Introduction

Cardiovascular disease is one of the major causes of both morbidity and mortality [1, 2]. In this regard, acute myocardial infarction (AMI) is the most common cardiovascular emergency encountered in hospitals. Apart from modifiable risk factors for AMI such as, smoking, obesity, diabetes, hypertension, and dyslipidemia [3], evidence suggests that psychosocial factors are independently related to AMI. Persons with several period of work stress had 1.3 times higher risk of developing AMI as compared to others. Similarly those with sustained stress at work were twice as likely to suffer from AMI [4]. Unhealthy habits such as extreme physical exertion and smoking, in addition to negative emotions like anger, anxiety and sadness have also been found to persuade AMI [5, 6]. Patients with AMI reported a higher subjective mental stress during two to four weeks preceding the acute cardiac event (53% of the patients with AMI reported ‘high’ levels of stress in contrast to only 20% of healthy controls reporting high stress for the same period [7]. Studies reported that the higher stress levels were associated with higher risk for AMI even after adjusting for cardiovascular risk factors [8].
Size (MILIS) suggested that among 849 patients with AMI, 48% reported one or more possible psychosocial trigger, emotional upset being most common (14%) [9]. Many studies have found possible psychosocial triggers in up to 10% of patients [10, 11].

AMI was also associated with a higher prevalence of depression and/or anxiety; type A behavior traits and job stress [12, 13]. Existing evidence suggests psychosocial risk factors to be common possible risk factors for AMI, and also for high post-AMI mortality. Therefore, we aimed to investigate whether psychosocial risk factors (stress at work and at home, financial stress, major life events and presence of depression in the past year) are associated with AMI at a teaching hospital, based in Karachi. We hypothesized that the presence of psychosocial factors would be different between those with AMI compared to controls.

Method

This case-control study was conducted in the Family Medicine clinics, Cardiology and Internal Medicine Clinics at the Aga Khan University Hospital Karachi (AKUH) during January 2011 to December 2011. AKUH is a 599 bedded, non-profit, private teaching institute which provides high quality patient care in a broad range of secondary and tertiary services to over 50,000 hospitalized patients and to approximately 600,000 outpatients annually. Before commencement of study, ethical review was sought from Ethical Review Committee of the Aga Khan University. Patients were recruited as cases and controls on the basis of the eligibility criteria. All participants provided a written informed consent before the study.

Case definition

Cases were those who presented with first ever AMI, above the age of 40 years and visited cardiology clinic at AKUH within a month of the attack (as identified and diagnosed on ECG changes [14] by attending physician). Patients with unproven AMI, psychiatric illness in the past and those on anti-psychotic medications were excluded from the study.

Control definition

Controls were selected from family medicine and internal medicine clinics of the AKUH and included patients above the age of 40 years without AMI. Patients with AMI, psychiatric illness in the past and those on anti-psychotic medications were excluded from the study.

Assessment of psychosocial factors and other covariates

A precoded, structured questionnaire was administered by the principal investigator. The questionnaire took approximately 20-30 minutes to complete. The first part of the questionnaire included patient demographics, the second part of the questionnaire was adapted from INTERHEART study questionnaire and it included the psychosocial factors associated with AMI (stress at work and at home, financial stress, major life events and presence of depression in the past year) [4]. In order to minimize the recall bias, we asked participants to report how often they had felt stress at work and home, using the following response options: 1) never; 2) sometimes (once a week); 3) often (twice per week); 4) sustained stress, in the past week, so the patients does not have to recall about longer past. Response to sometime, often and sustained stress was graded as presence of stress. Occurrence of major adverse life events was documented by asking participants whether they had experienced any specified life events in the past year such as: marital separation, family conflict, loss of job, financial problem, self-illness, personal injury, illness, death in family, illness of a family member, loss of a spouse, or loss of child [4]. Depression was assessed by 10 item questionnaire it was part of the INTERHEART study about the presence of symptoms in the past 12 months [4]. Those with five or more positive responses were categorized as having depression.

Sample size estimation

Sample size was calculated using data from INTERHEART study; the prevalence of psychosocial risk factors (stress at work and at home, financial stress, major life events and presence of depression in the past year) was reported to be in the range of 17.6% to 76% [4]. Using Epi info software, keeping 80% power, 5% level of significance and case to control of ratio 1:1, the estimated sample size to detect an odds ratio of 2.5 came out to be 153 cases and 153 for controls (306).

