https://jos.unsoed.ac.id/index.php/jipa

ARTICLE REVIEW

Suicidality and Somatic Comorbidities in Major Depressive Disorder: A Literature Review

Asti Yuliadha[1], Irin Riamanda[2]

ABSTRACT

Introduction: There is a strong interconnection between depression, as a significant mental health condition, and the vast majority of somatic symptoms. The presence of these conditions not only affects the quality of life but is also linked to poorer outcomes in treatment and increases the severity of depressive symptoms. On the other hand, suicidal behavior is notably prevalent among individuals with major depressive disorder (MDD). Even though somatic symptoms are common in MDD, their associations with suicide remain unclear. This literature review aimed to determine somatic comorbidities of MDD and their relation to suicidality. **Method**: This literature review was conducted using PubMed and Google Scholar to identify studies published within the last 5 years. Keywords combined terms for *MDD/depression*, *suicidality* (ideation/attempt/risk), and *somatic/medical comorbidity* using Boolean operators. Relevant studies were screened, key data extracted, and findings synthesized narratively. **Results:** The relationship between suicidality and somatic comorbidities in MDD is complex and multifaceted; it shares not only psychosocial factors but also a common biological and structural core. Chronic pain and cardio-metabolic conditions were the most commonly reported comorbidities. Greater somatic burden or multimorbidity tended to align with higher suicidal ideation and attempt risk. Understanding the interplay between these factors is crucial for effective clinical management and intervention strategies. **Conclusions:** These underscore the need for comprehensive assessment and tailored interventions that address both mental and physical health aspects. Regular comprehensive screening for suicidality and somatic conditions should be integral to managing MDD to improve patient outcomes effectively.

Keywords: Comorbidity, Major Depressive Disorder, Risk Factor, Somatic, Suicidal

1. Department of Psychiatry, Faculty of Medicine, Universitas Syiah Kuala, Banda Aceh, Indonesia
2. Department of Psychology, Faculty of Medicine, Universitas Syiah Kuala, Banda Aceh, Indonesia

* ✉ email: astiyuliadha@usk.ac.id

INTRODUCTION

The most frequent mental disorder worldwide is major depressive disorder (MDD), with a lifetime risk of 15– 18%, and about 5% suffer from major depression in any given year[1,2]. It's widely distributed in the population and usually associated with substantial symptom severity and role impairment[1,3,4]. Based on Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5), MDD is diagnosed when an individual has five of these symptoms, namely persistently low or depressed mood, anhedonia or decreased interest in pleasurable activities, feelings of guilt or worthlessness, lack of energy, poor concentration, appetite changes, psychomotor retardation or agitation, sleep disturbances, or suicidal thoughts. One must have a depressed mood or anhedonia, and this causes social or occupational impairment[5,6].

Somatic symptoms are common in patients with MDD, which can complicate treatment[4,7]. On the other hand, suicidal behavior is also notably prevalent among individuals with MDD, where MDD is an important risk factor for suicidal behavior[8]. However, the associations between somatic comorbidities in MDD and suicide remain unclear. This literature review aimed to determine somatic comorbidities of MDD and their relation to suicidality.

METHODS

Study design

This study was a literature review using a structured search strategy to identify published evidence on the relationship between suicidality (suicidal ideation, suicide attempt, or suicide-related outcomes) and somatic comorbidities/somatic symptom burden in individuals with major depressive disorder (MDD).

Data sources and search period

A literature search was conducted in PubMed and Google Scholar, covering publications over the last 5 years. Only articles with full-text availability were considered for inclusion.

Search strategy

Search terms were developed using three main concepts: MDD/depression, suicidality, and somatic comorbidity/physical illness/somatic symptoms. Boolean operators (AND/OR) were used, with following keywords: "*major depressive disorder*" OR *MDD* OR "*Depressive Disorder, Major*" OR *depression* AND *suicide* OR "*suicidal ideation*" OR "*suicide attempt*" OR "*suicide risk*" OR "*self-harm*" AND somatic OR "*somatic symptoms*" OR "*physical illness*" OR "*medical comorbidity*" OR *comorbid*.

