**Keywords:**depression; suicidal ideation; prevalence; risk factor; drug naïve; IQ

**Introduction**

 ‘Suicidality’, which includes suicidal ideation (SI), suicide attempt, and completed suicide, is a major global public health problem. Completed suicide is a major risk among patients with major depressive disorder (MDD), where 6.7% of males and 3.8% of females die by suicide (Nordentoft et al., 2011). Suicide risk assessment is an essential component of the management of depressed patients. As ‘Suicide completers’ with previous MDD had usually communicated their SI (Fang et al., 2018; Sokero et al., 2003), evaluating SI is an integral part of suicide risk assessment. The reported prevalence estimates of SI among MDD patients ranges from 8% to 66% (Dong et al., 2018; Farmer et al., 2001; Morris et al., 2010; Vuorilehto et al., 2014). Morris et al. (2010) found that 8% of MDD patients had SI, measured by three different scales. Farmer et al. (2001) found that 66% of people with depression had experienced SI in the previous week. Dong et al (2018) analyzed 33 published articles and found that the lifetime prevalence of SI in MDD patients was 53.1%, the one-month prevalence being 27.7%.

Studies have consistently reported that MDD is closely linked to suicide (Hawton and van Heeringen, 2009). Risk factors for suicide specific to MDD including depression severity (Brown et al., 2000; Hawton et al., 2013; Holma et al., 2010; Lim et al., 2014; Oquendo et al., 2004; Sokero et al., 2003; Sokero et al., 2005; Zhu et al., 2013), gender (Hawton et al., 2013; Kwon et al., 2016; Schaffer et al., 2000; Sokero et al., 2003), employment and marital status (Brown et al., 2000; Lim et al., 2014), age at onset (Zhu et al., 2013), stressful life events (Zhu et al., 2013), current alcohol dependence or substance abuse (Dumais et al., 2005; Hawton et al., 2013; Sokero et al., 2003; Sokero et al., 2005),impulsivity and hostility (Dumais et al., 2005), and comorbidity with an anxiety disorder (Hawton et al., 2013; Morris et al., 2010; Zhu et al., 2013). Further, several studies have reported inverse associations between cognitive ability/intelligence quotient (IQ) and suicide (Andersson et al., 2008; Sorberg et al., 2013; Sorberg Wallin et al., 2018). Low IQ level was associated with suicide risk in MDD (Hung et al., 2016)in a cohort study involving 633 participants with lifetime depression, whose cognitive abilities were assessed at age 7 years using the Wechsler Intelligence Scale for Children, low cognitive ability (IQ<85 v. IQ>115) being associated with SI (OR = 3.79).

Most studies which examined the prevalence of SI in depression have been conducted in medicated patients. Studies on suicide in the drug naïve MDD patients are limited. In a recent meta-analysis, Dong et al (2018) found that medicated inpatients/outpatients with MDD had a 27.7% one-month prevalence of SI in the Chinese Han population. The effect of drug treatment on SI in MDD patients has been found to vary between studies. Some, such as [Weitz](https://www.ncbi.nlm.nih.gov/pubmed/?term=Weitz%20E%5BAuthor%5D&cauthor=true&cauthor_uid=24953481) et al (2014) found that antidepressant medications could reduce SI, whereas others found that the risk of suicide in older people with MDD treated with a selective serotonin reuptake inhibitor treatment was greater than in patients not undergoing such treatment (KoKoAung et al., 2015).

The objectives of this study were to investigate associations between demographic and clinical factors with SI among drug naïve patients with MDD using a multi-center cross-sectional design. We recruited a large sample of patients in a Chinese Han population (n= 488) to investigate the prevalence of SI and to determine the socio-demographic, clinical and other correlates of SI.

**2. Methods**

**2.1 Study design and subjects**

Our study was part of a multi-center cross-sectional study. Participants were consecutively enrolled in the study from three psychiatric hospitals and the psychiatric departments of four general hospitals in seven cities, across China. The Institutional Review Board of each site approved this study, and all subjects gave signed, informed consent to participate in the study.

