ABSTRACT: 

Background: The incidence and prevalence of coronary heart disease (CHD) among Bedouins living in the Negev region were very low until the 1960s. During the past 50 years this pattern has changed: in parallel to the changes in lifestyle and nutrition in the Bedouin population, a rapid increase in incidence and mortality from CHD occurred. The relationship between the rise in CHD incidence and the degree of urbanization in this population has not been investigated to date. The study hypothesis was that the prevalence of risk factors and the outcome of myocardial infarction in Bedouins differ between those settled in permanent villages and those remaining in unrecognized villages.

Objectives: To compare the prevalence of cardiovascular risk factors, clinical characteristics, and in-hospital management of a first acute myocardial infarction (AMI) in two Bedouin groups: those residing in permanent villages versus those residing in unrecognized villages.

Methods: We conducted a retrospective analysis of in-hospital data of 352 patients admitted with a first AMI during the period 1997–2003 to Soroka Medical Center, the only medical facility in the region.

Results: There were no differences between the two groups regarding the major cardiovascular risk factors and outcome. A relatively greater number of patients from urban areas underwent catheterization of any sort during their hospitalization (primary, rescue, and risk stratification; \( P = 0.038 \)). No significant difference was found between the two groups in the type of catheterization performed \( (P = 0.279) \).

Conclusions: We found no differences in the clinical characteristics and in-hospital management of patients with AMI between Bedouins residing in permanent villages versus unrecognized villages.

KEY WORDS: cardiovascular disease, risk factors, acute myocardial infarction, Bedouin, rural, urban

Risk Factors and Outcome of Acute Myocardial Infarction in Bedouins Living in Permanent Compared to Unrecognized Villages in Southern Israel

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The Bedouin population in the southern region of Israel (the Negev) constitutes approximately 29% of the total population in the region. Originally nomads who reared livestock in the deserts, the scarcity of water and permanent pastoral land forced the Bedouins to constantly move with their tribes and flock. During the past half decade there has been a shift of a large proportion of the Bedouin population to permanent dwellings in towns. However, approximately 50% of the Bedouins still remain in more traditional villages that have not been officially recognized by the Israeli authorities. These villages are located close to main highways, have no running water or electricity, and lack rural health clinics [1,2].

Despite a paucity of data on the prevalence of coronary heart disease prior to the 1970s [3,4], it is clear that during the past 40 years there has been a gradual increase in the incidence of the disease. This is probably related to the shift from a nomadic lifestyle to living in permanent dwellings [5,6], which results in profound dietary and other lifestyle changes [7]. While the traditional Bedouin lifestyle is characterized by high levels of physical activity and a diet low in calories, fat and sugar, and rich in carbohydrates, those who moved to townships adopted a more westernized lifestyle that is associated with a greater incidence of cardiovascular disease, diabetes, hypertension and obesity. Previous studies [8,9] have shown that diabetes, which had hitherto been rare among the Bedouin, began to appear frequently and is now more common among Bedouin than in the Jewish population in southern Israel. In a previous study [6] it was found that 15% of the Bedouin population living in townships were obese (body mass index > 30) and 35% were overweight (BMI 25–29.9) compared to 0% obese and 23% overweight in a relatively traditionalist Bedouin group. Similarly, significantly higher levels of low-density lipoprotein-cholesterol were found among the urban dwellers. In countries such as Egypt and Tunisia, large differences in the number of diabetics have been noted between the traditional Bedouin population and those who live in cities [10].

BMI = body mass index

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According to Marmot [11], the standard of health is related to social, economic and political conditions. However, absence or inefficiency of medical services also contributes to mortality from coronary heart disease in low socioeconomic groups [12]. The aim of this study was to compare the prevalence of cardiovascular risk factors, clinical characteristics, and outcome among Bedouin living in permanent villages and those living in unrecognized tribal settings, who were hospitalized at Soroka Medical Center with a first acute myocardial infarction between 1997 and 2003.