Study selection process

All records were exported and duplicates removed. Titles/abstracts were screened for relevance, followed by full-text review for final eligibility.

REVIEWS

MDD and Somatic Comorbidities

MDD frequently coexists with various somatic disorders, which can complicate treatment and increase the severity of depressive symptoms. Somatic symptoms are common in primary care settings, often dominating the clinical picture of depression. Research indicates that approximately two-thirds of patients with depression present primarily with somatic complaints, such as fatigue, pain, and gastrointestinal issues, rather than typical psychological symptoms like sadness or anhedonia[4,7,9].

Somatic symptoms of MDD can be grouped into[7,10,11]:

1) vegetative symptoms, including sleep disturbance, changes in appetite, and lack of energy;
2) painful symptoms, including headache, backache, gastrointestinal disturbances, and musculoskeletal aches;
3) non-painful symptoms, including dizziness, palpitations, dyspnea, and shortness of breath

The present study from the population in Germany comprehensively illustrates the strong interconnection of depression with the vast majority of somatic diseases, where the three most frequent somatic comorbid diagnosis groups were dorsopathies, hypertension, and metabolic disorders. The diseases of the central nervous system (i.e., multiple sclerosis) and several neurological diseases, such as sleep disorders, migraine, and epilepsy, have strong associations with higher prevalences of depression[4]. The presence of somatic symptoms is related to worse outcomes in depression treatment, affects the quality of life, and patients often experience lower remission rates from antidepressant therapies. Somatic symptoms in MDD were predictors for greater severity, worse prognosis, and poorer treatment response, as well as the chronicity and delayed remission of MDD[12,13].

The connection between somatic symptoms and depression may involve several biological dysregulations. These somatic consequences could partly be due to metabolic, immuno-inflammatory, autonomic, and hypothalamic-pituitary-adrenal (HPA)-axis dysregulations, which have been suggested to be more often present among depressed patients, potentially linking emotional distress with physical health issues[14]. The potent interconnection of depression with other mental and peripheral disease symptoms may no longer be seen as simple co-occurrences or comorbidities; it may involve multiple bidirectional pathways with a similar genetic basis (Fig.1)[15].

Suicidality in MDD

Suicidal thoughts or behaviors are recognized as diagnostic criteria for MDD in the DSM-5 and have been reported in up to 50% of patients with MDD. The longer the episodes, the higher the occurrence. Suicidal behavior is defined as self-inflicted harm with or without concurrent suicidal ideation[16]. Suicidal ideation (SI), suicide plan (SP), suicide attempt (SA), and completed suicide (CS) are the four aspects of suicidality. SI refers to thoughts or wishes about ending one's life, SP refers to making plans for suicide, and SA refers to acts to end one's life[17].

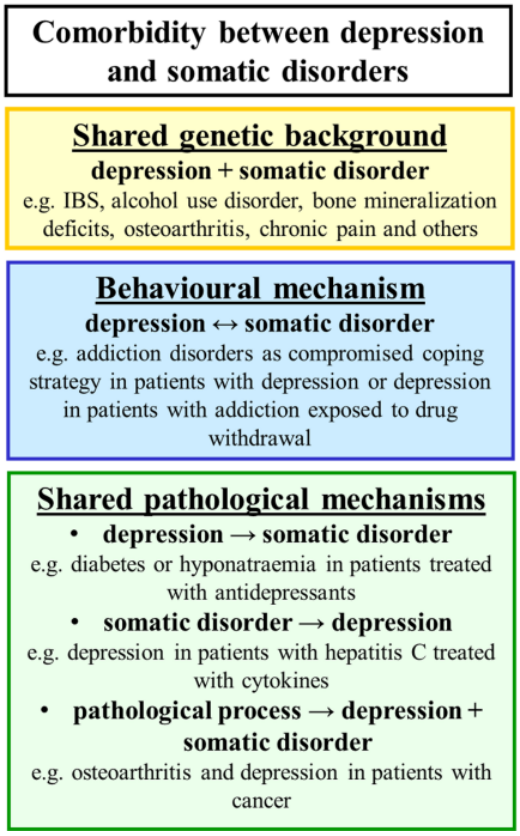


Figure 1. Main pathological mechanisms underlying comorbidity between MDD and somatic and mental disorders[15]

