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MENTAL HEALTH BURDEN IN RARE DISEASES: DEPRESSION AND EMOTIONAL SUPPORT NEEDS IN WOLFRAM SYNDROME PATIENTS

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ABSTRACT

This article analyzes the mental health burden in patients with Wolfram Syndrome (WS), a rare neurodegenerative disorder, based on data collected by the Brazilian Association of Wolfram Syndrome (ABSW). WS is characterized by diabetes mellitus, optic atrophy, hearing loss, and neurological dysfunctions, but its psychological impact is often overlooked. Data from 25 patients show that depression is highly prevalent (12 patients), comparable to core physical symptoms. The study highlights the urgent need to integrate emotional support into clinical treatment, including mental health screening, psychological follow-up, and the inclusion of mental health professionals in multidisciplinary teams. Patient accounts, such as Fernanda's, illustrate the emotional suffering, isolation, and lack of specialized support. The article concludes that mental health must be recognized as a clinical priority in the management of rare diseases, with the involvement of patient associations and systemic changes in care protocols.

Keywords: Mental Health. Rare Diseases. Wolfram Syndrome. Depression. Emotional Support.

CARGA PARA A SAÚDE MENTAL EM DOENÇAS RARAS: DEPRESSÃO E NECESSIDADES DE APOIO EMOCIONAL EM PACIENTES COM SÍNDROME DE WOLFRAM

RESUMO

Este artigo analisa a carga de saúde mental em pacientes com Síndrome de Wolfram (SW), uma doença neurodegenerativa rara, com base em dados coletados pela Associação Brasileira da Síndrome de Wolfram (ABSW). A SW é caracterizada por diabetes mellitus, atrofia óptica, perda auditiva e disfunções neurológicas, mas seu impacto psicológico é frequentemente negligenciado. Dados de 25 pacientes mostram que a depressão é altamente prevalente (12 pacientes), comparável aos sintomas físicos principais. O estudo destaca a necessidade urgente de integrar o apoio emocional ao tratamento clínico, incluindo triagem de saúde mental, acompanhamento psicológico e a inclusão de profissionais de saúde mental em equipes multidisciplinares. Relatos de pacientes, como o de Fernanda, ilustram o sofrimento emocional, o isolamento e a falta de apoio especializado. O artigo conclui que a saúde mental deve ser reconhecida como prioridade clínica no manejo de doenças raras, com o envolvimento de associações de pacientes e mudanças sistêmicas nos protocolos de atendimento.

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Palavras-chave: Saúde Mental. Doenças Raras. Síndrome de Wolfram. Depressão. Apoio Emocional.

CARGA DE SALUD MENTAL EN ENFERMEDADES RARAS: DEPRESIÓN Y NECESIDADES DE APOYO EMOCIONAL EN PACIENTES CON SÍNDROME DE WOLFRAM

RESUMEN

Este artículo analiza la carga de salud mental en pacientes con síndrome de Wolfram (SW), un trastorno neurodegenerativo poco frecuente, basándose en datos recopilados por la Asociación Brasileña del Síndrome de Wolfram (ABSW). El SW se caracteriza por diabetes mellitus, atrofia óptica, pérdida auditiva y disfunciones neurológicas, pero su impacto psicológico a menudo se pasa por alto. Los datos de 25 pacientes muestran que la depresión tiene una alta prevalencia (12 pacientes), comparable a los síntomas físicos centrales. El estudio destaca la urgente necesidad de integrar el apoyo emocional en el tratamiento clínico, incluyendo la evaluación de salud mental, el seguimiento psicológico y la inclusión de profesionales de la salud mental en equipos multidisciplinarios. Relatos de pacientes, como el de Fernanda, ilustran el sufrimiento emocional, el aislamiento y la falta de apoyo especializado. El artículo concluye que la salud mental debe reconocerse como una prioridad clínica en el manejo de las enfermedades raras, con la participación de las asociaciones de pacientes y cambios sistémicos en los protocolos de atención.

