The association of suicide risk with negative life events and social support according to gender in Asian patients with major depressive disorder

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\textbf{Abstract}

We investigated the associations between negative life events, social support, depressive and hostile symptoms, and suicide risk according to gender in multinational Asian patients with major depressive disorder (MDD). A total of 547 outpatients with MDD (352 women and 195 men, mean age of 39.58 \pm 13.21 years) were recruited in China, South Korea, Malaysia, Singapore, Thailand, and Taiwan. All patients were assessed with the Mini-International Neuropsychiatric Interview, the Montgomery–Asberg Depression Rating Scale, the Symptoms Checklist 90-Revised, the Multidimensional Scale of Perceived Social Support, and the List of Threatening Experiences. Negative life events, social support, depressive symptoms, and hostility were all significantly associated with suicidality in female MDD patients. However, only depressive symptoms and hostility were significantly associated with suicidality in male patients. Depression severity and hostility only partially mediated the association of negative life events and poor social support with suicidality in female patients. In contrast, hostility fully mediated the association of negative life events and poor social support with suicidality in male patients. Our results highlight the need of in-depth assessment of suicide risk for depressed female patients who report a number of negative life events and poor social supports, even if they do not show severe psychopathology.

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\section{Introduction}

One of the most serious adverse events of depression is suicide. Suicide is complexed with psychological, social, biological, cultural, and environmental factors involved (WHO, 2010). The severity or duration of depression (Sokero et al., 2003, 2005; Holma et al., 2010), low level of social support (Sokero et al., 2003, 2005), negative life events (Oquendo et al., 2005; Chan et al., 2011), impulsivity and hostility (Perroud et al., 2011; Jeon et al., 2013b), feelings of worthlessness (Jeon et al., 2014), and permissive attitude toward suicide (Jeon et al., 2013a) have all been reported as suicide-risk factors in individuals with major depressive disorder (MDD). Interactions among these risk factors also seem to be important. For example, the impact of stressful experiences may be buffered by social support (Hays et al., 2001). In addition, the impact of negative life events and social support might well vary depending on the clinical state of the patient (Leskela et al., 2006). Asian countries account for approximately 60% of the world’s suicides (Beautrais, 2006; WHO, 2010). However, studies on suicidality in Asian cohorts of individuals are still very limited in numbers with very rare multinational cooperation (Chen et al., 2015).
2012). It is well known that the role of depression or other psychiatric conditions in Asian populations is less influential in the determinism of suicidality than in Western countries (WHO, 2010). According to a recent review by Chen et al. (2012), the frequency of depression or another diagnosable mental disorder among suicides in Asian countries derived from psychological autopsy studies ranged from 37% to 97%, which was lower than that in Western countries. This suggests that social factors such as negative life events and social support might have more significant role in the determinism of suicidality in Asia than the West.

A number of studies have indicated that women are more vulnerable and more likely to react with depression when exposed to stressful life events (Kessler, 1997; Maciejewski et al., 2001; Nazroo et al., 1997; Sandanger et al., 2004). Kessler (1997) has suggested that higher vulnerability to stressful life events in women might be caused by less psycho-social stress-buffering resources such as social support. In a longitudinal twin study, Kendler et al. (2005) have found that the lack of social support has increased the risk of depression in women, but not in men. Dalgard et al. (2006) have reported that, in general, women are not more vulnerable to negative life events than men. However, when there is no social support, women are more vulnerable than men when exposed to negative life events. These studies suggest that negative life events and social support may have more significant and direct effect on suicidality in women than in men. However, no such study has been performed to study the effect of gender on suicidality when exposed to negative life events.

Therefore, the objectives of this study were: (1) to examine the associations among negative life events, social support, and suicide risk according to gender in multinational Asian MDD patients; and (2) to determine whether the severity of depressive symptoms and the level of hostility could fully or partially mediate the relationships among negative life events, social support, and suicide risk in Asian MDD patients.

2. Methods

2.1. Subjects

This study used data from the Study on the Aspects of Asian Depression (SAAD) (Jeon et al., 2013b). This was a multi-country, cross-sectional, and observational study of depression in clinical settings carried out between 2008 and 2011. Thirteen study sites were established across 6 Asian countries: China (3 sites), South Korea (4 sites), Malaysia (1 site), Singapore (1 site), Taiwan (2 sites), and Thailand (2 sites). This study was approved by the Institutional Review Board or Ethics Committee of Asan Medical Center and the relevant review board of each study site.