Statistical analysis

In descriptive statistics, frequencies and proportions were calculated for categorical variables. To observe for the difference between cases and controls several statistical tests were applied. Pearson chi square was applied to observe for the difference in the psychological factors between cases and controls. To study the association of psychosocial risk factors with AMI, logistic regression analysis was conducted. We ran a preliminary logistic regression analysis which was not adjusted for any covariates, to evaluate each variable for its crude association with AMI. Multivariable analysis was performed using multiple logistic regressions to study the influence of age, sex, weight, smoking, hypertension, diabetes and dyslipidemia, on the association of psychosocial risk factors and AMI. Results are presented as Odds ratio (ORs) and 95% confidence interval (CI). All tests were two tailed and a P value of <0.05 was considered statistically significant. Data were analyzed using the IBM SPSS Statistics version 19.0 (IBM Corp., Armonk, NY).

Results

This study included 153 cases of AMI aged ≥ 40 years as cases and 153 controls aged ≥ 40 years from AKUH, Karachi. The Socio-demographic characteristics of the study population (Table 1).

Psychosocial Risk Factors

Cases were often irritable (cases 96.1% v/s. 22.9% controls), often had difficulty falling asleep (cases 96.1% v/s. 22.9% controls) and often had anxiety (cases 96.7% v/s. 23.5% controls) as a result of conditions at work. Cases were often irritable (cases 96.1% v/s. 22.9% controls), often had difficulty falling asleep (cases 96.1% v/s. 22.9% controls) and often had anxiety (cases 96.7% v/s. 23.5% controls) as a result of conditions at home (Table 2).

As a result of conditions at work, cases were often irritable (cases 100% v/s. controls 39.1%), often had difficulty falling asleep (cases 95.2% v/s. controls 37.3%), and often had anxiety (cases 95.2% v/s. controls 40.9%).
Cases had more marital separation (7.8%) as compared to controls (4.6%). Family conflict was seen in 8.5% cases as compared to 3.9% controls. Loss of job was seen in 12.4% cases compared to 3.9% controls. More financial problems were seen in cases (8.5%) as compared to controls (7.8%). Similarly, cases suffered more from illness compared to controls (35.3% vs. 4.6%).

Among cases 11.8% had faced some injury compared to none among control (0%) while illness of family member was also reported to be higher in cases as compared to controls (32.7% vs. 20.3%). Loss of spouse was present in 3.9% of cases compared to 7.8% of controls. Child loss was found to be 4.6% among cases while none was reported in the control group (0%). Depression was seen in 91.5% of cases and 65.3% of controls respectively.

Univariable analysis
Cases were more likely to be irritable as a result of conditions at home (OR 8.26; 95% CI: 3.36-20.3), had decreased sleep (OR 2.02; 95% CI: 1.5-3.03) and more anxiety (OR 3.52; 95% CI: 1.25-5.27) compared to controls. Cases were less irritable as result of conditions at work (OR 1.15; 95% CI: 0.60-1.90) compared to controls, however, cases had decreased sleep as a result of conditions at work (OR 1.03; 95% CI: 0.89-2.08) and more anxiety compared to controls (OR 4.1; 95% CI: 2.7-6.5). All these variables were statistically significant (p<0.05).

Cases had less marital separations (OR 1.77; 95% CI: 0.67-4.63), less family conflicts (OR 2.27; 95% CI: 0.86-6.15), more loss of jobs (OR 3.47; 95% CI: 1.34-8.95), less financial problems (OR 1.09; 95% CI: 0.48-2.47), more self-illness (OR 4.70; 95% CI: 3.56-10.76), had more deaths in family (OR 1.91; 95% CI: 1.13-3.21) and had more illnesses in the family (OR 2.20; 95% CI: 1.32-3.69) compared to controls (Table 3). These all were statistically significant except, marital separations (p=0.24), less family conflicts (p=0.10) and less financial problems (p=0.83).

Multivariable logistic regression model
The final logistic regression model included irritability as a result of condition at home, illness in past, illness in family, death in family and loss of job.

Cases were four times more likely irritable as a result of conditions at home as compared to controls (ORadj=4.86, 95% CI: 3.24-7.53). Cases suffered three times more illness (ORadj=3.33, 95% CI: 2.86-5.23), had eight times more illness in family (ORadj=8.44, 95% CI: 6.21-10.1), seven times more deaths in family (ORadj=7.42, 95% CI: 3.98-10.12) and suffered more loss of job three times more (ORadj=3.71, 95% CI: 1.16-8.86) in last one year compared to controls (Table 3).