**PATIENTS AND METHODS**

We conducted a retrospective analysis of clinical data of Bedouins diagnosed with a first acute myocardial infarction and hospitalized at Soroka Medical Center between 1997 and 2003. From annual reports of the Registration and Medical Information Department of Soroka University Medical Center, we obtained data on all the patients hospitalized at Soroka between 1997 and 2003 following a first AMI as the primary cause for admission. The report is classified by ICD-9 codes; Bedouin patients were selected for the study according to their addresses as given in the report. Patients whose address was given as a post office box number were classified by the researchers according to their family name and relationship to a recognized tribe. Using the patient’s identity number, data on other variables were acquired from the computerized records of Soroka’s cardiac intensive care unit. When no patient data were available from the computerized records, treatment sheets from the admissions office were used and searched for the information required.

The patients were divided into two groups: those who lived in recognized (urban or permanent) villages in the Negev, and those from unrecognized (rural) villages in the Negev. The latter group covers different geographical areas belonging to different tribes. Patients whose place of residence was outside of the Negev area and patients with a previous diagnosis of AMI or other cardiovascular disease were excluded from the study.

Data from treatment carried out at the Soroka University Medical Center [13] on 90 of the Bedouin patients show that among those with ischemic heart disease 32% of those living in rural villages also suffered from diabetes, as compared to 45% of those living in townships. According to this, and regarding diabetes as one of the main risks in the study, 234 subjects were required from each group in order to provide 80% research power (α = 0.05, 1-β = 80%).

**STATISTICAL ANALYSIS**

Data input and processing were carried out using SPSS (Statistical Package of Social Science), version 12. Sociodemographic variables, cardiovascular risks, medication prior to hospitalization, patient function, and myocardial infarction characteristics were defined as independent variables, and the dependent variable was place of residence – either a rural settlement or a township. Variables with a large number of categories (for example, site of the infarction, Killip class) were reduced to a smaller number for clinical reasons as amalgamating categories. Hypertension and diabetes were defined by yes/no according to the diagnosis in the medical record. Univariate analysis was carried out to relate residential addresses with the dichotomic background variables using the chi-square test and the Student t-test for continuous variables.

The study was approved by the Soroka University Medical Center’s Institutional Review Board.

**RESULTS**

The study population included 352 patients hospitalized in the Soroka University Medical Center between 1997 and 2003 for whom the primary admission diagnosis was a first AMI. Overall, 48% of the patients were from urban villages (n=169) and 52% from rural villages (n=183). Table 1 shows no significant differences between the groups in age, gender, time from symptom onset until arrival to the emergency room, and clinical characteristics except for a higher percentage of overweight individuals in the urban group; hospitalized men living in urban villages were heavier than those from rural villages (P < 0.001). A greater number of patients from urban villages received aspirin and statins prior to their hospitalization.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Urban (n=169)</th>
<th>Rural (n=183)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>59.6 (14.94)</td>
<td>58.7 (13.44)</td>
<td>0.56</td>
</tr>
<tr>
<td>Male (%)</td>
<td>74.6</td>
<td>78.7</td>
<td>0.36</td>
</tr>
<tr>
<td>Smoking</td>
<td>48.5</td>
<td>55.2</td>
<td>0.42</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>33.1</td>
<td>31.7</td>
<td>0.77</td>
</tr>
<tr>
<td>Hypertension</td>
<td>35.5</td>
<td>33.9</td>
<td>0.75</td>
</tr>
<tr>
<td>Overweight</td>
<td>44.7</td>
<td>19.5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Time (hrs)**</td>
<td>5 (5.78)</td>
<td>6 (8.96)</td>
<td>0.28</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>20.7</td>
<td>16.4</td>
<td>0.30</td>
</tr>
<tr>
<td>Aspirin</td>
<td>18.3</td>
<td>9.8</td>
<td>0.02</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>19.5</td>
<td>13.7</td>
<td>0.14</td>
</tr>
<tr>
<td>Statins</td>
<td>8.9</td>
<td>2.7</td>
<td>0.01</td>
</tr>
<tr>
<td>Thiazide</td>
<td>1.2</td>
<td>0.5</td>
<td>0.52</td>
</tr>
</tbody>
</table>

The data given above are either averages (± standard deviation) or percentages

*Medication for cardiovascular risk factors prior to hospitalization

**Time lapse between onset of symptoms and arrival time at the emergency room**

ACE = angiotensin-converting enzyme

**Table 1. Demographic data, risk factors, and medication* for patients by type of settlement**
tion. No significant differences were found between the two groups with regard to other medications.