Palabras clave: Salud Mental. Enfermedades Raras. Síndrome de Wolfram. Depresión. Apoyo Emocional.

1 INTRODUCTION

This analysis highlights the urgent need to integrate mental health care into the management of Wolfram Syndrome, based on original data collected by the Brazilian Association of Wolfram Syndrome. Rafaela Waltrick Ungaretti Lopes, founder of ABSW, leads this critical discussion.

Rare diseases present a complex and often underappreciated challenge for patients, families and healthcare systems alike. While medical advancements have improved outcomes in many areas, the emotional and psychological burden of living with a rare disease remains an overlooked aspect of care. Wolfram Syndrome, a rare and progressive neurodegenerative disorder characterized by diabetes mellitus, optic nerve atrophy, hearing loss, neurological decline and diabetes insipidus, is a striking example of this gap.

Despite the multisystemic nature of the condition, little attention has been paid to the emotional impact of the disease on patients and their families. A systematic review shows that depression and anxiety affect up to 42% of patients with rare diseases—rates significantly higher than in the general population.[1] Wolfram Syndrome, in particular, has been associated with severe psychiatric manifestations in up to 60% of patients, including major depression and suicidal ideation.[2] [3]

In the absence of formal mental health support structures, patient-led initiatives such as the Brazilian Association of Wolfram Syndrome (Associação Brasileira da Síndrome de Wolfram - ABSW), founded and directed by Rafaela Waltrick Ungaretti Lopes, have emerged as critical advocates for the community. This article presents original data collected by the ABSW from 25 individuals with Wolfram Syndrome in Brazil, highlighting the prevalence of depression and the urgent need for integrated mental health care in rare disease management.

2 METHODS AND DATA

Since 2022, the ABSW has conducted a survey of 25 patients diagnosed with Wolfram Syndrome. Data were gathered using standardized questionnaires developed by the association, which collected information on demographics, symptom prevalence and mental health status. All participants provided informed consent for their data to be anonymized and analyzed for this study.

The data were analyzed descriptively, with frequencies calculated for key symptoms, including depression. The originality of this dataset lies in its patient-led design and focus on a rare condition for which few mental health studies exist.

3 RESULTS

3.1 SYMPTOM PREVALENCE

Table 1 presents the number of patients who reported each major symptom associated with Wolfram Syndrome.

Table 1

Symptom Frequency in Wolfram Syndrome (n=25)

Symptom	Number of Patients
Diabetes mellitus	24
Optic atrophy	23
Hearing loss	21
Urinary symptoms	17
Depression	12
Neurological symptoms	11
Gastrointestinal symptoms	9
Diabetes insipidus	6
Balance difficulties	6
Swallowing difficulties	6
Muscle weakness	6
Respiratory symptoms	5

These findings reveal that the emotional toll of Wolfram Syndrome extends far beyond its physical manifestations, underscoring the importance of addressing mental health as a core component of rare disease management.

3.2 CRITICAL ANALYSIS AND REFLECTION

The progression of Wolfram Syndrome—marked by the unpredictable emergence of symptoms such as diabetes, vision loss, hearing decline and neurological impairments—creates a profound emotional burden for patients. The data presented confirm what many patients have long reported that the psychological impact of Wolfram Syndrome is severe, persistent and largely unaddressed by the healthcare system.

Rafaela Waltrick Ungaretti Lopes, as a patient diagnosed with Wolfram Syndrome and the founder of ABSW, brings a unique and deeply informed perspective to this discussion. Her insights cultivated a decade of direct engagement with patients and their families and highlighted challenges faced by the Wolfram Syndrome community. Rafaela emphasizes that living with the disease is a constant battle against unpredictable and accumulating symptoms, a reality that profoundly impacts mental well-being. She stresses the pivotal role of a well-informed and emotionally prepared family in supporting the patient, contrasting this with the unintentional limitations imposed by unprepared families who may inadvertently reinforce feelings of incapacity. Crucially, Rafaela observes a systemic oversight within the medical community: the tendency for healthcare professionals to prioritize the physical manifestations of the disease while rarely addressing the emotional state of patients. This critical lacuna, she argues, must be urgently filled, as true health cannot be achieved without comprehensive mental health care.