Participants who were prospectively enrolled in the study were recruited from outpatient who sought psychiatric treatment at study sites. After the study details had been fully explained, written informed consent was obtained from each participant. The inclusion criteria were as follows: (i) age 18–65 years; (ii) a positive response ("yes") to the Mini-International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998) question A1 (depressed mood) and/or A2 (loss of interest); and (iii) a diagnosis of MDD according to the DSM-IV criteria (American Psychiatric Association, 1994) that was assessed by the MINI. The exclusion criteria were as follows: (i) unstable medical condition; (ii) mood disorder due to medical conditions and/or substance abuse; (iii) psychotic or bipolar disorder; (iv) clinically significant cognitive impairment; (v) treatment with psychotropic medication within previous month; (vi) treatment with a benzodiazepine drug within previous week; and (vii) treatment with a long-acting antipsychotic medication within previous 3 months. All other psychiatric and comorbid conditions were permitted. Participants completed several self-report questionnaires in the presence of a study coordinator. A face-to-face diagnostic evaluation was then conducted with the site investigator before the participant met with their treating clinician.

2.2. Suicidality

Suicide ideation and behaviors were assessed with the MINI suicidality module (Sheehan et al., 1998). The suicidality module comprised six questions. Each item had a different score: wish for death with a score of 1, wish for self-harm with a score of 2, suicidal thought with score of 6, suicide plan with a score of 10, suicide attempt in the past month with a score of 10, and lifetime suicide attempt with a score of 4. Three questions began with ‘In the past month.’ Question of ‘Did you think about suicide?’ was used to test suicidal ideation. Question of ‘Did you have a suicide plan?’ was used to examine suicidal plan. Question of ‘Did you attempt suicide?’ was used to examine suicide attempts. Question of ‘Did you ever make a suicide attempt in your lifetime?’ was used to examine lifetime suicide attempt. The scores of the six questions were added together to quantify suicide risk. Total scores ranged from 0 (no current risk) to 1–5 (low), 6–9 (moderate), and 10 or more (high). Suicide risk was then coded as 0 if the total scores indicated no current risk. It was coded as 1 if the risks were low, as 2 if they were moderate, and as 3 if they were high.

2.3. Negative life events

Negative life events were assessed with the List of Threatening Experiences (LTE) questionnaire (Brugha and Cragg, 1990), a 12-item instrument to measure common life events that tend to be threatening. The 12 items were: serious illness or injury to subject, serious illness or injury to a close relative, death of a close relative, separation due to marital difficulties, broke off a steady relationship, serious problem with a close friend or relative, unemployment, subjects sacked from job, change of residence, major financial crisis, problem with police and court appearance, and something valuable lost or stolen. Respondents were asked to select life events that had occurred within 12 months prior to the onset of their depressive symptoms. Each life events was scored dichotomously (yes/no) with the exact month of the year in which it occurred. LTE was found to have high test–retest reliability (Cohen’s kappa = 0.96) and good agreement with informant information (Cohen’s kappa = 0.84).

2.4. Social support

Perceived social support was assessed with the Multidimensional Scale of Perceived Social Support (MSPSS) (Zimet et al., 1990), a 12-item scale to measure perceived social support from family, friends, and a significant other. Respondents answer items on a 7-point Likert-type scale (options ranging from ‘very strongly disagree’ to ‘very strongly agree’). MSPSS was found to have good internal reliability (Cronbach’s coefficient alpha = 0.92) and strong factorial validity, confirming the three-subscale structure of the MSPSS (factor loading of 0.74–0.85 for family subscale, 0.87–0.89 for friends subscale, and 0.72–0.88 for a significant other subscale).

2.5. Depression severity

Depression severity was assessed with the Montgomery–Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979), a 10-item depression rating scale to assess core symptoms of depression. Each item was scored 0 to 6, with 0 denoting the absence of symptoms, while 6 indicating the presence of the most severe form of symptoms. MADRS was found to have high inter-rater reliability (r = 0.89). It had significant correlation with the Hamilton Rating Scale (r = 0.70, p = 0.001).

2.6. Hostility

Hostility was assessed with the Hostility subscale of the Symptoms Checklist 90-Revised (SCL-90-R) (Derogatis, 1997). It was rated from 0 (no distress) to 4 (extreme distress). The Hostility subscale of SCL-90-R was found to have good internal reliability (Cronbach’s coefficient alpha = 0.84) and high test–retest reliability (r = 0.78).