Suicidal behavior is notably prevalent among individuals with MDD, where MDD is an important risk factor of suicidal behavior[8]. Research indicates that 16% to 33.7% of individuals with MDD have attempted suicide at least once in their lifetime, which is significantly higher than the general population's rates[18,19]. A systematic review found that the lifetime prevalence of suicide attempts in MDD patients is approximately 31%, with a 12-month prevalence rate of 8%[19]. One cohort study's finding suggested that high mortality, morbidity, health care resource utilization (HCRU), and work loss associated with MDD may be substantially accentuated in patients with MDD and suicidal behavior. When

comparing the all-cause mortality to MDD episodes with and without suicide behavior records, the difference was more than doubled. Younger age at the onset of depression and a history of suicidal behavior are also significant predictors of future suicidal action[8].

The increased suicidality in MDD could be due to several reasons. Symptoms in MDD, such as feelings of hopelessness, worthlessness, delusionally depressive thoughts, anxiety, and sleep disturbances, directly and indirectly increase the risk of suicide attempts. In addition, psychosocial factors associated with MDD, such as disruption of marital and family connections, could also increase the risk of suicidality[20,21]. The increased risk of suicidality in MDD could be associated with biological factors, such as the uncoupled N-acetyl aspartate–glutamatergic metabolism in the anterior cingulate cortex and the impaired executive functions and impulsivity control caused by decreased structural connectivity in the fronto-subcortical circuit[22,23].

Suicidality and Somatic Comorbidities in MDD

Somatic symptoms have been linked to an elevated likelihood of suicidal ideation and suicide attempts, with active suicidal ideation estimated from 24 to 34%[24]. Suicidality and somatic comorbidities in MDD patients are associated with increased healthcare resource utilization, higher all-cause mortality rates; one study indicated that patients exhibiting suicidal behavior had a mortality rate 2.6 times higher than those without such behaviors[8], greater functional impairment and disability compared to those with either condition alone[4]. Suicidal ideation was associated with much more frequent and severe somatic symptoms in MDD patients of both sexes than in those without it. Current suicidal risk was associated with chest pain in men, and neck or shoulder pain in women[12].

Comorbid somatic symptoms are common in patients with mood disorders and vice versa. It is commonly recognized that people with mood problems are more likely to attempt suicide, and this risk appears to increase when somatic symptoms are present. This could be a result of comorbid somatic symptoms that tend to be associated with a more severe illness burden, which is linked to a higher prevalence of suicidality[24,25]. Pain is frequently found in clinical MDD patients, and chronic pain is strongly associated with suicidality. Most patients with depression have one or more pain complaints; those who suffer from chronic pain are more likely to suffer from a variety of negative health outcomes, including suicide [12,26]. Approximately 30% of patients treated for an episode of MDD experience painful physical symptoms, and painful symptoms are associated with suicidal ideation[27]. Another study found that multiple somatic pain was significantly associated with lifetime suicide attempts. It had a greater prevalence among individuals reporting a higher number of somatic pain conditions and comorbid MDD[28].

One study that examined somatic symptoms and sleep quality as indicators of depression and suicide risk in Korean military conscripts found that moderate to high levels of somatic symptoms and poorly perceived health were linked to the risk of depression and suicide. A higher risk of depression was associated with poor sleep quality, but sleep quality was not significantly related to suicide risk after accounting for depression. The association between sleep problems and suicide is mainly due to its association with depression[29].