3.3 PATIENT'S VOICE: A DIRECT EXPERIENCE WITH THE EMOTIONAL IMPACT OF WOLFRAM SYNDROME

Beyond the statistical data, the direct account of a young woman living with Wolfram Syndrome offers an invaluable, humanizing insight into the daily emotional realities of the condition.

Fernanda Mattos dos Reis, 23, diagnosed in 2017, eloquently articulates the profound psychological toll that accompanies the onset and progression of the disease.

Her testimony highlights the emotional suffering from the earliest moments of discovering the condition:

> "Years before being diagnosed, in 2017, we were already studying my health... it became very draining. At the time of diagnosis, it was a gigantic impact. You face a new reality, you have to adapt and try to be strong—and it's not easy to be strong every day."

Fernanda's experience underscores a critical gap in conventional medical care: the absence of specialized emotional support. She states:

> "I never had psychological or psychiatric support. I only started this support after joining the association's support group. Since March 2025, I have been having individualized sessions with the ABSW psychologist."

This personal narrative powerfully emphasizes the importance of such care, revealing the isolation many patients face:

> "Having psychological support is essential. Many patients deal with it alone, feeling in the dark, as I felt. Not wanting to worry my family, I hid my frustration. This pushes us into a bubble that is difficult to escape. Support helps us share what we feel and receive advice."

Her reflections also extend to the often-overlooked burden on family members:

> "It's already difficult to be a patient with Wolfram Syndrome, but it's even harder for family members, who suffer alone. They feel helpless. With the association's support group, my family began to understand better and feel more secure."

Her conclusion is a sincere portrait of the condition's burden:

> "Before, I was happy and didn't know it. Today, I say I am a sad person. I find it humanly impossible to be happy with so many things happening. I have anxiety, I have socially isolated myself. Every day I ask God for strength to continue."

When asked what she would like doctors to know, her response serves as a direct plea for a more empathetic and holistic approach to care:

> "Doctors need to understand that each patient is unique and treat them with individuality and empathy. Welcome and often listen to what the patient has to say. Emotions affect us greatly and severely impact symptoms. If the doctor only wants to treat the symptom that is his specialty and doesn't want to understand the others... it becomes difficult."

Fernanda's account reinforces the urgency of integrating mental and physical health in the management of rare diseases like Wolfram Syndrome. Her experience echoes the data presented and humanizes the statistical reality described earlier, providing a compelling argument for systemic change.

