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Are Huntington's Disease Patients, in Comparison to Patients with Other Neurodegenerative Diseases, at High Risk to Commit Suicide?

Nassim Said*

Corresponding Author: Nassim Said, School of Health Sciences, University of Georgia, Tbilisi.

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Abstract

Objective: *To determine whether the patients with Huntington's disease are at a high risk of committing suicide than patients with other neurodegenerative disorders.*

Methodology: *The literature was searched using the electronic database PubMed to extract studies related to our topic. Those studies were selected for our research which met a proper exclusion and inclusion criteria. The included studies were then critically reviewed and analysed to extract the most important and valuable knowledge to produce desired results.*

Results: *The results of our study were based on the reviews that were included in this research. Most of the literature fulfilled our required criteria that Huntington's disease patients were at a high risk of suicide compared to other neurodegenerative diseases. There was minimal literature found contrary to this statement.*

Conclusion: *After the data extracted from our reviewed literature and critical review of the studies, it can be concluded that patients with Huntington's disease are at a high risk of suicide relative to patients with other neurodegenerative disorders.*

Background

Huntington's disease is a genetically acquired, persistent neurodegenerative disease caused by motor dysfunction, behavioral disorder, and physical presentation **(**such as chorea, dystonia, and incoordination**)**. Although suicide is a significant public health problem, HD patients have a greater chance of suicide, not only in the specific population but also in people with other neurological disorders such as ALS, Parkinson's disease, and Alzheimer's disease. George Huntington, who reported a tendency for insanity and suicide' as one of the three primary characteristics in explaining the condition, first identified this high likelihood of suicide. Some early studies have shown that suicide is the third leading cause of death in patients with HD. These behavioral variations put an extra burden on the patient and parents, relatives, and companions. **(**Kachian, Cohen-Zimerman, Bega, Gordon, & Grafman, 2019**)**.

George Huntington published a report of inherited chorea in 1872, now referred to as the Huntington disease **(**HD**)**. He identified his inherited generation, its associated psychological and cognitive symptoms, and the disease's presentation in adult life between the ages of 30 and 40 years. HD is caused by a rehashed expansion of the autosomal dominantly acquired CAG trinucleotide in the Huntingtin **(**HTT**)** gene on chromosome 4. He acknowledged the disease's increasing nature, asserting that it adheres to the disturbing realization once it starts. That results in the development of abnormally long polyglutamine repetition of mutant huntingtin **(**mHTT**)** protein. Many with more than 39 CAG repetitions are confident that the disorder will exist, while between 36 and 39, decreased penetrance repetitions are seen. Anticipation can be seen as the gene is passed down the paternal line. A child with an extensive pathogenic repeat duration will have a parent with a CAG repeat length in the middle range. This is because men's sperm reveals more comprehensive heterogeneity in repetition and more generous repeat sizes than somatic tissues. HD is a neurodegenerative disease with the prevailing transmission with a significant variation in age of onset, but with a mean starting age of 40. There is a 50% risk of incurring the disease in children of HD gene carriers. **(**Fiedorowicz et al., 2011**)**.

An autosomal-dominant, progressive neurodegenerative disease, which includes chorea and dystonia, no coordination, cognitive disorder, and behavioral issues, is Huntington's disease with a separate phenotype. Usually, the symptoms happen in middle age after affected people have had children, but the condition can display at any moment between childhood and senescence. Huntington, the mutant protein in Huntington's disease, arises from an extended repeat of CAG, leading to the variable-length N-terminus polyglutamine chain. Evidence demonstrates that there is a toxic functional advantage to this tail. Huntington's disease's precise pathophysiological mechanisms are insufficiently assumed, but research provides insight into causative determinants and likely improvements in the disorder's transgenic animal models. **(**Paulsen, Hoth, Nehl, Stierman, & Group, 2005**)**.

Methods

An electronic database was used to search and extract the required data and studies in this research paper. The search engine PubMed was used to obtain beneficial and suitable research studies on our research topic. The data search was initiated using appropriate mesh terms or keywords, which could help us find the most convenient and relevant articles. The keywords we used for our study were Huntington's disease, neurodegenerative diseases and suicidal risk. These keywords yielded many relevant studies; only the mesh term "Huntington's disease and risk of committing suicide" provided us around 62065 results on PubMed. However, as we had to focus on articles that can fulfill our

research criteria, so initially, after removing the duplicates, many studies that did not meet inclusion criteria were excluded. After removing duplicates and irrelevant studies, a proper inclusion and exclusion criterion was designed so that we could have relevant research findings.

The criteria for inclusion included:

1. Articles written in English
2. Full-text review articles
3. Articles that were published in peer-reviewed journals
4. Articles that included the case definition of Huntington's disease and neurodegenerative diseases.
5. Articles that included at least two keywords

The articles that were not associated with Huntington's disease and suicide were excluded from this research paper. The research articles which didn't meet the inclusion criteria and the items that were not written and published in English were excluded from the study. All the studies with a diagnosis other than Huntington's disease were also excluded. After going through this process of identifying, exclusion, and selecting relevant articles, six articles were finally included in this research study. Out of six lessons, one systematic review was formed, and one comparative study, two cohort studies, one case study and one RCT were also included in the study. These studies have been critically reviewed, their outcomes have been objectively evaluated, and their findings have been systematically analyzed. Once these findings have been objectively checked and confirmed, our research paper has taken their useful knowledge out and used it. These studies provided us with in-depth information and relevant data, which was necessary to produce a clear outcome in our research.

