### **Original article**

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# Factors associated with increased suicide risk in Obsessive-Compulsive Disorder

### Summary

### **Objectives**

Obsessive-Compulsive Disorder (OCD) is in itself at greater risk for suicide (suicidal ideation, suicide attempts and completed suicide) as compared to the general population. However, the majority of individuals with OCD do not have current or lifetime suicidal ideation nor did attempt suicide in their lifetime.

### Methods

The present paper aims to provide an updated review on factors (socio-demographic and personal factors, OCD-related variables, comorbidities, emotion-cognitive factors, and biological variables) contributing to the increased suicide risk in patients with OCD.

### **Results**

Several factors have been found to be strongly associated with suicide risk in patients with OCD, such as the severity of OCD, the unacceptable thoughts symptom dimension, having a comorbid Axis I disorder (Bipolar Disorder, Major Depressive Disorder, Substance Use Disorder), the severity of comorbid depressive and anxiety symptoms, a previous history of suicide attempts, having high levels of alexithymia and hopelessness.

#### Conclusions

Several contributing factors should be evaluated and identified in the clinical practice in order to improve early detection of suicide risk. Risk identification and stratification of risk remain essential components of suicide prevention and should guide the clinical approach to patients with OCD. Whether and how these risk factors for suicide in patients with OCD work together, and whether the specific factors act as moderators or mediators, remains to be fully clarified.

#### Key words

Obsessive-Compulsive Disorder (OCD) • Suicide • Risk factors

### Introduction

Obsessive-Compulsive Disorder (OCD) has been considered for long time a disorder without a notable suicide risk. According to recent metaanalyses, patients with OCD may actually be considered at risk for suicidal ideation, suicide attempts and committed suicide.

Harris et al. <sup>1</sup> found that patients with OCD has 10-times higher risk of suicide compared to the general population. Khan et al. <sup>2</sup> estimated the incidence of suicide attempts among subjects with anxiety disorders, and found a 4% incidence in the subset of patients with OCD. This is a notable result as these patients were enrolled in clinical trials and, since the risk of suicidal behaviors is often an exclusion criterion, it means they were likely not deemed at risk. In more recent years, two independent systematic reviews <sup>34</sup> confirmed a significant association between OCD, suicidal ideation and suicide attempts.

The concept that patients with OCD are not at risk of committing or attempting suicide, with the clinical consequence of underestimating and un-

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<sup>1</sup> Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy; <sup>2</sup> Rita Levi Montalcini Department of Neuroscience, University of Torino, Italy; <sup>3</sup> Department of Psychiatry, Sántha Kálmán Szakkórház, Nagykálló, Hungary; <sup>4</sup> Department of Neurosciences, Mental Health and Sensory Organs, Suicide Prevention Center, Sant'Andrea Hospital, Sapienza University of Rome, Rome, Italy; <sup>5</sup> Department of Clinical and Theoretical Mental Health, Kútvölgyi Clinical Center, Semmelweiss University, Budapest, Hungary





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Department of Biomedical and Neuromotor Science, Section of Psychiatry, University of Bologna, viale C. Pepoli 5, 40123 Bologna, Italy • Tel. +39 051 2083058 • Fax +39 051 521030 • E-mail: umberto.albert@unibo.it dertreating this aspect, has been questioned. Clinicians should consider that patients affected from OCD are at risk and all aspects of suicidality should be evaluated in these patients. However, having a mental disorder is one of the contributing factors for suicide risk; other risk factors can interact with the diagnosis of OCD and determining the risk of suicide in each subject.

The present paper aims to provide an updated review of the literature concerning the relationship between suicide risk and OCD. Specifically, we will focus our attention on factors (socio-demographic and personal factors, OCDrelated variables, comorbidities, psychopathological and biological variables) contributing to the increased suicide risk in OCD (either in terms of suicidal ideation, suicidal attempts, or completed suicides).