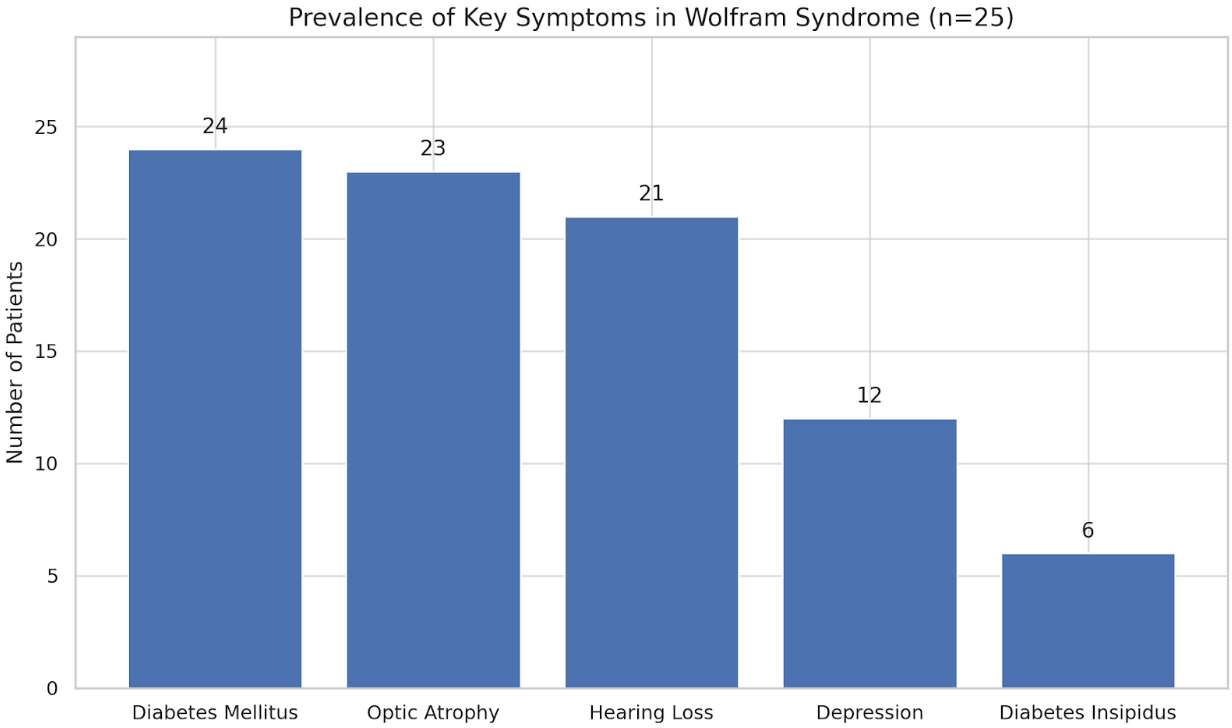
These personal observations are not isolated; they align strongly with a growing body of international research on the psychological burden of rare diseases. A UK survey, for instance, revealed that over 90% of rare disease patients felt their emotional well-being was overlooked by their doctors.[4] Similarly, a longitudinal study from Finland confirmed that psychological symptoms in patients with rare conditions remain consistently elevated over time.[5] A cross-sectional study conducted during the COVID-19 pandemic further highlighted this issue, finding that 42% of patients with rare conditions reported depression.[6] Specifically concerning Wolfram Syndrome, studies consistently confirm that psychiatric illness is a common manifestation and that neuropsychiatric symptoms, including depression and suicidal behavior, may affect more than half of patients.[2] [3]

In response to these critical findings and the unmet needs identified through both patient testimonies and broader research, the ABSW has established a structured psychological support program. This program offers group and individual sessions, directly addressing the emotional needs of patients and their families.

3.4 VISUAL DATA DEEPEN THE ANALYSIS

Figure 1

Prevalence of Key Symptoms in Wolfram Syndrome (n=25)