Discussion
In this case-control study of 153 cases and 153 controls, we found that psychosocial risk factors namely; irritability, illness, illness of family members and death in family in the past one year were positively associated with AMI.

Irritability as a result of conditions at home was associated with four time’s higher risk of AMI in our study. Similar findings were reported by Shen et al [15] and INTERHEART [4]. Gafarov et al also found that among men with first AMI, there was high level of stress in the family [16].

Loss of job was not statistically significant in the study. This is in contrast to the United States Health and Retirement Survey which concluded that involuntary job losses can double the risk of AMI [17]. It is evident that losing a job increases the risk of developing AMI [18]. The results of INTERHEART study [4] although were positive for an association between loss of job and AMI but it showed lower risk compared to other psychosocial risk factor for AMI.

The current study found that serious illness of a family member is associated with AMI. A study conducted by Deljanin et al concluded that serious illness of family members is a risk for AMI [19]. Similarly, illness in the past and illness in the family are associated with AMI as was seen in INTERHEART study [4] and Toftet al [9] in their study which supports our results.

The loss of a significant person in one’s life has been shown to acutely increase the risk of cardiac events seen by Mostofsky et al [20]. Similarly death in family was also found to be a significant factor in our study which is supported by a Danish registry-based study too [21] but is in contrast to INTERHEART study [4] where death in family was similar among cases and controls.

Depression has been associated with an increased risk of coronary heart disease in both men and women [22-24]. Similar findings are reported by the pooled results from meta-analysis which support the role of depression in the development of AMI [25, 26]. A study done by Arifi et al showed that high depression score was associated with the development of AMI and all-cause mortality [27]. INTERHEART study [4] reported more cases of AMI than controls with feeling sad, blue, or depressed for more than 2 weeks or more in a row which is comparable to our study.

Strengths and limitations
This study has identified various psychosocial risk factors for AMI. Psychosocial risk factors are independent risk factors for AMI and since low to middle income countries have a high risk of AMI despite low risk factor burden, psychosocial risk factors can prove to be serious risk factors leading to AMI and hence a rise in morbidity and mortality of patients.

Limitations of our study were that since the study population mainly belonged to metropolitan city of the country and visiting cardiology and family medicine clinics located in the best of tertiary care centers of the country. Hence study population is not truly representative. Moreover, since this study was conducted in urban city of Karachi, therefore, the results might be different for the rural areas of the city. Although, the cutoff scores for risk of AMI is being validated and extensively reported, however, the psychometric properties of the INTERHEART questionnaire are not available to us, which we consider as a potential limitation. Another limitation is possibility of recall bias which cannot be excluded. Moreover, we cannot comment on causality of these factors with AMI, therefore, further studies like cohort studies are needed to find casual relations between the factors and AMI.
Table 1 Socio-demographic characteristics of cases (153) and controls (153).

| Variables       | Cases | Controls | P-value |
|-----------------|-------|----------|---------|
| Age             |       |          |         |
| 50-65 years     | 93    | 122      | 0.0001  |
| 65+ years       | 60    | 31       |         |
| Gender          |       |          | <0.001  |
| Male            | 104   | 109      |         |
| Female          | 49    | 44       |         |
| Marital Status  |       |          | <0.001  |
| Never married   | 6     | 6        |         |
| Currently married | 110 | 103      |         |
| Widowed         | 37    | 44       |         |
| Occupational Status | |      |         |
| Unemployed      | 49    | 43       | 0.001   |
| Employed        | 104   | 110      |         |
| 10,000-30,000   | 36    | 19       |         |
| 30,000-50,000   | 62    | 67       | <0.001  |
| >50,000         | 18    | 30       |         |
| Unknown         | 37    | 37       |         |

Conclusion

Psychosocial risk factors such as stress at work and at home, financial stress, major life events and presence of depression in the past year are associated with AMI. The importance of psychosocial risk factors is much more important, under recognized and might contribute to a substantial proportion of AMI. Strategies should be planned out by family physicians and all health care providers to identify and screen for these psychosocial risk factors which in turn will assist in reducing the overall burden of cardiovascular diseases.
Table 2 Association of psychosocial risk factors and AMI.