### Methods

We performed a systematic review of the literature by searching PubMed from the date of the first available article to January 8, 2018. The search terms [suicide] OR [suicidality] OR [suicide attempts] OR [suicidal ideation] OR [suicidal thoughts] were combined with [OCD] OR [obsessive\*compulsive disorder] OR [obsessive\*compulsive symptoms]. We included: 1) studies with appropriate definition of OCD (diagnosis made through specific structured interviews and/or established international criteria); 2) performed in adolescents and/or adults; 3) with a cross-sectional or prospective designs; 4) performed in clinical samples or in the general population (epidemiological studies); 5) which employed a quantitative measure of suicidality; and/or 6) reported an outcome measure of the association between suicidality and OCD (e.g. odds ratios) or examined factors associated with suicidality.

### Estimates of suicide risk in OCD

A recent systematized review of the available literature <sup>4</sup> investigated suicide risk in OCD patients in both clinical and epidemiological samples; estimates of suicidal ideation and suicide attempts rates in clinical samples were based on 37 studies while 14 epidemiological studies provided data on the association in the general population between a baseline diagnosis of OCD and suicidal ideation or suicide attempts.

### Suicidal ideation and suicide attempts in OCD: clinical samples

The prevalence of current suicidal ideation ranges between 6.4 <sup>5</sup> and 75% <sup>6</sup> with an estimated mean of 25.9% (median: 15.6%) <sup>4</sup>; while the lifetime suicidal ideation is estimated to be 44.1% (median: 36.4%) <sup>4</sup>, varying from 26.3 <sup>7</sup> to 73.5% <sup>8</sup>. Lifetime suicide attempts rate is estimated at 14.2% (median 10.8%) <sup>4</sup>, ranging from 6 <sup>9</sup> to 51.7% <sup>10</sup>. Concerning family history of suicide, the rates of suicide attempts range from 11.5  $^{11}$  to 27.1%  $^{12}$  (mean 17.9, median 18.2%)  $^4$  and rates of completed suicide among family members varying between 8.9  $^{13}$  and 16.1%  $^{14}$ .

### Suicidal ideation, suicide attempt and suicide rates in OCD: epidemiological samples

All epidemiological studies (among which three performed on national registers – the Swedish National Patient Register <sup>15</sup>, the Danish Register <sup>16</sup> and the British National Psychiatric Morbidity Survey <sup>17</sup>) found that OCD increases significantly the odds of having a lifetime suicidal ideation as compared to the general population [OR ranging from 1.9 (Cl 1.3-2.8) to 10.3 (Cl 5.37-19.8)]; the increased risk remains significant even after controlling for demographic variables and comorbid psychiatric disorders [Adjusted Odds Ratio ranging from 3.8 (Cl 2.8-5.1) to 5.58 (Cl 2.7-11.6)]<sup>4</sup>. Having a history of OCD is associated with an increased risk of lifetime suicide attempts [OR from 1.6 (Cl 1.0-2.6) to 9.9 (Cl 4.5-21.8)], although it is not clear whether this increased risk remains significant when controlling for comorbid psychiatric disorders<sup>4</sup>.

The two prospective studies on national registers <sup>15 16</sup> reported a higher risk of death by suicide in patients with OCD than expected [OR: 3.02 (CI 1.85-4.63) to 9.83 (CI 8.72-11.08)], and results remained significant even for pure OCD [OR: 13.18 (CI 10.76-16.16)].

Data coming from the analysis of prevalence rates and odds ratios show that, at least in part, suicide risk in OCD is influenced by several other psychiatric disorders, including unipolar and bipolar depression. Additionally, a substantial proportion of OCD patients never manifest suicidal ideation in their lifetime, even when the severity of the disorder is significant. This implies that a number of potential contributing factors to the increase of suicide risk are to be screened and identified. Risk identification and stratification of risk remain essential for suicide prevention and should guide the clinical approach to subjects with psychiatric disorders.

In the following paragraphs, we will present data concerning which factors are associated with a higher risk of suicidal ideation, attempting suicide or committing suicide in individuals with OCD. Socio-demographic and personal factors, OCD-related variables, comorbidities, psychopathological variables (emotion-cognitive and temperamental factors) as well as biological variables will be presented separately.