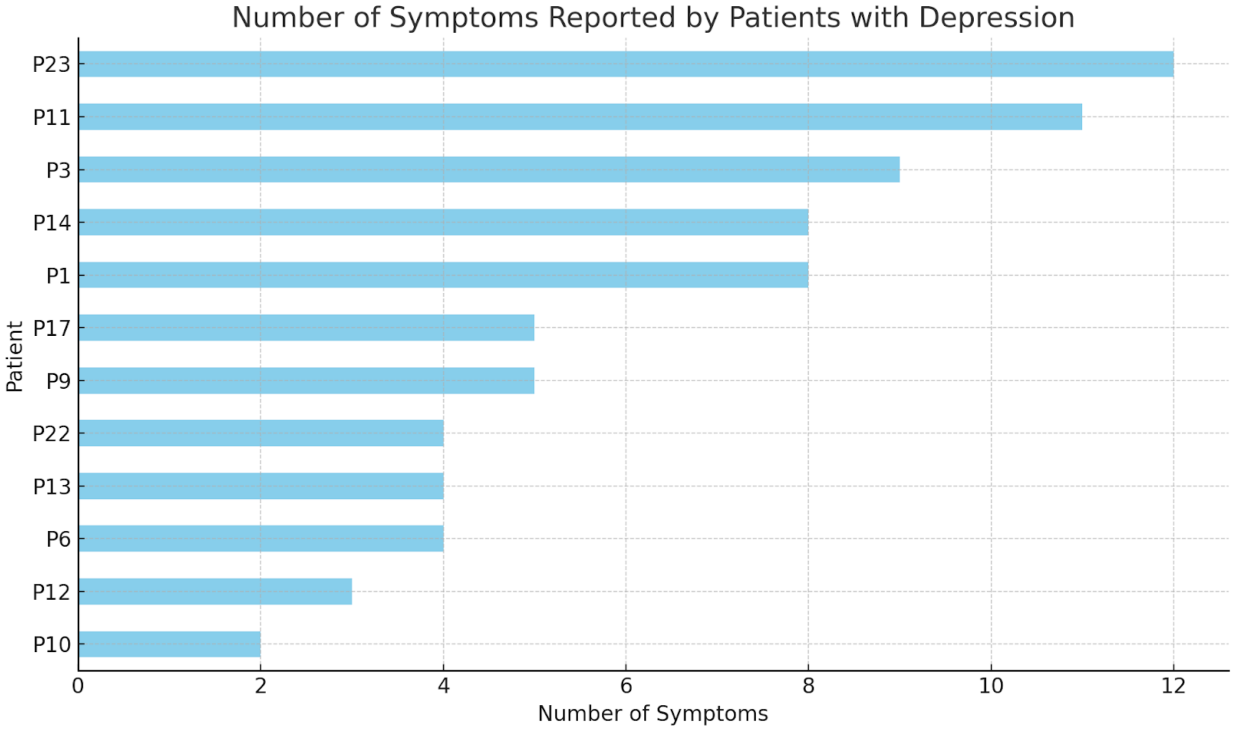
This bar chart illustrates the number of patients reporting each of the five key symptoms of Wolfram Syndrome: Diabetes Mellitus, Optic Atrophy, Hearing Loss, Depression and Diabetes Insipidus. The data highlights the high prevalence of depression, comparable to other core physical symptoms.

Graph 1 (Figure 1) shows that depression appears as frequently as core physical symptoms. Wolfram Syndrome is historically known by the acronym DIDMOAD—diabetes insipidus, diabetes mellitus, optic atrophy and deafness—an acronym that emphasizes the most recognized physical symptoms of the disease. However, the data presented here suggest that depression, due to its high prevalence, should be considered an equally relevant clinical symptom.

This finding signals a critical warning: the clinical definition of the disease must be broadened to include mental health as a central dimension of patient care—not merely as a psychological side effect or late-stage complication. This challenges traditional assumptions that emotional suffering in rare diseases is secondary or anecdotal.

Figure 2

Number of Symptoms Reported by Patients with Depression



This horizontal bar chart displays the number of concurrent symptoms reported by individual patients who also experience depression. It shows that many patients with depression live with multiple symptoms, suggesting a compounded emotional burden.

The Graph 2 (Figure 2) adds a deeper layer, showing that patients with depression often live with five or more concurrent symptoms—an accumulation that likely compounds emotional suffering. This highlights how symptom burden can contribute directly to psychological distress, not merely as a consequence but as a parallel burden requiring equal attention.

Graph 2 also reveals an important point: patients with few physical symptoms reported experiencing depression. This indicates that the diagnosis itself and the stigma of living with a rare disease can, on their own, trigger severe emotional suffering. This observation reinforces that depression in these patients should not be understood merely as a consequence of clinical progression, but also as a result of social isolation, uncertainty and the lack of specialized support.

These patterns suggest the need for symptom clustering analysis in clinical evaluations and call for integrated care models that address physical and emotional health simultaneously.

