyperglycemia as well, is an issue that has been widely investigated and discussed upon, however, no definite answer has yet
been achieved. One of the major questions is the role of elevated glycemia in atherosclerosis among nondiabetic people (3). The role and importance of asymptomatic hyperglycemia as a risk factor for coronary disease has been largely investigated, however, the results are quite inconsistent (4-6).

The question of the relationship between asymptomatic hyperglycemia and coronary disease has been raised in numerous publications. Many of them confirm a significant relationship between fasting glycemia and cardiovascular disease, coronary disease, and an excessive risk of dying from coronary disease (7). A study performed by Waddell and Field (8) in patients with known cardiovascular diseases revealed a relationship with carbohydrate metabolism impairment even in patients with normal fasting glycemia (9). Earlier, it was not clear whether asymptomatic hyperglycemia was an independent risk factor for coronary disease. Current studies have produced results which show that asymptomatic hyperglycemia is an independent risk factor for coronary disease in women but not in men (10).

Clinically diagnosed diabetes and asymptomatic hyperglycemia are associated with an increase in coronary disease mortality. The magnitude of this association is greater in women than in men, when related to coronary disease. However, the absolute excess risk for all diabetics and those with asymptomatic hyperglycemia is higher for men than for women (10).

Atherogenic metabolic disorders which follow diabetes, including dyslipidemia, hyperuricemia, hypertension, adiposity, hyperinsulinemia and high normal glycemia, can manifest much before the occurrence of overt diabetes (11).

The factors of hyperglycemia in AMI patients without previously noted abnormal glucose hemostasis are different (12). AMI has an extremely unfavorable effect on glucose metabolism. In such conditions, there is very often an increase in catecholamine concentration, suppression of insulin release, development of peripheral insulin resistance, and increase in growth hormone and cortisol concentrations (13,14).

A decreased secretion of insulin can be dangerous. During ischemia the passage of glucose into cells becomes critical, since the heart switches from aerobic metabolism with primary utilization of fatty acids to anaerobic metabolism that depends on glucose as energy source. Insulin facilitates glucose uptake, whereas ketones, free fatty acids and their oxidation products that develop during insulin deficiency inhibit its transfer across the cell membrane. The result of hormonal and physiologic changes during AMI is intolerance which, in such cases, is usual even in nondiabetics (12,13,15).

Transitory hyperglycemia and glycosuria are common during the acute stage of AMI and are usually explained as a manifestation of stress. However, studies have shown that such patients are actually latent diabetics in whom the myocardial incident and accompanying stress have worsened the diabetic state and precipitated hyperglycemia and glycosuria (9).

Numerous studies in AMI patients with previously normal fasting glycemia, i.e. without diabetes in their history, confirm a significantly higher rate of impaired glucose tolerance test (ivGTT, oGTT) results as compared with people without AMI (16-19).

During the period from 1962 to 1969, 63 patients were treated at the Department of Medicine in Zenica for AMI, accounting for 2.33% of the total number of hospitalized patients. Of these 63, 17 (27%) patients had elevated glycemia without diabetes in their history (20).

The aim of the study was to determine the number of patients with hyperglycemia diagnosed for the first time during AMI.

**PATIENTS AND METHODS**

The study included 412 nondiabetic patients treated for AMI at the Department of Medicine, Cantonal Hospital in Zenica during 1991, 1993 and 1996. Twenty-nine, 50 and 34 nondiabetic patients with hyperglycemia suffering from AMI were treated in 1991, 1993 and 1996, respectively. The European nomenclature for diagnosing diabetes from 1993, i.e. fasting venous blood glycemia $\geq 6.7$ mM/L or accidentally found glycemia at any time of the day $\geq 10.0$ mM/L, was used on making the diagnosis of diabetes and hyperglycemia in nondiabetic patients (30). The study was based on the results of fasting glycemia.
The diagnosis of AMI was based on clinical picture, electrocardiogram (ECG) on admission, values of relevant enzymes and echocardiography in unclear cases. During hospitalization, ECG was regularly monitored until discharge, at least one on admission, then at the middle of the hospitalization period, and at discharge. The diagnosis of AMI was confirmed by relevant laboratory parameters, along with CPK, LDH and AST enzyme values. The latter were determined when available at the laboratory, depending directly on the necessary chemical reagent supply, especially in 1993 during the war. Echocardiography was performed in patients with ambiguous AMI diagnosis.

Results were analyzed by χ²-test.

RESULTS

All AMI patients treated at the Department of Medicine in Zenica during in 1991, 1993 and 1996 are presented in Table 1.

Table 2 shows the number and percentage of patients with hyperglycemia during AMI, who had never had elevated levels of blood glucose or diabetes diagnosed until the current AMI, according to year of hospitalization. Analysis of the results yielded statistically significant between-year differences in the percentage of patients with transitory hyperglycemia during AMI: 1991:1993 ÷²=4.591, p<0.05; 1993:1996 ÷²=4.321, p<0.05; and 1991:1996 nonsignificant. The results revealed the total number of inpatiently treated nondiabetics with AMI to include a statistically significantly greater percentage of patients with transitory hyperglycemia during AMI in the war year 1993 as compared with 1991 and 1996.