The diagnosis of MDD was established with an acute episode which met DSM–IV criteria for MDD, as assessed by two independent experienced psychiatrists using the Structured Clinical Interview for DSM-IV (SCID) at study intake point. Recruitment criteria also included: 1) age 18–65 years, Han Chinese; 2) patients had no prior treatment with antidepressant medication; 3) current depressive symptoms were of moderate severity or greater as measured with the 17-item HAMD score ≥18. Exclusion criteria were: 1) pregnancy or lactation; 2) the patient refused to provide written informed consent.

For all participants, trained research staﬀ gathered general information, including age, sex, high, weight, education level, marital status, current/history physical disease, and stressful life event; together with information on age at onset of MDD, duration of disease, family history of psychiatric illness, depression severity, anxiety symptoms, psychiatric symptoms and measured IQ.

**2.2 Measures**

Questionnaires employed in this study included the 17-item HAMD (Hamilton, 1960), the and 14-item Hamilton Anxiety Rating Scale (HAMA) (Hamilton, 1959): psychotic symptoms were assessed with the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962).

All patients were assessed for cognitive ability using the Chinese version of the Wechsler Adult Intelligence Scale-Ⅲ (WAIS-Ⅲ) (Wechsler et al., 2002), including the verbal (information, similarities, arithmetic, vocabulary, comprehension) and performance (picture completion, coding, picture arrangement, block design, object assembly) subtests. Individual scores were scaled according to age, and the verbal IQ (VIQ), performance IQ (PIQ) and full-scale IQ (FIQ) scores were derived.

The HAMD item 3 was used to asses SI. The item has the following alternative statements: 0=absent, 1 =feels life is not worth living, 2=wishes he/she were dead or any thoughts of possible death of self, 3=suicide ideas or gesture and 4=attempts at suicide (any serious attempt rates 4). In this study, we defined someone who had suicidal ideation by a score of ≥3 on HAMD item 3 (Vuorilehto et al., 2014). That is to say, if a patient had scores of 3 or 4 he/she would allocated to the group with SI, participants with lower scores being allocated into the group without SI.

**2.3 Statistics**

Descriptive statistics, means and standard deviations (SD) for continuous variables, and percentages for discrete variables, are presented. Variables were compared between groups using t-tests for continuous variables and chi-squared comparisons for categorical variables. When significance was found, the effects of the relevant variables were added to the logistic regression analysis model as covariates. Bivariate logistic regression analysis was used to assess which factors were most strongly associated with SI. We used three models to explore the associations in different levels: in model 1, age, sex, marital status, stressful life event, current/history physical disease, and scores on HAMD/HAMA/BPRS were entered as independent variables; in model 2, education years, scores on HAMD and VIQ/PIQ/FIQ were entered as covariates; in model 3, age, sex, education years, marital status, stressful life event, current/history physical disease and scores on HAMD/HAMA/BPRS and VIQ/PIQ/FIQ were entered as covariates. For all statistical analyses, a P level of less than 0.05 indicated statistical significance. Analysis was performed by SPSS 22.0.

**3. Results**

**3.1 Prevalence of SI in the patients**

A total of 488 drug naïve MDD patients, comprising 203(41.6%) male and 285(58.4%) female participants, ranging from 18 to 65 years old (36.2±12.9), with a minimum HAMD score at 18 (25.1±4.9) were recruited for this study. The prevalence of SI was 32.8% (160/488) in drug naïve patients with MDD, which includes 3.1% (15/488) patients with a suicide attempt.

**3.2 Demographic and clinical characteristics between the patients with and without SI**

Table 1 shows that there were more female patients in group with SI than without (66.2% vs 54.6%, p=0.014), and that marital status (measured by married, divorced and never married) was different between patients with or without SI (x2=6.93, df=2, p=0.031). The differences in marital status but not sex remained significant after using logistic regression to adjust for characteristics including age, sex, stressful life event, current/history physical disease, and scores on HAMD/HAMA/BPRS (p=0.013). Further analysis showed that divorced status was a risk factor, compared to married status, for patients with SI (Wald x2=8.683, df=1, p=0.003; OR=4.674; 95% CI: 1.676~13.036).