## Factors associated with increased risk of suicide

### Socio-demographic and personal characteristics

Table I shows the socio-demographic or personal factors associated with the increased suicide risk in pa-

Factor	Suicidal ideation	Suicide attempts	Completed suicides
Male gender	Maina et al., 2006 18		Fernandez de la Cruz et al., 2017 $^{\scriptscriptstyle 15}$
Female gender		Fernandez de la Cruz et al., 2017 $^{\scriptscriptstyle 15}$	
Older age	Maina et al., 2006 18		
Marital status: single	Torres et al., 2011 14	Alonso et al. 2010 27	
No children	Torres et al., 2011 14		
Poor educational level, lower social class	Maina et al., 2006 <sup>18</sup> Torres et al., 2011 <sup>14</sup>		
Childhood trauma	Ay & Erbay, 2018 <sup>21</sup>	Khosravani et al., 2017 6	

TABLE I. Socio-demographic variables or personal factors found to be associated with increased suicide risk in OCD patients.

tients with OCD. Being male is a risk factor for both suicidal ideation and for death by suicide <sup>15</sup><sup>18</sup>, while being female is a risk factor for lifetime suicide attempts <sup>15</sup>, confirming data from the general population <sup>19</sup>.

Having a low educational level, being older, having a low social economic status and not having children have been found to be significant risk factors for current and lifetime suicidal ideation <sup>14 18</sup>.

As regards the impact on marital status of suicide risk, Torres et al. <sup>14</sup> reported a significant correlation between being single and a higher risk of lifetime suicide attempts, contrasting with data by Maina et al. <sup>18</sup>. An explanation may be that the family plays an important supportive role in OCD, tackling suicide-related sentiments when they emerge, urging patients to seek for professional help. Another factor associated with increased risk of suicide (both suicidal ideation and suicide attempts) is a personal history of childhood trauma <sup>6 21</sup>. In particular, childhood sexual abuse predicts later suicidal ideation and attempts among individual with OCD <sup>6 21</sup>.

### OCD-related variables

The disorder-specific (OCD-related) variables associated with increased suicide risk in patients with OCD are reported in Table II.

Six studies investigated the relationship between OCD severity (in terms of Y-BOCS total score) and suicidal ideation/suicide attempts showing that higher levels of illness severity are associated with higher rates of life-time suicide attempts <sup>12</sup> <sup>23</sup> and suicidal ideation <sup>18</sup> <sup>24-26</sup>. Whether or not the effect is mediated by the concomitant presence of comorbid depression, the chronicity of

Factor	Suicidal ideation	Suicide attempts
Severity of OCD: Y-BOCS total scores	Maina et al., 2006 <sup>18</sup> Balci & Sevincok, 2010 <sup>26</sup> Hung et al., 2010 <sup>24</sup> Gupta et al., 2014 <sup>25</sup>	Velloso et al., 2016 <sup>12</sup> Dhyani et al., 2018 <sup>23</sup>
Contamination/washing dimension	Gupta et al., 2014 25	
Symmetry/ordering dimension	De Berardis et al., 2014 <sup>13</sup> Gupta et al., 2014 <sup>25</sup>	Alonso et al., 2010 27
Unacceptable thoughts	Balci & Sevincok, 2010 <sup>26</sup> Torres et al., 2011 <sup>14</sup> Kim et al., 2016 <sup>30</sup> Velloso et al., 2016 <sup>12</sup> Khosravani et al., 2017 <sup>10</sup>	Velloso et al., 2016 <sup>12</sup> Khosravani et al., 2017 <sup>10</sup>
Hoarding dimension	Torres et al., 2011 14	Chakraborty et al., 2012 29
Poor insight	Gupta et al., 2014 <sup>25</sup> De Berardis et al., 2015 <sup>11</sup>	
Premenstrual worsening of OCD symptoms	Moreira et al., 2013 33	Moreira et al., 2013 33

TABLE II. Disorder-specific (OCD-related) variables found to be associated with increased suicide risk in OCD patients.

OCD: Obsessive-Compulsive Disorder; Y-BOCS: Yale-Brown Obsessive-Compulsive Scale

the disorder/duration of untreated illness or other mediating factors is to be fully understood.