Results

These clinical findings, which we have addressed so far, have shown that the literature and evidence-based studies available so far strongly support that patients with Huntington's disease are at a high risk of suicide relative to patients with other neurodegenerative disorders.

The evidence supports the long-lasting debate that HD patients have greater chances of suicidal thoughts and behavior than the overall community and other clinical groups. The new findings have also confirmed studies suggesting higher rates of suicidal ideation in people in danger and diagnosed with Huntington's chorea. Suicidal ideation in HD has been correlated with clinical symptoms, including depression, anxiety, and aggression. Within the past decades, we've witnessed the formation

of much-needed broad, observational studies of HD patients. However, there's still a significant lack of lessons specifically designed to research the roots of the increased risk and to assess alternative suicide prevention measures in patients with HD. Supported the reported findings, suicidal thoughts and actions should be closely monitored in clinical practice. Prospective study should discuss apparent differences within the existence of greater chances of suicide among HD patients.

Discussion

Kachian et al. **(**2019**)** determined the control and causative determinants of self-destructive ideation and HD participation. Depression, anxiety, and aggression were the key vital variables linked with suicide in HD. Within the general population, depression has been documented as a causative determinant for suicidal ideation. The chance of self-destructive thought and performance was better for HD patients than for the general population and other clinical populations. However, there is still a considerable lack of precisely planned studies investigating the reasons for increased chance and looking at alternative suicide inhibition procedures in patients with HD. In clinical training, the stated results, suicidal feelings, and the action should be vigilantly monitored. In prospective research, obvious differences in the nature of the high risk of suicide among patients with HD should be discussed. **(**Kachian et al., 2019**)**.

Fiedorowicz et al. **(**2010**)** reported that a high risk of suicide has been documented in Huntington's chorea patients with frequencies more significant within the general population and other neurodegenerative diseases. This research showed that depression and a history of suicide attempts in prodromal HD were significant risk determinants for suicidal activity. These were amidst the primary strong risk determinants for depression reported in the medical literature, supporting the pattern of assessing the risk of suicide in this population as individuals rather than as individuals with prodromal HD. The results showed that conventional suicide risk measures are often fairly administered to people with prodromal HD and unquestionably HD depression and a history of suicide attempts as predictors of suicidal behavior in prodromal HD, two of the foremost established predictors within the suicide literature. Self-murder tries and completions were combined, portraying suicidal acts, into one variable. Almost like those who kill, but not similar, those who plan to kill constitute a gaggle, which was the report's limitation. **(**Fiedorowicz et al., 2011**)**.

Paulsen et al, reported that in individuals at risk for and diagnosed with Huntington's chorea, there were elevated rates of suicidal ideation. Suicide is suggested to occur between seven and 200 times more frequently in Huntington's Chorea patients than in the general population. These results

demonstrate the vulnerability of this specific group of genetically at-risk individuals who are beginning to show signs and symptoms of Huntington's chorea. Historically, the time around the beginning of Huntington's illness has been referred to as a time of high suicide risk. The most critical sample size ever analyzed was used concerning suicidal ideation in Huntington's chorea. In contrast to other broad studies, this research explicitly questioned everyone about current suicidal ideas with survey data obtained from relationships. **(**Paulsen et al., 2005**)**

A study conducted by Hubers et al. **(**2013**)** determined that suicidal ideation was found primarily in HD. In mutation carriers with depressed moods and in those taking benzodiazepines, diagnosis of suicidal ideation was the priority. This study's findings determined that mutation carriers with baseline self-destructive ideation were more prone to have a depressed mood, were more often anxious and aggressive, had more repeated self-destruction attempts in the past, and had a lower expected duration of the disease contrasted to suicidal ideation-free mutation carriers. As only one item evaluated suicidal ideation, the prevalence of suicidal ideation was potentially underestimated, and therefore the participants were representative of all carriers of HD mutations. **(**Hubers et al., 2013**)**.

Wetzel et al. **(**2011**)** examined the consequence of mental comorbidity and its part in self-destructive ideation. Depression, anxiety, and violence have been associated with suicidal ideation in HD. There has been evidence of a high level of suicide risk. The majority of HD studies focused on HD's cognitive and motor characteristics; less attention was given to the outcomes of clinical manifestations. Recent studies have attempted to identify the HD stages at which patients are at high risk of suicidal ideation, but no study has investigated potential suicidal risk factors. In the current research, the prevalence and presentation of psychiatric comorbidity in self-destructive ideation have been investigated. The so-called "rational suicide" consideration could also be associated with suicidal ideation in HD. People with a terminal illness decide to terminate life to avoid the danger of suffering, injury, and stress from other relationships. **(**Wetzel et al., 2011**)**.

Chu et al. **(**2019**)** conducted a study showing that impulsivity was included in Huntington's chorea **(**HD**)** related cognitive deficits, closely resembling variables that are both inclined to measurable chance. Men appear to be extra severe perpetrators of acts of violence than women, and women are less likely to be arrested for violence than men. This finding is not accurate in the case of girls with Huntington's chorea, and has been investigated in the three subsequently described clinical cases of HD women and their forensic history. In this vulnerable category of patients, assessment and earlier treatment in appropriate hospital environments would better include and modify procedures, resulting in lower levels of risk of recurrence. **(**Chu, O'Neill, Purkayastha, & Knight, 2019**)**.

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