Compared to patients without SI, patients with SI had significantly higher scores on HAMD/HAMA/BPRS (t=-8.14, p<0.001, t=-3.28, p<0.001, and t=-5.71, p<0.001, respectively). Through stepwise multiple logistic regression analysis for associations with SI by model 1, we added the demographic and clinical data including sex, age, marital status, stressful life event, current/history physical disease, and scores on HAMD/HAMA/BPRS together into the model and found that the severity of depression measured by HAMD (Wald x2=25.424 df=1, p<0.001; OR=1.143, 95% CI: 1.085~1.204) and psychotic symptoms (Wald x2=7.239, df=1, p=0.007; OR=1.044; 1.012~1.077) remained significant (Table 2).

**3.3 IQ in MDD patients with and without SI**

As shown in table 1, patients with SI had significantly lower scores on VIQ, PIQ and FIQ than patients without SI (t=-3.86, df=348, p<0.001; t=-3.90, df=347, p<0.001; t=-4.21, df=327, p<0.001 respectively). We included education years and scores of HAMD/VIQ/PIQ/FIQ together into a single stepwise bivariate logistic regression analysis of risk factors, (model 2) and found that severity of depression (Wald x2=33.166 df=1, p<0.001; OR=1.197, 95% CI: 1.126~1.272) and FIQ (Wald x2=3.913 df=1, p=0.012; OR=0.983, 95% CI: 0.966~1.000) were significantly associated with SI. Further, when adding these potential risk factors including sex, age, education years, marital status, stressful life event, current/history physical disease, and scores on HAMD/HAMA/BPRS/VIQ/PIQ/FIQ together into model 3, we found that severity of depression (Wald x2=32.912 df=1, p<0.001; OR=1.312, 95% CI: 1.196~1.440) and FIQ (Wald x2=4.518 df=1, p=0.034; OR=0.980, 95% CI: 0.962~0.998) remained significant for SI.

**4. Discussion**

To our knowledge, this is the ﬁrst study to investigate associations between socio-demographic/clinical variables, including IQ levels, and SI in Chinese Han drug naïve MDD patients. The major finding of this study is a frequency of SI of 32,8% in the previous week in drug naïve patients with MDD. In addition, in the binary stepwise logistic regression models, we found that divorce, severity of depression symptoms, comorbid psychotic features and low IQ levels were all signiﬁcantly associated with SI.

We found that 3.1% (15/488) of patients had made a suicide attempt in the last week, considerably lower than the 27.7% one-month SI rate in a recent meta-analysis (Dong et al., 2018). Moreover, a recent epidemiological survey enrolled 3275 MDD patients showed that the previous two weeks prevalence of SI was 53.4%, higher than our findings (Fang et al., 2018). Bi et al (2012) examined 1970 Han Chinese women with recurrent medicated MDD between the ages of 30 and 60 years old and found that the frequency of SI was 61.8%. The different results may be explained by differences in the patient sample and measurements of SI, the inclusion of medicated patients, and different periods for assessing SI. Our findings are based on a cut-off score of 3 on the HAMD suicide item. However, when taken together, all studies have found a high prevalence of SI in both drug naïve and medicated patients with MDD in the Chinese population.

A recent Chinese study showed that the odds ratio of suicidality in females was more than twice that in males (OR =2.62; 95% CI 1.45±4.76) (Li et al., 2017). Furthermore, Chinese national reports on suicide showed that in those younger than 60 years, female rates exceed male rates by an average of 26% (Law and Liu, 2008). We found that female patients were more often in the SI group than in the group without SI, but this difference between groups was not significant after stepwise bivariate logistic regression analysis..

A recent meta-analyses of 36 studies found that suicide risk was higher in divorced individuals than married individuals, in both men and women (OR = 2.99, 95% CI: 1.97~4.55) (Kyung-Sook et al., 2018). Studies have suggested that the effects of marital dissolution (i.e. divorce) are not only the loss of a social relationship but also a serious stressor (Hagedoorn et al., 2006), often associatedwith loss of financial or instrumental support (Andres et al., 2010). Our study found that divorced marital status was a significant risk factor for SI in MDD patients.

In addition, the robust association between depressive symptom severity and SI n the present study is consistent with previous studies. Valuck et al.(2012) found that 25% to 30% of MDD patients expressed some degree of SI according to the 9-item Patient Health Questionnaire, and reported a substantial correlation between severity of depressive symptoms and SI. Wang et al. (2015) have replicated the significant association between depression severity and SI. Interestingly, Ribeiro et al. (2018) conducted a recent meta-analysis of 166 published studies from 1971 to 2014, and found that depressive symptoms were significant predictors of SI (OR = 1.57, 95% CI: 1.45~1.70; OR = 2.48, 95% CI: 1.32~4.67 respectively).