OCD is a heterogeneous disorder, with several symptom dimensions. Contrasting findings have been found on the role of obsessive thinking/compulsive behaviour and suicidal ideation. In particular, Gupta et al.<sup>25</sup> found a positive significant association between contamination obsessions/washing behaviors and lifetime suicidal ideation, while other studies identified the presence of symmetry as risk factor <sup>13 25 27</sup>. Alonso et al. <sup>27</sup> found that symmetry obsessions/ordering symptoms are associated with lifetime suicide attempts. Chaudhary et al. <sup>28</sup> have observed that suicidality is most common in patients reporting obsessions on cleanliness and contamination (57%), religious obsessions (45%), sexual obsessions (33%) and repeated rituals (31%). Hoarding obsessions and compulsions predicted lifetime suicide attempts in one study <sup>29</sup>. A clear association between unacceptable (aggressive, sexual, or religious obsessions) thoughts and suicidal behaviors has been found 10 12 14 26 30, both in terms of suicidal ideation and suicide attempts. Moreover, suicidal ideation was predicted by lack of insight <sup>11 25</sup>. Moreira et al. <sup>33</sup> investigated the worsening of OCD symptoms in the premenstrual period as risk factor for suicidal ideation and suicide attempts. This relationship might be due to the hormonal changes preceding the menstrual period, which may heighten patients' susceptibility to obsessions/compulsions cycle, causing an exacerbation of symptoms.

### Comorbidities

The impact of psychiatric or medical comorbidities on suicide risk or suicidal behaviors in patients with OCD has been extensively investigated (Tab. III). Having at least one current or lifetime comorbid mental disorder impacts on suicidal behaviors <sup>12 15 34 35</sup>, in terms of higher number of suicide attempts and higher prevalence of suicidal thoughts <sup>34</sup>.

Several studies have analyzed the effects of specific comorbidities and suicidal behaviors. In particular, patients with OCD and comorbid bipolar disorder <sup>36-38</sup> or major depressive disorder (MDD) <sup>14 18 26 39-41</sup> have an increased risk of suicidal attempts and suicidal ideation; moreover, patients with MDD and OCD have an increased risk of lifetime suicide attempts <sup>14 27 39 41</sup>. Furthermore, the severity of depressive symptoms is positively associated with suicidal ideation and lifetime suicide attempts in patients with OCD <sup>10 12 14 18 24-28 30</sup>.

As regards the impact of comorbidity with anxiety disorders on suicidal behaviors, having a PTSD or GAD increases the risk of suicidal ideation and lifetime suicide attempts <sup>14 42</sup>. On the other hand, the presence of comorbid anxiety disorders seems to be a protective factor for completed suicides <sup>15</sup>. The severity of comorbid anxiety disorders is correlated with suicidal ideation <sup>14</sup> <sup>18</sup> <sup>24-26</sup> <sup>43</sup> and with suicide attempts <sup>12</sup> <sup>14</sup>, although this has not been confirmed by Weingarden et al. <sup>43</sup>.

Patients with a comorbid substance and alcohol use disorders show a higher risk of suicidal ideation <sup>7 14 36</sup>, suicide attempts <sup>7 15 36</sup> and death by suicide <sup>15</sup>.

A significant correlation was found between cigarette smoking and suicide attempts in OCD patients by Dell'Osso et al. <sup>44</sup>. In particular, the risk of suicide is higher in former cigarette smokers with OCD.

A significant association between higher lifetime suicide attempts and comorbid eating disorders in OCD was found by Sallet et al. <sup>50</sup>. The prevalence of lifetime suicide attempts was higher in bulimic-OCD patients (33%), followed by anorexic-OCD patients (19%), and then by binge eating disorder-OCD patients (16%).

Personality disorders are correlated to a higher risk of both suicide attempts and completed suicide in patients with OCD, although it is unclear whether specific personality disorders account for this increased risk <sup>15</sup>.