| Variables                                      | Cases | Controls | P-value |
|------------------------------------------------|-------|----------|---------|
| **Irritability as a result of condition at home** |       |          |         |
| Never/sometimes                               | 6     | 118      | 0.085   |
| Often*                                        | 147   | 35       |         |
| **Sleep disturbance as a result of condition at home** |       |          |         |
| Never/sometimes                               | 6     | 118      | 0.085   |
| Often*                                        | 147   | 35       |         |
| **Anxiety as a result of condition at home**   |       |          |         |
| Never/sometimes                               | 5     | 117      | 0.065   |
| Often*                                        | 148   | 43       |         |
| **Irritability as a result of condition at work** |       |          |         |
| Never/sometimes                               | 0     | 104      | 0.006*  |
| Often*                                        | 104   | 43       |         |
| **Sleep disturbance as a result of condition at work** |       |          |         |
| Never/sometimes                               | 5     | 69       | 0.025*  |
| Often*                                        | 99    | 41       |         |
| **Anxiety as a result of condition at work**   |       |          |         |
| Never/sometimes                               | 5     | 65       | 0.010*  |
| Often*                                        | 99    | 45       |         |
| **Marital separation**                        |       |          |         |
| Yes                                           | 12    | 7       | 4.6%    |
| No                                            | 141   | 146     | 95.4%   |
| **Family conflict**                           |       |          |         |
| Yes                                           | 13    | 6       | 3.9%    |
| No                                            | 140   | 147     | 96.1%   |
| **Loss of job**                               |       |          |         |
| Yes                                           | 19    | 6       | 3.9%    |
| No                                            | 134   | 147     | 96.1%   |
| **Financial problem**                         |       |          |         |
| Yes                                           | 13    | 12      | 7.8%    |
| No                                            | 140   | 147     | 92.2%   |
| **Self-illness**                              |       |          |         |
| Yes                                           | 55    | 7       | 4.6%    |
| No                                            | 98    | 146     | 95.4%   |
| **Injury**                                    |       |          |         |
| Yes                                           | 18    | 0       | 0%      |
| No                                            | 135   | 153     | 100%    |
| **Death in family**                           |       |          |         |
| Yes                                           | 50    | 31      | 20.3%   |
| No                                            | 103   | 122     | 79.7%   |
| **Illness of family member**                  |       |          |         |
| Yes                                           | 31    | 55      | 35.9%   |
| No                                            | 122   | 98      | 64.1%   |
| **Loss of spouse**                            |       |          |         |
| Yes                                           | 6     | 12      | 7.8%    |
| No                                            | 147   | 141     | 92.2%   |
| **Child loss**                                |       |          |         |
| Yes                                           | 7     | 0       | 0%      |
| No                                            | 146   | 153     | 100%    |
| **Depression**                                |       |          |         |
| Yes                                           | 140   | 100     | 65.3%   |
| No                                            | 13    | 53      | 34.6%   |

* Significant variables at p-value=0.05
+ Often=twice per week
Table 3 Risk factors associated with AMI in univariable and multivariable analysis.

| Variable                          | Unadjusted OR | 95% CI      | Adjusted OR | 95% CI      |
|-----------------------------------|---------------|-------------|-------------|-------------|
| Irritability as a result of condition at home |               |             |             |             |
| Never/sometime                    | Ref           |             | Ref         |             |
| Often+                            | 8.26          | 3.36-20.3   | 4.86        | 3.24-7.53   |
| Self-illness                      |               |             |             |             |
| No                                | Ref           |             | Ref         |             |
| Yes                               | 4.70          | 3.56-10.76  | 3.33        | 2.86-5.23   |
| Illness of family member         |               |             |             |             |
| No                                | Ref           |             | Ref         |             |
| Yes                               | 2.20          | 1.32-3.69   | 8.44        | 6.21-10.1   |
| Loss of job                       |               |             |             |             |
| No                                | Ref           |             | Ref         |             |
| Yes                               | 3.47          | 1.34-8.95   | 3.71        | 1.16-8.86   |
| Death in family                   |               |             |             |             |
| No                                | Ref           |             | Ref         |             |
| Yes                               | 1.91          | 1.13-3.21   | 7.42        | 3.98-10.12  |

+ Often=twice per week
I=unadjusted OR
II=adjusted OR

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