2.7. Statistical analysis

Differences between male and female participants were compared using t-test for continuous variables and Chi-squared test for categorical variables. Multiple regression analysis was conducted to determine the association between independent variables (depression severity, hostility, social support, and negative life events) and suicide risk (dependent variable) in female or male participants. All independent variables were concurrently entered into the model. AMOS software (version 18.0; SPSS Inc., Chicago, IL) was used for path analyses. To evaluate the direct effect of negative life events and poor social support on suicidality and their indirect effect via depression severity and hostility, we ordered the variables as follows: negative life events/social support → depression/hostility → suicidality. All statistical analyses except the path analyses were performed using SPSS (version 21.0; SPSS Inc., Chicago, IL). Statistical significance was considered when p value was less than 0.05.

3. Results

Of 2,023 outpatients who were screened for eligibility, 637

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(31.5%) were eligible. Of the 637 outpatients, 556 were enrolled in the study. The remaining 81 outpatients were not enrolled due to refusal or unwillingness to cooperate (n=58) or insufficient patience to be interviewed (n=14) or insufficient time to participate (n=9). After interviews, nine participants were excluded from further analysis because the site investigator judged them as not having MDD. The remaining 547 participants (352 women and 195 men with mean age of 39.58 ± 13.21 years, age range of 18 to 65 years) were included in the analysis.

There was no significant difference in the distribution of suicidality or the scores of MADRS, Hostility, MSPSS, or LTE between female and male participants (Table 1). No significant difference in the frequencies of each type of life events according to gender was found either, except that a predominance of problems with police and court appearance in male participants was found (Table 2).

In multiple regression analysis, MADRS (β = 0.03, 95% CI = 0.02 to 0.04) and Hostility (β = 0.26, 95% CI = 0.16 to 0.37) scored were positively associated with suicidality in female patients. However, MSPSS (β = −0.14, 95% CI = −0.21 to −0.08) and LTE (β = −0.09, 95% CI = −0.15 to −0.03) scores were negatively associated with suicidality in female patients. In male patients, MADRS (β = 0.03, 95% CI = 0.01 to 0.05) and Hostility (β = 0.16, 95% CI = 0.01 to 0.32) scores were positively associated with suicidality, whereas MSPSS (β = −0.06, 95% CI = −0.15 to −0.03) and LTE (β = −0.16, 95% CI = −0.10 to −0.08) scores were negatively associated with suicidality (Table 3).

Path analysis was conducted in female and male patients separately to evaluate the direct and indirect effect of negative life events and poor social support on suicidality. In women, depression severity that was predicted by more negative life events (β = 0.12, 95% CI = 0.02–0.20, P = 0.020) and poor social support (β = −0.14, 95% CI = −0.26 to −0.08, P = 0.043) significantly predicted suicidality (β = 0.25, 95% CI = 0.17–0.35, P = 0.003). Hostility predicted by more negative life events (β = 0.29, 95% CI = 0.18–0.39, P = 0.011) and poor social support (β = −0.11, 95% CI = −0.20 to −0.01, P = 0.023) also significantly predicted suicidality (β = 0.25, 95% CI = 0.14–0.36, P = 0.012). In addition to indirect effect via depression severity and hostility, more negative life events (β = −0.14, 95% CI = −0.23 to −0.05, P = 0.011) and poor social support (β = −0.21, 95% CI = −0.31 to −0.11, P = 0.009) also directly predicted suicidality (Fig. 1A). In men, depression severity (β = −0.26, 95% CI = −0.09–0.37, P = 0.021) and hostility (β = 0.17, 95% CI = 0.02–0.31, P = 0.043) significantly predicted suicidality. More negative life events (β = 0.25, 95% CI = 0.09–0.38, P = 0.016) and poor social support (β = −0.27, 95% CI = −0.41 to −0.14, P = 0.009) predicted hostility. However, they did not predict depression severity. More negative life events and poor social support indirectly predicted suicidality via hostility, but they had no direct effect on suicidality (Fig. 1B).

Both models showed reasonable fit to the data (Chi-square = 9.580, Q = 4.790; GFI = 0.989, AGFI = 0.920, CFI = 0.942, NFI = 0.931 for women; and Chi-square = 14.0996, Q = 2.499; GFI = 0.971, AGFI = 0.927, CFI = 0.844, NFI = 0.879 for men).