Suicidal ideation increases the risk of attempting suicide <sup>23 39</sup> and a history of previous suicide attempts is strongly related to later suicidal ideation, suicide attempts and even death by suicide <sup>15 27 39</sup>. Moreover, in the Swedish study that used a matched case-cohort design with a follow-up of 44 years, authors found that a previous suicide attempt increases the risk of 4.7 for death by suicide in patients with OCD <sup>15</sup>. A positive family history for suicide attempts is also correlated with both suicidal ideation and suicide attempts in OCD patients <sup>12</sup>.

Only one study <sup>35</sup> found that also comorbid medical disorders may be associated with increased risk of suicide; in fact, subjects who attempted suicide had more comorbid medical disorders than individuals who never attempted suicide.

### Psychopathological variables

Several different psychopathological variables are associated with increased suicide risk in OCD patients (Tab. IV). De Berardis et al. <sup>11</sup> found a significant association between suicidal ideation and inflated responsibility in individuals with OCD and alexithymia, independently from depressive symptoms. Alexithymia is a multifaceted construct including difficulty in identifying and describing feelings, difficulty in distinguishing feelings from bodily sensations, reduction in fantasy, and concrete and minimally introspective thinking. Alexithymia itself is associated with suicidal ideation <sup>11 13 30</sup> and lifetime suicide attempts <sup>30</sup>. Moreover, a study found that alexithymic individuals with OCD exhibit dysregulation of the cholesterol balance <sup>13</sup>, which in turn is associated with suicidal ideation. Although the exact relationship between alexithymia, altered lipid profile and suicide in OCD is not clear, it is possible that the increased risk for suicide is mediated by the alterations of cholesterol levels associated with alexithymia.

Factor   Suicida Ideation   Suicida Ideation   Suicida Ideation   Completed suicides     Current/illetime comorbid psychiatric disorders   Torres et al., 2013 <sup>34</sup> Torres et al., 2017 <sup>35</sup> Fernandez de la Cruz et al., 2017 <sup>35</sup> Comorbid Psychiatric Dall'Osso et al., 2017 <sup>35</sup> Comorbid Psychiatric Dall'Osso et al., 2017 <sup>35</sup> Comorbid Mood Disorders/ Comorbid Major Depressive Disorder   Maina et al., 2007 <sup>30</sup> Maina et al., 2007 <sup>30</sup> Torres et al., 2011 <sup>46</sup> Kamath et al., 2007 <sup>30</sup> Alonso et al., 2017 <sup>30</sup> Alonso et al., 2017 <sup>30</sup> Severity of comorbid depressive symptoms   Maina et al., 2007 <sup>30</sup> Maina et al., 2007 <sup>30</sup> Balci & Sevincok, 2010 <sup>47</sup> Viswanath et al., 2007 <sup>30</sup> Hung et al., 2014 <sup>46</sup> Kim et al., 2014 <sup>46</sup> Balci & Sevincok, 2010 <sup>47</sup> Veloso et al., 2016 <sup>47</sup> Fernandez de la Cruz et al., 2017 <sup>46</sup> Fernandez de la Cruz et al., 2017 <sup>46</sup> Severity of comorbid anxiety symptoms   Maina et al., 2007 <sup>46</sup> Kim et al., 2014 <sup>46</sup> Kim et al., 2014 <sup>46</sup> Sevirity of comorbid anxiety symptoms   Maina et al., 2006 <sup>47</sup> Veloso et al., 2016 <sup>47</sup> Fernandez de la Cruz et al., 2017 <sup>46</sup> Fernandez de la Cruz et al., 2017 <sup>46</sup> Substance/alcohol use disorders   Gentil et al., 2009 <sup>7</sup> Torres et al., 2011 <sup>46</sup> Sevirity of comorbid eating disorders   Gentil et al., 2009 <sup>7</sup> Fernandez de la Cruz et al., 2017 <sup>46</sup> Fernandez de la Cruz et al., 2017 <sup>46</sup> Alore <sup>47</sup> Comorbid eating	TABLE III. Comorbidities found to be assoc	clated with increased suicide	e risk in OCD patients.	
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	Medical comorbidities		Dell'Osso et al., 2017 35	

ABLE III. Comorbidities	found to be	associated with	n increased	suicide ris	sk in OC	D patient
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PTSD: Post-Traumatic Stress Disorder; GAD: Generalized Anxiety Disorder