Table 3 shows correlation of fasting glycemia on admission and at discharge in nondiabetic patients with AMI who experienced hyperglycemia during hospital treatment. Analysis of the results produced statistically significant differences in the number of patients with first-ever hyperglycemia during AMI on admission and at discharge (÷²=73.28, p<0.001). A significantly lower number of inpatiently treated nondiabetics with AMI and hyperglycemia were recorded at discharge as compared with their number on admission to the Department. Accordingly, the hyperglycemia that occurred during AMI normalized in 90.27% of nondiabetic patients with AMI by the time of discharge.
DISCUSSION

It is well known that hyperglycemia may occur in some people suffering from severe diseases or when exposed to other stress situations, although they have not been diagnosed as diabetics before. This was noticed in some individuals who had experienced AMI.

During the study period, out of 412 nondiabetics with AMI, hyperglycemia occurred in 113 (27.43%) patients during their treatment at Coronary Unit. A statistically significantly higher number of people in the group of nondiabetics with AMI and hyperglycemia during their hospitalization were recorded in 1993 as compared with 1991 and 1996 (Table 2). In the majority of nondiabetics with AMI this first-ever hyperglycemic episode normalized before their discharge from the hospital. Upon admission, hyperglycemia occurred in 113 nondiabetics with AMI and normalized by discharge in 102 (90.27%) of these patients. At discharge, hyperglycemia persisted in only 11 (9.73%) patients (Table 3). Thus, there were significantly more nondiabetics with AMI and hyperglycemia on admission than at discharge \( (p<0.001) \). The average length of hospitalization in AMI patients was 21 days.

Ellenberg et al. described definite diabetes in 20% and transitory hyperglycemia in another 20% of 75 AMI cases they studied (21). Sowton found hyperglycemia in 73% of 40 nondiabetics right after AMI (18). Datey et al. report on hyperglycemia to be often associated with AMI. However, its meaning and possible relation to diabetes remained unclear. They further emphasize that hyperglycemia followed AMI in 65% of cases. Other authors report on a high incidence of hyperglycemia. Raab and Rabinowitz found hyperglycemia in all 12 AMI cases they analyzed during a two-week period after the attack (22). Eckerstrom reports an incidence of 74% in 212 study cases. However, his results are based exclusively on fasting glycemia (23). Datey et al., Soler and Frank, and Husband et al. found hyperglycemia to be common among AMI patients (24-26). Sewdarsen et al. have reported on a 49% prevalence of hyperglycemia among patients without a previous history of diabetes (27). Hyperglycemia noted among these patients can be caused by previously unrecognized diabetes or can be the result of hormonal response to stress (24).

Behar et al. found a 4% prevalence of asymptomatic hyperglycemia among 14,326 patients aged 45-74, who had a documented coronary disease (AMI and angina pectoris in their history), examined from February 1990 till October 1992. There was no age or sex difference. Asymptomatic hyperglycemia was defined as fasting glycemia \( \geq 140 \) mg% in patients without previous diagnosis of diabetes (28). In a sample of 1,034 consecutively treated adult patients, after exclusion of those admitted for primary diagnosed diabetes, Cloresa et al. found hyperglycemia in 37.5% of the total number of patients and in 33% of surgical patients.

Our results on the occurrence of hyperglycemia in nondiabetics during AMI are consistent with those from the literature mentioned above. The occurrence of hyperglycemia during AMI in patients without previously diagnosed diabetes was confirmed. Such hyperglycemia is a consequence of the manifestation of the previously undiagnosed diabetes or more often represents stress hyperglycemia caused by heart attack. It could be presumed that 11 of the total of 113

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### Table 3. Distribution of fasting hyperglycemia among nondiabetic patients with acute myocardial infarction on admission and at discharge

<table>
<thead>
<tr>
<th>Fasting glycemia on admission</th>
<th>Total number of patients</th>
<th>Fasting glycemia at discharge (mM/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>11-15</td>
</tr>
<tr>
<td>Total number of patients</td>
<td>113*</td>
<td>2*</td>
</tr>
<tr>
<td>%</td>
<td>100</td>
<td>1.77</td>
</tr>
<tr>
<td>&gt;20 mM/L</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>≥16 - ≤ 20 mM/L</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>≥ 11 - &lt;16 mM/L</td>
<td>8</td>
<td>–</td>
</tr>
<tr>
<td>≥ 6.7 - &lt;11 mM/L</td>
<td>97</td>
<td>–</td>
</tr>
</tbody>
</table>

*p<0.001
hospitalized nondiabetics with AMI in whom hyperglycemia occurred and normalized by the time of discharge, actually were diabetic patients who had previously failed to be diagnosed as such. Yet, normalization of such hyperglycemia within a certain period of time is not excluded. Most probably, 102 patients in the group of AMI nondiabetics in whom hyperglycemia normalized during the treatment for AMI, had stress hyperglycemia. A possibility for some of them to develop diabetes later could not be excluded.

A significantly higher percentage of hyperglycemic nondiabetics with AMI in the war year 1993 could be explained by the strong impact of stress caused by the war conditions. Poor nutrition and consequently better glycoregulation could have covered up the clinical picture of diabetes in this period, which then was more frequently manifested during AMI.

CONCLUSION

The analysis of fasting glycemia during AMI in hospitalized patients without diabetes in 1991, 1993 and 1996 produced the following results:

- in the study sample of 420 AMI nondiabetics, hyperglycemia occurred in 113 (27.43%) patients, which is consistent with literature reports;
- hyperglycemia that occurred during hospital treatment for AMI normalized by discharge in 90.27% of nondiabetics with AMI; and
- there was a significantly higher percentage of nondiabetics with AMI and hyperglycemia in the war year 1993 as compared with 1991 and 1996.

REFERENCES