4. Discussion

Our results revealed that negative life events, social support, depressive symptoms, and hostility were all significantly associated with suicidality in female patients with MDD. However, only depressive symptoms and hostility were significantly associated with suicidality in male patients. Negative life event and poor social support predicted suicidality in women with MDD both directly and indirectly via mediation of depression severity and hostility. However, negative life events and poor social support only indirectly predicted suicidality in men with MDD via mediation of hostility.

Table 1
Demographic and clinical characteristics of patients with major depressive disorder according to gender.

<table>
<thead>
<tr>
<th></th>
<th>Male (N=195)</th>
<th>Female (N=352)</th>
<th>X² or t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>14.49</td>
<td>0.013</td>
<td></td>
<td></td>
</tr>
<tr>
<td>South Korea</td>
<td>14.09</td>
<td>0.009</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malaysia</td>
<td>14.29</td>
<td>0.007</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Singapore</td>
<td>14.30</td>
<td>0.006</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thailand</td>
<td>14.72</td>
<td>0.002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taiwan</td>
<td>14.79</td>
<td>0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, Mean (SD)</td>
<td>40.03 (13.19)</td>
<td>40.01 (13.19)</td>
<td>−1.04</td>
<td>0.297</td>
</tr>
<tr>
<td>MINI Suicidality, N (%)</td>
<td>4.49</td>
<td>0.213</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2
Prevalence (%) of each type of stressful life event of patients with major depressive disorder according to gender.

<table>
<thead>
<tr>
<th></th>
<th>Male (N=195)</th>
<th>Female (N=352)</th>
<th>X² or t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious illness or injury to subject</td>
<td>33 (16.9)</td>
<td>81 (23.0)</td>
<td>2.82</td>
<td>0.093</td>
</tr>
<tr>
<td>Serious illness or injury to a close relative</td>
<td>18 (9.2)</td>
<td>49 (13.9)</td>
<td>2.57</td>
<td>0.109</td>
</tr>
<tr>
<td>Separation due to marital difficulties</td>
<td>11 (5.4)</td>
<td>33 (9.4)</td>
<td>2.37</td>
<td>0.124</td>
</tr>
<tr>
<td>Broke off a steady relationship</td>
<td>23 (11.8)</td>
<td>48 (13.6)</td>
<td>0.38</td>
<td>0.539</td>
</tr>
<tr>
<td>Serious problem with a close friend, neighbor or relative</td>
<td>30 (15.4)</td>
<td>56 (15.9)</td>
<td>0.03</td>
<td>0.872</td>
</tr>
<tr>
<td>Unemployed/seeking work for more than one month</td>
<td>22 (11.3)</td>
<td>33 (9.4)</td>
<td>0.51</td>
<td>0.477</td>
</tr>
<tr>
<td>Subject sacked from job</td>
<td>10 (5.1)</td>
<td>22 (6.3)</td>
<td>0.29</td>
<td>0.592</td>
</tr>
<tr>
<td>Change of residence</td>
<td>10 (5.1)</td>
<td>35 (9.9)</td>
<td>3.85</td>
<td>0.050</td>
</tr>
<tr>
<td>Major financial crisis</td>
<td>33 (16.9)</td>
<td>59 (16.8)</td>
<td>0.002</td>
<td>0.961</td>
</tr>
<tr>
<td>Problems with police and court appearance</td>
<td>14 (7.2)</td>
<td>4 (1.1)</td>
<td>14.40</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Something valuable lost or stolen</td>
<td>11 (5.6)</td>
<td>19 (5.4)</td>
<td>0.01</td>
<td>0.905</td>
</tr>
</tbody>
</table>

The role of adverse life events as a precipitating factor for depression is well documented (Jeon et al., 2013b; Kendler et al., 2002). Negative life events such as job loss and financial problems are important precipitating factors of suicide among Asian men (Phillips et al., 2002; Wong et al., 2008; Im et al., 2011), whereas family conflicts are important precipitants for Asian women (Phillips et al., 2002; Zhang et al., 2010; Im et al., 2011). In this study, serious interpersonal problems, serious illness or injury to subject, and major financial crisis were common life problems that male and female patients had faced before the onset of depression.