Higher levels of frustration and hopelessness could be reasons for the higher frequency of suicidal ideation and suicide attempts among people with somatic symptoms, and these can evolve into feelings of despair, which may contribute to increased suicidality[24]. One example is pain symptoms, where chronic pain leads to suffering, overwhelming disability, and personal impairment, pervading all aspects of social

and emotional life. Multiple pain conditions may induce impulsivity, anger, and catastrophic thinking, and this could increase the risk of suicide. Moreover, a common biological core may interrelate impulsivity, overt aggression, and pain. Pain is associated with genetic variants influencing the opioid, serotonergic, and adrenergic systems, as well as endogenous opioid system dysfunction. The altered metabolism of serotonin, noradrenergic, and dopaminergic activities can also play an important role in impulsive behaviors. This suggests that impulsivity, overt aggression, and pain share a common biological and structural core, which involves different factors, including serotonergic and adrenergic systems[28,30]. Based on the literature review above, it can be concluded that there are biopsychosocial factors that play a role in the relationship between suicide and somatic comorbidity in MDD.

Clinical Implications

Integrated care is crucial in managing MDD alongside somatic comorbidities due to the complex interplay between mental and physical health. This approach not only enhances treatment outcomes but also addresses the various needs of patients, leading to improved quality of life[4,31,32]. Treatment considerations for suicidality and somatic comorbidities in MDD involve a multifaceted approach combining pharmacotherapy, psychotherapy, lifestyle interventions, and collaborative care models. Regular screening for depression in primary care settings is essential, given the high comorbidity rates with somatic symptoms. Early detection allows for timely intervention, which can prevent worsening of symptoms and reduce the risk of suicidal behavior[4,33].

CONCLUSION

The relationship between suicidality and somatic comorbidities in MDD is complex and multifaceted. Realizing a higher rate of comorbid somatic symptoms in MDD, and people with MDD are more likely to attempt suicide, underscores the need for comprehensive assessment and tailored interventions that address both mental and physical health aspects. Regular screening for suicidality and somatic conditions should be integral to the comprehensive management of MDD, and it needs a multidisciplinary approach. This integrated care is expected to improve patient outcomes effectively.

ACKNOWLEDGMENTS

None.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

FUNDINGS

None.

REFERENCES

1. R. C. Kessler *et al.*, “The Epidemiology of Major Depressive Disorder,” *JAMA*, vol. 289, no. 23, p. 3095, Jun. 2003, doi: 10.1001/jama.289.23.3095.
2. T. Asif, D. Adavalath, and P. Cherukunnath, “Somatic Symptoms in Depression and Their Correlation with Suicidality - A Cross-Sectional Study,” *J. Evol. Med. Dent. Sci.*, vol. 9, no. 38, pp. 2824–2828, Sep. 2020, doi: 10.14260/jemds/2020/615.
3. G. S. Malhi and J. J. Mann, “Depression.,” *Lancet (London, England)*, vol. 392, no. 10161, pp. 2299–2312, Nov. 2018, doi: 10.1016/S0140-6736(18)31948-2.
4. A. Steffen, J. Nübel, F. Jacobi, J. Bätzing, and J. Holstiege, “Mental and somatic comorbidity of depression: A comprehensive cross-sectional analysis of 202 diagnosis groups using German nationwide ambulatory claims data,” *BMC Psychiatry*, vol. 20, no. 1, pp. 1–15, 2020, doi: 10.1186/s12888-020-02546-8.
5. American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*, 5th ed. Washington, DC: American Psychiatric Association, 2013.
6. N. Bains and S. Abdijadid, “Major Depressive Disorder,” *StatPearls Publishing [Internet]*, 2023. .
7. X. Wu *et al.*, “Identifying the Subtypes of Major Depressive Disorder Based on