Factor	Suicidal ideation	Suicide attempts	
Inflated responsibility	De Berardis et al., 2015 11		
Ego-dystonic perfectionism	Kim et al., 2016 30	Kim et al., 2016 30	
Alexithymia	Kim et al., 2016 <sup>30</sup> De Berardis et al., 2014 <sup>13</sup> De Berardis et al., 2015 <sup>11</sup>	Kim et al., 2016 <sup>30</sup>	
Shame	Weingarden et al., 2016 43		
Hopelessness	Kamath et al., 2007 <sup>39</sup> Balci & Sevincok, 2010 <sup>26</sup> Gupta et al., 2014 <sup>25</sup>	Dhyani et al., 2018 23	
Hostility	Gupta et al., 2014 25		

Kim et al. <sup>30</sup> found an association between suicidal behaviors and perfectionism, defined as a tendency to set extremely high personal standards and being critical of themselves in a perpetuating cycle of dissatisfaction. Weingarden et al. <sup>43</sup> found a significant association between shame and suicidal ideation in OCD patients and hypothesized that shame may strengthen the destabilizing effects of egodystonic emotions and acts.

Also hopelessness and hostility can impact on suicidal ideation and suicide attempts in patients with OCD <sup>23 25 26 39</sup>. In particular, Gupta et al. <sup>25</sup> found a correlation between hostility and suicidal ideation and found that the Beck Hopelessness Scale (BHS) predicts suicidal ideation in patients with OCD better than the Y-BOCS <sup>23</sup>. Khosravani et al. <sup>6</sup> found that the presence of early maladaptive schemas, such as mistrust/abuse schemas, is significantly correlated with an increased risk for suicidal ideation and suicide attempts in patients with OCD. Cyclothymic affective temperament represents a major risk factor for suicide in patients with OCD <sup>8</sup> as in patients with MDD <sup>51 52</sup>.

### **Biological variables**

In addition to the well documented serotonergic dysregulation in OCD <sup>3 54</sup>, two recent studies reported a statistically significant correlation between lower HDL-Cholesterol levels and suicidality in OCD patients; De Berardis et al. <sup>13</sup> found a statistically significant correlation between lower HDL-C levels, alexithymia, and higher suicidal ideation, while Aguglia et al. <sup>55</sup> found a significant correlation between higher lifetime suicide attempts and lower HDL-C levels and higher blood levels of triglycerides. While the two studies investigated two different dimensions of suicidality, they agree on specific serum lipid alterations that seem to correlate with suicidal behavior. No other biological variables have been investigated concerning the risk for suicide in OCD.

### Discussion

Patients with OCD are at high risk for suicide, and not only due to the presence of other comorbid mental disorders <sup>34</sup>. This new evidence is in contrast with the former assumption that patients with OCD are not exposed to suicidal risk. Therefore, clinicians should always evaluate the suicidal risk in patients with OCD in terms of suicidal ideation, past history of suicide attempts and family history of suicide (attempts and/or committed). Suicidality is a dynamic dimension, and the use of specific instruments, such as the Columbia Suicide Severity Rating Scale (C-SSRS) for evaluating the different dimension analysis of suicidal ideation and its severity, should be implemented in clinical practice<sup>56</sup>. Clinicians dealing with OCD patients should keep in mind that most patients may not spontaneously report suicidal ideation, and a direct inquire is mandatory as it is generally considered to be when interviewing subjects with a major depressive episode.

The majority of patients with OCD do not have current or lifetime suicidal ideation nor did attempt suicide in their lifetime. This implies that identifying predictors of suicidal ideation and suicide attempts in OCD could result in improving our ability to screen subjects at greater risk needing intensive and careful monitoring. Of course, early recognition and diagnosis of OCD and effective pharmacological and psychological treatments of the disorder remain essential for the prevention of suicidality. We do not have pharmacological agents with an evidence-based demonstration of effectiveness in treating suicidality, apart from lithium in affective disorders and clozapine in schizophrenia. Therefore, the evaluation of risk factors remains crucial for suicide prevention.