We found that MDD patients with psychotic features had a higher rate of SI than patients without psychosis. A comprehensive review of 24 studies (Zalpuri and Rothschild, 2016) indicated that psychotic depressed patients had higher rates of suicide, suicide attempts, and SI when compared to MDD patients without psychosis, particularly during the acute episode of the illness. Another meta-analysis of twenty studies reported by Gournellis et al. (2018), provides additional evidence that psychotic depressed patients have a two-fold higher risk of suicide attempt, both during lifetime and in the acute phase, when compared to depressed patients without psychosis.

We found that patients who had low FIQ scores, but not low VIQ and PIQ scores, had higher SI prevalence than those with high FIQ scores. Children or young adults with relatively low cognitive ability, as measured by scores on IQ tests, may be more likely to develop a psychiatric disorder than children or young adults with relatively better cognitive abilities (Franz et al., 2011; Horwood et al., 2008; Weeks et al., 2014). Some studies have indicated that lower IQ is associated with a greater risk of SI and suicide attempt (Batty et al., 2010; Sorberg et al., 2013; Hung et al., 2016; Sorberg Wallin et al., 2018). One putative explanation draws on ‘cognitive reserve’ theories, which posit that strengthened neural connections (presumably manifested by higher scores on IQ tests) protect against the development of psychiatric disorders and attenuate the severity of disorders following their onset (Barnett et al., 2006; Stern, 2002). Another possible explanation is that the association between low IQ and an increased risk of suicide may be because people with low IQ experience SI for more prolonged periods than those with high IQ or because low IQ increases the likelihood that people experiencing SI act upon them (Gunnell et al., 2009). However, Park et al (2015) found that there were no significant differences in any type of IQ between completed suicide patients and non-suicide patients, in a mixed diagnostic sample.

Possible associations between IQ and psychiatric and suicidal outcomes are not fully understood. In a systematic review Scult et al. (2017) of the potential linkage between cognitive function and subsequent depression, which involved 29 publications, representing 121,749 participants, the association between lower cognitive function and later depression was confounded by the presence of contemporaneous depressive symptoms at the time of cognitive assessment. Furthermore, most studies on IQ and suicidal outcomes have been conducted in Western and/orEnglish-speaking populations, whereas cultural differences might be relevant in understanding differences or similarities between studies.

There are several limitations which should be considered. First, this is a cross-sectional study which cannot show direct causality between SI and the risk factors in patients with MDD. Second, the SI data were collected through use of HAMD item 3 rather than structured specific SI instrument. Third, we did not assess the severity of SI. Fourth, all participants were from 7 hospitals located in provincial capital cities, and so may not constitute a representative sample of patients in China. Fifth, the associations between SI and cognitive functions was not explore through more detail cognitive assessment.

In conclusion, whilst acknowledging these limitations, our study is the first to investigate SI and relevant risk factors including IQ in drug naïve Chinese Han MDD patients. We found that marital status, severity of depression, psychotic features and IQ levels were associated with the presence of SI. Future research using a prospective study design is warranted to examine how these and other factors might contribute to suicide risk and other clinical outcomes.