Somatic Symptoms: A Longitudinal Study Using Latent Profile Analysis," *Front. Psychiatry*, vol. 13, no. July, pp. 1–9, 2022, doi: 10.3389/fpsyt.2022.759334.
8. J. Lundberg *et al.*, "Determinants and Outcomes of Suicidal Behavior among Patients with Major Depressive Disorder," *JAMA Psychiatry*, vol. 80, no. 12, pp. 1218–1225, 2023, doi: 10.1001/jamapsychiatry.2023.2833.
9. A. Tylee and P. Gandhi, "The importance of somatic symptoms in depression in primary care.," *Prim. Care Companion J. Clin. Psychiatry*, vol. 7, no. 4, pp. 167–76, 2005, doi: 10.4088/pcc.v07n0405.
10. B. W. Dunlop *et al.*, "Somatic symptoms in treatment-naïve Hispanic and non-Hispanic patients with major depression," *Depress. Anxiety*, vol. 37, no. 2, pp. 156–165, Feb. 2020, doi: 10.1002/da.22984.
11. D. Novick *et al.*, "Which somatic symptoms are associated with an unfavorable course in Asian patients with major depressive disorder?," *J. Affect. Disord.*, vol. 149, no. 1–3, pp. 182–188, Jul. 2013, doi: 10.1016/j.jad.2013.01.020.
12. H. J. Jeon *et al.*, "Gender differences in somatic symptoms and current suicidal risk in outpatients with major depressive disorder," *Psychiatry Investig.*, vol. 13, no. 6, pp. 609–615, 2016, doi: 10.4306/pi.2016.13.6.609.
13. E. Bekhuis, L. Boschloo, J. G. M. Rosmalen, M. K. de Boer, and R. A. Schoevers, "The impact of somatic symptoms on the course of major depressive disorder," *J. Affect. Disord.*, vol. 205, pp. 112–118, Nov. 2016, doi: 10.1016/j.jad.2016.06.030.
14. B. W. Penninx, Y. Milaneschi, F. Lamers, and N. Vogelzangs, "Understanding the somatic consequences of depression: biological mechanisms and the role of depression symptom profile," *BMC Med.*, vol. 11, no. 1, p. 129, Dec. 2013, doi: 10.1186/1741-7015-11-129.
15. L. S. Kalinichenko, J. Kornhuber, and C. P. Müller, "The system's genetics of depression and its somatic and mental comorbidities," *Transl. Neurosci.*, vol. 13, no. 1, pp. 198–200, Jul. 2022, doi: 10.1515/tnsci-2022-0229.
16. S. McManus *et al.*, "Prevalence of non-suicidal self-harm and service contact in England, 2000–14: repeated cross-sectional surveys of the general population," *The Lancet Psychiatry*, vol. 6, no. 7, pp. 573–581, Jul. 2019, doi: 10.1016/S2215-0366(19)30188-9.
17. K. Posner, M. A. Oquendo, M. Gould, B. Stanley, and M. Davies, "Columbia Classification Algorithm of Suicide Assessment (C-CASA): Classification of Suicidal Events in the FDA's Pediatric Suicidal Risk Analysis of Antidepressants," *Am. J. Psychiatry*, vol. 164, no. 7, pp. 1035–1043, Jul. 2007, doi: 10.1176/ajp.2007.164.7.1035.
18. Y. Zhou *et al.*, "The association of clinical correlates, metabolic parameters, and thyroid hormones with suicide attempts in first-episode and drug-naïve patients with major depressive disorder comorbid with anxiety: a large-scale cross-sectional study," *Transl. Psychiatry*, vol. 11, no. 1, 2021, doi: 10.1038/s41398-021-01234-9.
19. H. Cai *et al.*, "Prevalence of Suicidality in Major Depressive Disorder: A Systematic Review and Meta-Analysis of Comparative Studies," *Front. Psychiatry*, vol. 12, no. September, 2021, doi: 10.3389/fpsyt.2021.690130.
20. K. Okamura, K. Ikeshita, S. Kimoto, M. Makinodan, and T. Kishimoto, "Suicide prevention in Japan: Government and community measures, and high-risk interventions," *Asia-Pacific Psychiatry*, vol. 13, no. 3, Sep. 2021, doi: 10.1111/appy.12471.
21. A. Omary, "Predictors and Confounders of Suicidal Ideation and Suicide Attempts among Adults with and without Depression," *Psychiatr. Q.*, vol. 92, no. 1, pp. 331–345, Mar. 2021, doi: 10.1007/s11126-020-09800-y.
22. W. Myung *et al.*, "Reduced frontal-subcortical white matter connectivity in association with suicidal ideation in major depressive disorder," *Transl. Psychiatry*, vol. 6, no. 6, pp. e835–e835, Jun. 2016, doi: 10.1038/tp.2016.110.
23. C. P. Lewis *et al.*, "Altered anterior cingulate glutamatergic metabolism in depressed adolescents with current suicidal ideation," *Transl. Psychiatry*, vol. 10, no. 1, p. 119, Apr. 2020, doi: 10.1038/s41398-020-0792-z.
24. M. E. Torres, B. Löwe, S. Schmitz, J. N. Pienta, C. Van Der Feltz-Cornelis, and J. G. Fiedorowicz, "Suicide and suicidality in somatic symptom and related disorders: A systematic review," *J. Psychosom. Res.*, vol. 140, p. 110290, Jan. 2021, doi: 10.1016/j.jpsychores.2020.110290.
25. D. G. Öyekçin and E. M. Sahin, "Suicidal Ideations and Attempts in Patients Admitted to Psychiatry Outpatient Clinic," *Nobel Med.*, vol. 3, no. 1, pp. 75–83, 2013.
26. T. Jolly *et al.*, "Risk of Suicide in Patients With Major Depressive Disorder and Comorbid Chronic Pain Disorder: An Insight From National Inpatient Sample Data," *Pain Physician*, vol. 25, no. 6, pp. 419–426, 2022.
27. W. M. Bahk, S. Park, D. I. Jon, B. H. Yoon, K. J. Min, and J. P. Hong, "Relationship between painful physical symptoms and severity of