Table 2 shows the clinical data of all patients. In total, 29 patients died during hospitalization (8.2%). No difference was found in location of MI or in clinical outcome.

A relatively greater number of patients from urban areas underwent catheterization of any sort during their hospitalization (primary, rescue, and risk stratification; \( P = 0.038 \)). No significant difference in the type of catheterization was found between the two groups (\( P = 0.279 \)).

Based on these data, a multivariable analysis was carried out and a model explaining catheterization procedures versus the following variables was constructed: age, type of settlement, first hospitalization ward, site of infarction, and time between onset of symptoms and arrival at the emergency room. The final model is illustrated in Table 3.

Using the Logistic Regression Stepwise Forward method, it seemed that the time variable may be a confounder regarding catheterization in the first hospitalization ward. For this reason, the analysis was carried out in layers as in Table 4, showing a significant relationship between the ward where catheterization is carried out after time standardization, and a significant relationship between catheterization in the primary hospital ward and arrival time at the emergency room less than 6 hours after the onset of symptoms (\( P = 0.026 \)). A greater percentage of catheterizations were carried out in the coronary care unit in patients arriving at the emergency room sooner after the onset of symptoms.

**DISCUSSION**

This study investigated the characteristics of hospitalized patients with a first AMI from the southern Israel Bedouin population in urban as compared to rural villages. In contrast to our original assumptions, we found no differences between the two groups in the prevalence of major risk factors for AMI, though there appears to be a greater prevalence of overweight among urban patients. Among patients who received medication for risk factors prior to hospitalization, aspirin and statins were prescribed more frequently to the urban population. We found no difference in the mode of treatment or in-hospital clinical outcome between the two groups.

Differences were found, however, in the rate of catheterization during hospitalization. A model in a multivariable analysis was built to explain this finding [Table 3], and it was found that a greater percentage of catheterizations are carried out in the coronary care unit in patients arriving at the emergency room sooner after the onset of symptoms, dismissing the possibility of time being a confounding factor [Table 4].
The literature suggests that urban settlement dwellers have difficult socioeconomic conditions [14–17]. The shift to permanent living conditions and an unsettling gradual change in lifestyle, accompanied by social and economic pressures, are assumed to directly or indirectly affect health. Previous studies have shown a greater prevalence of cardiovascular risk factors in urban compared to rural Bedouin [6]. We therefore speculated that while such changes may affect the incidence of the disease in the two populations (which was not assessed in this study), the prevalence of known cardiovascular risk factors among those who developed the disease is not different.

One surprising finding in this study was the absence of any difference in arrival times at the hospital after the onset of chest pain [Table 1]. Previous studies have shown that Bedouin are forced to make relatively more use of hospital services than other populations of the Negev, possibly due to the lack of availability of first-aid facilities [17]. There are eight clinics in rural villages, and most of the residents are forced to use clinics in urban villages or to make their own way to the hospital if the distance from their place of residence is not too great. Another factor that affects the arrival time at the emergency room after onset of symptoms is connected to the availability of transportation. In the Acute Coronary Syndrome Israel Survey – 2002 (ACSIS), it was found that 38% of the patients hospitalized following AMI used private transport to get to the hospital. No ambulance service is available in rural villages and the residents have to get to the hospital on their own. This may explain the prolonged arrival time at the hospital from the onset of symptoms compared to the non-Bedouin patients in Israel [18]. Factors such as the distance between the settlement and the emergency room and even a communications system to call for assistance does not seem to affect the arrival time at the hospital, since the distances between the settlements and the hospital are about equal and most families have access to a mobile telephone.

In a cross-sectional study carried out in 1995 among 322 Bedouin in the United Arab Emirates, where the population is characterized by a rapid rise in quality of life, high incidences of ischemic heart disease, diabetes, hypertension and obesity were found, which were more prevalent among Bedouin living in urban villages compared to those living a more traditional lifestyle [19]. In another cross-sectional survey in Bahrain in 1998 among 2128 residents, most of whom were Bedouin, high rates of diabetes (25–48%) were found in various ethnic groups and very high levels of cholesterol in those who were diabetic [20]. In their comprehensive survey, Steptoe and Marmot [21] suggested six reasons for the effects of socioeconomic situation on the development of coronary heart disease: genetic factors, prenatal and childhood factors, exposure to infection and hazard, access to health care, health behaviors, and psychobiological processes. It is important to note that to date no comprehensive epidemiological survey related to the characteristics of this rise in the incidence of ischemic heart disease among Bedouins in Israel has been conducted and, likewise, the causes of ischemic heart disease peculiar to the Bedouin population have not been investigated.