Concerning sociodemographic factors, we found male gender, older age and poor socioeconomic status to be associated with suicide risk. The possible explanations for higher suicide mortality of males may be the more common use of alcohol and violent suicide method by males and the higher prevalence of borderline personality disorder in women <sup>20</sup>, which is more frequently correlated with attempted suicides than with completed ones. Some of the data taken in consideration may actually support this hypothesis, as Fernandez de la Cruz et al. <sup>15</sup> actually found overlapping confidence intervals between genders in OR for suicide attempts after adjustments for personality disorders.

Since no significant difference was found between age at diagnosis, suicidal ideation in older age may be considered a consequence of OCD which has not been resolved, and therefore which could have had a longstanding negative impact on quality of life. As of the poorer educational level as a risk factor, this specific group of subjects may lack the means or the knowledge to further understand their illness, or to recognize when to seek help in case of exacerbations, which may impact their quality of life and the course of the illness.

When examining OCD-related variables, we found that severity of symptoms and the specific symptom dimension of aggressive obsessions are related to higher suicide risk. It is possible that other factors, such as hopelessness, could mediate the effect of specific symptom dimensions on suicide risk. It may be that individuals with a higher severity of symptoms, or higher severity of specific symptom dimensions (such as thoughts that are deemed unacceptable, or symptoms that severely impact a multitude of aspects of their day-to-day life, such as hoarding symptoms), are more likely to feel hopeless, and therefore may consider - or even act - against their own self in an attempt to regain control of their life. In this context, lack of insight may play a role as a risk factor as proper insight could promote a deeper knowledge and understanding of the illness, which could therefore lead to the better use of all the means available to patients to get help and appropriate treatment.

From our review of the literature we found that comorbid disorders (and, specifically, comorbid depression - both in major depressive disorder but also in bipolar disorder) are predictors of higher suicide risk. Clinicians should always inquire about suicidal ideation or previous suicide attempts in individuals with comorbid depression, keeping in mind that often these individuals are affected by bipolar disorder and that the pharmacological treatment for OCD (moderate-to-high doses of SSRIs) may worsen suicidal ideation, induce mixed states and expose the patient to a higher risk of committing suicide. Comorbid substance use disorders are also significant risk factors for suicidality. It may be that the development of an addiction to a substance and the distress caused by egodystonic obsessions and compulsions in OCD may work in synergy and amplify each other. Substance abuse may therefore be considered, in OCD patients who develop addiction, as a mean to escape from their obsessions and compulsions through the intoxication of the mind, which could cause an exacerbation of symptoms as soon as the effect of the substance wears off, thus reinforcing the cycle, eventually leading some patient to consider, attempt or even complete suicide. Comorbid cigarette smoking seems also to be a risk factor; it may be hypothesized that those who are at a higher risk for smoking are at a higher risk for impulsive behaviors <sup>45</sup>; however, those who are no longer smoking may be those who are either determined enough to make long-term, definitive choices (both healthier choices, such as no longer smoking, but also harmful ones, such as attempting suicide), or they may be those who no longer feel that they have an easily accessible mean, such as a cigarette, to help coping with the stress of OCD symptoms and behaviors. Smoking could be not an important contributing factor for the elevated suicidality of OCD patients as, in spite of the fact that smoking is a risk factor for all forms of suicidal behavior both on clinical <sup>46</sup> and on population level <sup>47</sup>, it has been repeatedly shown that OCD patients smoke much less than other psychiatric patients and the general population <sup>48 49</sup>. Further studies are needed to better understand the relationship between smoking and suicidality in OCD patients.

Comorbid somatic diseases are also associated with suicidality in OCD. Since the presence of medical comorbidities is associated with an increased risk of suicide attempt <sup>35</sup>, it is possible that the treatment of medical comorbidities could strongly affect the risk for suicide attempts in OCD patients, and should be a priority, although this assumption needs to be further confirmed. Concerning psychopathological variables, from our review of the literature we identified hopelessness and personality traits, such as alexithymia or ego-dystonic perfectionism, as emotion-cognitive factors increasing the risk of suicide in individuals with OCD. Regretfully, it is not common in clinical practice to screen for the presence of these factors, nor it is routine clinical practice to distinguish between ego-dystonic perfectionism from OCD symptoms. Some clinicians with a cognitive-behavioral background may assess cognitive constructs such as inflated responsibility and evaluate its impact on the severity of the disorder (including suicide risk). Given that suicide risk is higher in people with these cognitive-emotional risk factors, we suggest adding their evaluation in the baseline assessment of individuals presenting with severe OCD.