depressive symptomatology and suicidality," *Psychiatry Res.*, vol. 189, no. 3, pp. 357–361, 2011, doi: 10.1016/j.psychres.2011.01.009.
28. M. J. Park *et al.*, "Multiple types of somatic pain increase suicide attempts and depression: A nationwide community sample of Korean adults," *Compr. Psychiatry*, vol. 90, pp. 43–48, 2019, doi: 10.1016/j.comppsych.2018.12.006.
29. E.-J. Shim *et al.*, "Somatic symptoms and sleep quality as indicators of depression and suicide risk among Korean military conscripts," *Psychiatry Res.*, vol. 287, p. 112912, May 2020, doi: 10.1016/j.psychres.2020.112912.
30. F. Margari *et al.*, "Aggression, impulsivity, and suicide risk in benign chronic pain patients - a cross-sectional study.," *Neuropsychiatr. Dis. Treat.*, vol. 10, pp. 1613–20, 2014, doi: 10.2147/NDT.S66209.
31. M. Latas *et al.*, "Diagnostic psychiatric and somatic comorbidity in patients with depression in the Western Balkan countries," *PLoS One*, vol. 19, no. 1, p. e0295754, Jan. 2024, doi: 10.1371/journal.pone.0295754.
32. M. Berk *et al.*, "Comorbidity between major depressive disorder and physical diseases: a comprehensive review of epidemiology, mechanisms and management.," *World Psychiatry*, vol. 22, no. 3, pp. 366–387, Oct. 2023, doi: 10.1002/wps.21110.
33. K. Maehder, B. Löwe, M. Härter, D. Heddaeus, M. Scherer, and A. Weigel, "Management of comorbid mental and somatic disorders in stepped care approaches in primary care: a systematic review," *Fam. Pract.*, vol. 36, no. 1, pp. 38–52, Jan. 2019, doi: 10.1093/fampra/cmy122.