3.5 RECOMMENDATIONS FOR CLINICAL CARE

Improving care for patients with Wolfram Syndrome and other rare conditions requires a shift in clinical priorities. Emotional well-being must be recognized as a key outcome in rare disease treatment.

Future efforts should also focus on developing and implementing culturally sensitive mental health screening tools and interventions tailored specifically for rare disease populations, considering the unique challenges they face. The inclusion of psychologists in multidisciplinary care teams and the creation of national protocols to guide emotional support. Healthcare professionals must also receive training to improve their ability to listen, empathize and provide comprehensive care that validates the emotional experiences of patients.

In addition, supporting and collaborating with institutions led by patients that offer psychosocial support is essential, especially in the absence of public health structures. These initiatives play a critical role in bridging the gap between patients' emotional needs and the healthcare system's current limitations.

Such endeavors can reduce suffering, enhance adherence to treatment and improve quality of life. Recognizing mental health as a clinical priority is essential for advancing equity and compassion in rare disease care.

4 CONCLUSION

The data presented in this article reveal a troubling reality: depression is a highly prevalent symptom among patients with Wolfram Syndrome, occurring at rates comparable to core physical manifestations such as optic atrophy and hearing loss. This finding reinforces that emotional suffering is not a peripheral consequence of the disease, but rather a significant clinical expression of its progression.

Despite this, mental health remains systematically neglected in medical protocols for rare diseases. The absence of psychological screening, the lack of preparedness among healthcare professionals to address emotional issues and the scarcity of specific public policies contribute to the worsening of patient suffering. The invisibility of emotional impact, combined with limited access to therapeutic resources, deepens patients' isolation, anxiety and loss of autonomy.

The case of Wolfram Syndrome, analyzed here using original data collected by the Brazilian Association of Wolfram Syndrome (ABSW), clearly illustrates how holistic care—both physical and emotional—remains a significant gap in clinical practice. Recognizing depression as part of the disease's symptom constellation should prompt a reevaluation of current models of care.

Ignoring this dimension compromises not only patients\' quality of life but also treatment effectiveness and the therapeutic alliance necessary for long-term engagement.

4.1 KEY MESSAGES

- Depression is highly prevalent in Wolfram Syndrome, occurring at rates comparable to core physical symptoms, yet it remains systematically neglected in medical protocols.
- Patient-led initiatives, such as the Brazilian Association of Wolfram Syndrome (ABSW), are crucial for bridging the gap in mental health support for rare disease patients.
- Integrated care models that address both physical and emotional health, including early mental health screening and the inclusion of psychologists in multidisciplinary teams, are urgently needed.
- Recognizing mental health as a clinical priority is essential for advancing equity and compassion in rare disease care.

CONTRIBUTORS AND SOURCES

Rafaela Waltrick Ungaretti Lopes, the sole author, is the founder and director of the Brazilian Association of Wolfram Syndrome (ABSW), board member of The Snow Foundation (largest independent supporter of Wolfram syndrome research) and a patient diagnosed with Wolfram Syndrome. Her extensive experience living with the condition and her direct engagement with the patient community over more than a decade provide a unique and profound understanding of the challenges faced by individuals with this rare disease. She designed and led the data collection from 25 Brazilian patients, which forms the basis of this analysis. The sources of information include this original dataset, her lived experience and a review of existing literature on Wolfram Syndrome and mental health in rare diseases. Rafaela Waltrick Ungaretti Lopes is the guarantor of this article.

PATIENT INVOLVEMENT

While patients were the source of the anonymized data analyzed in this article and the author herself is a patient, there was no direct involvement of other patients in the writing or conceptualization of this specific manuscript beyond the initial data provision. One patient, Fernanda, was consulted via messaging by Rafaela to enrich certain informational aspects of the article and informed consent was obtained for this interaction and the use of survey data.

CONFLICTS OF INTEREST

We have read and understood BMJ policy on declaration of interests and have no conflicts of interest to declare.

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