Inconsistent with our results that negative life event and poor social support had significant indirect effect on suicidality via increasing depressive symptoms, Leskela et al. (2006) have reported that the influence of adversity and perceived social support on the

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outcome of MDD differed according to the levels of depressive symptoms. However, there was no separate analysis by gender in the cited study. We also found direct role of adverse life events and poor social support on suicidality in women via the mediation of depression severity and hostility, but not in men. In male patients, the severity of depressive symptoms was the most important risk factor for suicide. However, negative life events or poor social support was not independent risk factor of suicide. Our findings are in line with previous studies that have reported more susceptibility of women’s psychopathology (e.g., increased anxiety

Table 3
Correlates of suicidality in female and male patients with major depressive disorder.

<table>
<thead>
<tr>
<th></th>
<th>Male (N=195)</th>
<th></th>
<th>Female (N=352)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \beta ) coefficients (95% CI)</td>
<td>( \beta ) coefficients</td>
<td>( P )</td>
<td>( \beta ) coefficients (95% CI)</td>
</tr>
<tr>
<td>MADRS</td>
<td>0.03 (0.01-0.05)</td>
<td>0.25</td>
<td>&lt; 0.001</td>
<td>0.03 (0.02, 0.04)</td>
</tr>
<tr>
<td>Hostility</td>
<td>0.16 (0.01-0.32)</td>
<td>0.15</td>
<td>0.043</td>
<td>0.26 (0.16, 0.37)</td>
</tr>
<tr>
<td>MSPSS</td>
<td>-0.06 (-0.15-0.04)</td>
<td>-0.09</td>
<td>0.198</td>
<td>-0.14 (-0.21 to -0.08)</td>
</tr>
<tr>
<td>LTE</td>
<td>-0.02 (-0.10-0.08)</td>
<td>-0.02</td>
<td>0.745</td>
<td>-0.09 (-0.15 to -0.03)</td>
</tr>
</tbody>
</table>

MADRS; Montgomery–Asberg Depression Rating Scale; MSPSS: Multidimensional Scale of Perceived Social Support; LTE: List of Threatening Experiences

Fig. 1. Path diagrams (A) showing that depressive symptoms and hostility partially mediated the effects of negative life events and social support on suicidality in female patients with major depressive disorder and (B) showing that hostility fully mediated the effects of negative life events and social support on suicidality in male patients. All values were standardized regression weights. Only the significant paths are displayed.
and depression symptoms) than men's one to the influence of surrounding stress or social network (Haw and Hawton, 2008; Kendler et al., 2005; Kessler, 1997; Maciejewski et al., 2001; Nazroo et al., 1997; Sandanger et al., 2004). However, the finding that there was direct association between negative life events and poor social support and suicidality in female MDD patients but not in male MDD patients is novel.

The most marked gender difference in this study is that a more significant and direct association of negative life events and poor support with suicidality was found in female MDD patients compared to that in male MDD patients. This indicates that the suicide risk might increase in female patients if they report a number of negative life events and poor social supports, even if their depressive symptoms and hostility are not severe. In contrast, suicide risk might increase in male patients with a number of negative life events and poor social support only when their hostility is increased. Therefore, when treating a female patient with MDD, creating a strong social support system and using problem solving methods for common adverse life events such as financial difficulties and family conflicts could be useful to prevent suicide. In the mean time, when treating a male patient with MDD, it is important to establish the negative life events they have been facing and to try to help them deal with these problems in a less maladaptive way so that hostility will not be increased.

Our study had several limitations. First, this study was cross-sectional in design, making it impossible to identify causal relationships between social support, depression, and hostility. A prospective study is needed to classify whether poor social support is a predictive factor for depressive symptoms and hostility and vice versa. Second, suicidality could have been under-reported due to possible biased self-reporting on embarrassing behavior such as suicide attempt. Finally, the study sample from each of the six countries may not have been drawn from the same population. Recruitment was biased toward MDD patients who used health care institutions. There might be differences in health care systems across the six countries used in the study.

Despite these limitations, this study extended the findings of previous research by examining the direct and indirect effect of negative life events and poor social support on suicidality according to gender in multinational Asian patients with MDD. Our results highlight the need of in-depth assessment for suicide risk in depressed female patients who report a number of negative life events and poor social support, even if they do not present severe psychopathology. As a clinical implication, problem-solving for life problems and creating social support system as well as treating depressive symptoms are important to prevent suicide in Asian patients with MDD.

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