Among Bedouins, the division into higher or lower socioeconomic groups is problematic since those who live in urban villages have a low socioeconomic status in comparison to the general population of Israel.

**CONCLUSIONS AND RECOMMENDATIONS**

Contrary to our preliminary speculations, we found that patients with AMI from urban and rural villages in southern Israel have a similar prevalence of cardiovascular risk factors, time to arrival at hospital, in-hospital treatment, and short-term clinical outcome.

Preventive treatment in both populations needs to be similar. A prospective study evaluating AMI characteristics would serve to support the results of the present study. Similarly, a follow-up study of the patients after their release from hospital would clarify the differences between the two groups and levels of primary health care, morbidity, quality of life, and death. We suggest developing strategies to reduce time to arrival at the hospital, such as better education on AMI symptoms and access to ambulance services.

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**Capsule**

**Platelet CD154 potentiates interferon-α secretion by plasmacytoid dendritic cells in systemic lupus erythematosus**

Duffau et al. have shown that in SLE patients, platelets were activated by circulating immune complexes composed of autoantibodies bound to self-antigens through an Fc-γ receptor IIa (CD32)-dependent mechanism. Further, platelet activation correlated with severity of the disease and activated platelets formed aggregates with antigen-presenting cells, including monocytes and plasmacytoid dendritic cells. In vitro, activated platelets enhanced interferon-alpha secretion by immune complex-stimulated plasmacytoid dendritic cells through a CD154-CD40 interaction. Finally, in lupus-prone mice, depletion of platelets or administration of the P2Y(12) receptor antagonist (clopidogrel) improved all measures of disease and overall survival; transfusion of activated platelets worsened the disease course. Together, these data identify platelet activation as an important contributor to SLE pathogenesis and suggest that this process and its sequelae may provide a new therapeutic target.

*I Eitan Israeli*  

**Capsule**

**Immunogenicity of induced pluripotent stem cells**

Induced pluripotent stem cells (iPSCs), reprogrammed from somatic cells with defined factors, hold great promise for regenerative medicine as the renewable source of autologous cells. Whereas it has been generally assumed that these autologous cells should be immune-tolerated by the recipient from whom the iPSCs are derived, their immunogenicity has not been vigorously examined. Zhao and colleagues show that, whereas embryonic stem cells (ESCs) derived from inbred C57BL/6 (B6) mice can efficiently form teratomas in B6 mice without any evident immune rejection, the allogeneic ESCs from 129/SvJ mice fail to form teratomas in B6 mice due to rapid rejection by recipients. B6 mouse embryonic fibroblasts (MEFs) were reprogrammed into iPSCs by either a retroviral approach (ViPSCs) or a novel episomal approach (EiPSCs) that causes no genomic integration. In contrast to B6 ESCs, teratomas formed by B6 ViPSCs were mostly immune-rejected by B6 recipients. In addition, the majority of teratomas formed by B6 EiPSCs were immunogenic in B6 mice with T cell infiltration, and apparent tissue damage and regression were observed in a small fraction of teratomas. Global gene expression analysis of teratomas formed by B6 ESCs and EiPSCs revealed a number of genes frequently overexpressed in teratomas derived from EiPSCs, and several such gene products were shown to contribute directly to the immunogenicity of the B6 EiPSC-derived cells in B6 mice. These findings indicate that, in contrast to derivatives of ESCs, abnormal gene expression in some cells differentiated from iPSCs can induce a T cell-dependent immune response in syngeneic recipients. Therefore, the immunogenicity of therapeutically valuable cells derived from patient-specific iPSCs should be evaluated before any clinic application of these autologous cells into the patients.

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**Original articles**


“Art enables us to find ourselves and lose ourselves at the same time”  

*Thomas Merton (1915-1968), Anglo-American Catholic writer, Trappist monk and social activist*