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**Table 1.** **Demographic, clinical characteristics and IQ between groups with and without suicidal ideation in drug-naïve patients with MDD**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| variables | With SI(N=160, 32.8%) | Without SI(N=328, 67.2%) | ⅹ2 | df | p |
| Male, N (%) | 54 (33.8) | 149 (45.4) | 6.04 | 1 | 0.014\* |
| Education years, N (%) |  |  | 4.37 | 2 | 0.113 |
| <10 | 65 (40.6) | 105 (32.2) |  |  |  |
| 10-12 | 37 (23.1) | 100 (30.7) |  |  |  |
| >12 | 58 (36.3) | 121 (37.1) |  |  |  |
| Marital status, N (%) |  |  | 6.93 | 2 | 0.031\* |
| Married | 99 (62.3) | 199 (60.7) |  |  |  |
| Divorced  | 12 (7.5) | 9 (2.8) |  |  |  |
| Never married  | 48 (30.2) | 119 (36.5) |  |  |  |
| Current/history physical disease, N (%) | 28 (19.0) | 34 (11.2) | 5.17 | 1 | 0.023\* |
| Stressful life event, N (%) | 71 (45.5) | 108 (34.1) | 5.82 | 1 | 0.016\* |
| Family history of MD, N (%) | 18 (11.9) | 22 (7.1) | 2.94 | 1 | 0.086 |
| Age, Mean (SD) | 36.85 (12.46) | 35.89 (13.14) | -0.77 | 486 | 0.440 |
| Age at onset, Mean (SD) | 34.89 (12.42) | 33.86 (13.16) | -0.82 | 415 | 0.415 |
| Duration of months illness, Mean (SD) | 25.46 (5.56) | 25.14 (9.30) | -0.08 | 472 | 0.937 |
| BMI, Mean (SD) | 21.74 (3.07) | 22.25 (5.68) | 1.05 | 471 | 0.296 |
| HAMD, Mean (SD) | 27.51 (4.97) | 23.90 (4.40) | -8.14 | 486 | 0.000\*\* |
| HAMA, Mean (SD) | 22.76 (7.03) | 20.78 (5.83) | -3.28 | 485 | 0.001\*\* |
| BPRS, Mean (SD) | 35.37 (8.23) | 31.38 (6.59) | -5.71 | 474 | 0.000\*\* |
| VIQ, Mean (SD) | 99.84 (18.36) | 107.03 (15.43) | 3.86 | 348 | 0.000\*\* |
| PIQ, Mean (SD) | 94.95 (14.83) | 101.11 (13.45) | 3.90 | 347 | 0.000\*\* |
| FIQ, Mean (SD) | 98.06 (15.63) | 105.43 (14.87) | 4.21 | 327 | 0.000\*\* |

Note: MDD=major depressive disorder, SI=suicidal ideation, BMI=body mass index, HAMD= Hamilton depression rating scale, HAMA= Hamilton anxiety rating scale, BPRS= brief psychiatric rating scale; VIQ= verbal IQ; PIQ= performance IQ; FIQ=full-scale IQ;

\*p < 0.05; \*\*p < 0.01;

 Since some subjects did not complete the questionnaire or clinical measures fully, numbers vary slightly in different categories.

**Table 2. Stepwise logistic regression analysis of with or without suicidal ideation in drug-naïve patients with MDD**

|  |  |  |  |
| --- | --- | --- | --- |
| variables | Model1.demographic and clinical profiles  | Model2. demographic, clinical features and IQ | Model3. demographic, clinical features and IQ |
|  | OR | 95% CI | p | OR | 95% CI | p | OR | 95% CI | p |
| **marital status** |  |  | 0.013\* |  |  |  |  |  |  |
| Married |  |  |  |  |  |  |  |  |  |
| Divorced | 4.704 | 1.686~13.121 | 0.003\*\* |  |  |  |  |  |  |
| Never married | 1.147 | 0.703~1.871 | 0.584 |  |  |  |  |  |  |
| BPRS | 1.044 | 1.012~1.077 | 0.007\*\* |  |  |  |  |  |  |
| HAMD | 1.143 | 1.085~1.204 | 0.000\*\* | 1.197 | 1.126~1.272 | 0.000\*\* | 1.312 | 1.196~1.440 | 0.000\*\* |
| FIQ |  |  |  | 0.983 | 0.966~1.000 | 0.012\* | 0.980 | 0.962~0.998 | 0.034\* |

Note:

MDD=major depressive disorder, HAMD= Hamilton depression rating scale, HAMA= Hamilton anxiety rating scale, BPRS= brief psychiatric rating scale; VIQ= verbal IQ; PIQ= performance IQ; FIQ=full-scale IQ;

\*p < 0.05; \*\*p < 0.01;

Model1: adjusted for Age, sex, marital status, stressful life event, current/history physical disease, and scores on HAMD/HAMA/BPRS.

Model2: adjusted for scores on HAMD, education years and VIQ/PIQ/FIQ.

Model3: adjusted for age, sex, education years, marital status, stressful life event, current/history physical disease and scores on HAMD/HAMA/BPRS and VIQ/PIQ/FIQ.