Early maladaptive schemas, such as mistrust/abuse schemas, are also predictors of suicidality. Mistrust/ abuse schema refers to an attitude recognized by avoidance of relationships with others for fear of being betrayed or misled, which in turn may be related to having suffered from physical and/or sexual abuse experiences, severe punishments or living in an emotionally or physically unsafe environment<sup>6</sup>. This finding is particularly interesting and clinically useful if considered together with results concerning the role of childhood trauma and comorbid PTSD as two independent risk factors for suicide behaviors in OCD. Addressing adverse childhood experiences in patients at higher risk for suicide because of having suffered a childhood trauma could result in reduced suicide rates.

Very few biological variables have been investigated concerning suicide risk and OCD; only low HDL-cholesterol levels have been found associated with an increase in suicidal ideation and suicide attempts. A possible explanation could be that altered cholesterol levels may impact vascular serotonin sensitivity, neuronal membrane balance and viscosity, and this may result in decreased serotonin activity, which could lead to more impulsive behaviors, such as suicidal ideation and attempts. Further studies are needed to better assess the cause and effect relationship between suicidality and altered serum lipid levels.

A few studies evaluated the relative weight of each risk factor in increasing risk suicide risk: family history for suicidality <sup>12</sup>, previous suicide attempts <sup>15</sup> and comorbid major depression or bipolar disorder <sup>14</sup> appear the most important risk factors and should not be disregarded when assessing individuals with OCD.

Another under investigated area in OCD is whether addressing and modifying one risk factor result in reducing rates of suicide attempts. We could identify only one study investigating the effects of an intervention on risk factor modification; in this study, a one-session anxiety sensitivity cognitive concerns intervention produced significantly greater reduction in anxiety sensitivity, and changes in anxiety sensitivity cognitive concerns mediated the changes in suicidality at one-month followup <sup>57</sup>. Unfortunately, no other studies assessed or proposed similar interventions on other risk factors.

We strongly advocate future similar longitudinally studies examining whether specific programs and interventions on risk factors will result in a reduced suicide risk in OCD patients, as some identified risk factors, such as severity of the disorder, comorbid depression (or other disorders), cigarette smoking, alexithymia and hopelessness, among others, are all potentially modifiable (e.g. simple interventions such as smoking cessation programs could reduce suicide risk).

A general limitation of this review is that several of the identified risk factors were not confirmed in other studies; moreover, the statistical procedure of several studies did not allow for the control of potentially confounding factors, so that many identified predictors of suicide ideation or attempts in OCD may actually result to be proxies to other true independent risk factors. Notwithstanding these limitations, we think that our contribution could be of great value to clinicians in that it could prompt a greater attention to suicide risk in OCD.

### Conclusions

Patients with obsessive-compulsive disorder have a greater risk for suicide (suicidal ideation, suicide attempts and completed suicide) as compared to the general population, and this increased risk is even greater in individuals who have specific characteristics, which we may assume are risk factors for suicidality in OCD. These factors should be routinely assessed in clinical practice: the severity of OCD, the symptom dimension of unacceptable (aggressive, sexual, religious obsessions) thoughts, having a comorbid Axis I disorder (especially bipolar disorder or major depressive disorder, but also substance use disorder), the severity of comorbid depressive and anxiety symptoms, a previous history of suicide attempts, and some psychopathological variables, such as alexithymia and hopelessness, all increase the risk of having suicidal ideation or attempting suicide. Whether and how these risk factors for suicide in OCD work together, and whether the specific factors act as moderators or mediators, remains to be elucidated. Nevertheless, identifying individuals who are at greater risk could result in improving our ability to prevent suicide in OCD.

### **Conflict of Interest**

The authors have no conflict of interests.

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