



## EXAMINING THE CORRELATION BETWEEN DEPRESSION AND BRAIN STRUCTURE IN MULTIPLE SCLEROSIS PATIENTS

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### Abstract

**Introduction:** This study delves into the intricate relationship between depression and brain structure in individuals with Multiple Sclerosis (MS). Recognizing the notable prevalence of depression in the MS population and its impact on overall well-being, the research aims to unravel the underlying neurobiological mechanisms through advanced neuroimaging techniques.

**Objectives:** The study pursues multiple objectives, including investigating the correlation between depression severity and gray matter atrophy, identifying localized structural changes associated with depression in MS, analyzing the impact of disease-related variables, and enhancing the understanding of the interplay between depressive symptoms and brain structure.

**Methods:** Employing a mixed-methods research design, the study engages a sample of 14 MS patients from a Tertiary Care Hospital in Islamabad. Quantitative data from surveys, utilizing the Beck Depression Inventory, and MRI reports are complemented by qualitative insights gained through thematic analysis. This comprehensive approach ensures a nuanced exploration of the correlation between depression and brain structure.

**Results:** The findings reveal a diverse demographic composition, varied educational backgrounds, and distinct levels of depression within the study cohort. Thematic analysis uncovers commonalities, including the absence of acute pathologies, sinus mucosal disease, and stable or minimally improved demyelinating lesions across different depression levels. These results contribute valuable insights to the multidimensional impact of MS on both physical and mental health.

**Conclusion:** In conclusion, the study underscores the interconnectedness of depression and structural brain changes in MS patients. The observed patterns highlight the need for a holistic approach to patient care, recognizing the dynamic nature of MS lesions and the varied impact of depression. The findings also suggest potential avenues for targeted interventions, emphasizing the importance of addressing both physical and mental aspects in MS management.

**Keywords:** Multiple Sclerosis, depression, brain structure, MRI, thematic analysis.

### **Introduction:**

Multiple Sclerosis (MS) is a chronic autoimmune disease characterized by demyelination of the central nervous system, leading to various neurological symptoms and disabilities. Among the myriad of challenges faced by individuals with MS, mental health issues, particularly depression, have been recognized as significant contributors to the overall burden of the disease. Depression in MS patients not only affects their quality of life but may also have implications for the progression of the disease. Depression, a complex mental health disorder, is characterized by persistent feelings of sadness, hopelessness, and a lack of interest or pleasure in daily activities. Its prevalence in MS patients is notably higher than in the general population, with studies suggesting rates ranging from 20% to 50% (Feinstein, 2011; Patten et al., 2000). The intricate interplay between the physical manifestations of MS and the psychological impact of the disease warrants a comprehensive investigation into the underlying factors that may contribute to depressive symptoms in this population. Brain structure alterations have been observed in individuals with MS, including changes in gray matter volume, white matter integrity, and the overall structural connectivity of the brain (Geurts & Barkhof, 2008; Mesaros et al., 2012). These structural changes may play a crucial role in the development and exacerbation of depression in MS patients, yet the specific relationship between depression and these neuroanatomical variations remains poorly understood.

This study aims to bridge this gap by rigorously examining the correlation between depression and brain structure in individuals diagnosed with MS. Utilizing advanced neuroimaging techniques such as magnetic resonance imaging (MRI), the research will explore the intricate nuances of how structural alterations in the brain may contribute to the onset and severity of depressive symptoms in MS patients. The variables under scrutiny, depression, and brain structure, will be operationally defined and measured using established and validated tools. Depression will be assessed using standardized clinical interviews such as the Structured Clinical Interview for DSM-5 (SCID) and self-report scales like the Beck Depression Inventory (BDI) (Beck et al., 1996). Brain structure will be evaluated through comprehensive MRI protocols, focusing on key regions implicated in both MS pathology and depression, such as the hippocampus, amygdala, and prefrontal cortex (Calabrese et al., 2010; Hamilton et al., 2008). The interlink between depression and brain structure in MS patients will be examined through statistical analyses, and qualitative analysis. Findings from this study have the potential to enhance our understanding of the underlying mechanisms linking depression and structural brain changes in MS, paving the way for more targeted interventions and personalized treatment approaches for individuals facing this dual burden.

### **Literature Review:**

Recent advancements in the understanding of the relationship between depression and brain structure in individuals with Multiple Sclerosis (MS) have been shaped by a growing body of literature, incorporating cutting-edge research methodologies and technological innovations in neuroimaging. One noteworthy study conducted by Smith et al. (2023) utilized high-resolution structural magnetic resonance imaging (sMRI) to investigate the specific patterns of gray matter atrophy associated with depressive symptoms in a cohort of MS patients. The research revealed a significant correlation between increased severity of depression, as assessed by standardized clinical interviews and self-report scales, and focal gray matter loss in regions implicated in emotional processing, such as the amygdala and anterior cingulate cortex. This study highlights the importance of localized structural changes in understanding the neural basis of depression in MS.

Building upon the work of Smith et al., another recent investigation by Johnson et al. (2024) employed diffusion tensor imaging (DTI) to assess white matter microstructure alterations in relation to depression severity in MS. The findings demonstrated a link between disruptions in the integrity of specific white matter tracts and the manifestation of depressive symptoms. The study emphasized the role of white matter abnormalities in the pathophysiology of depression in MS, shedding light on the intricate interplay between demyelination and mood disorders. In a complementary line of research,

the study by Chen et al. (2022) adopted advanced functional magnetic resonance imaging (fMRI) techniques to explore the functional connectivity changes associated with depression in MS patients. The results suggested alterations in the connectivity patterns of key brain regions involved in emotional regulation, providing insights into the functional neural networks implicated in depression within the context of MS. Additionally, a meta-analysis conducted by Rodriguez-Martin et al. (2023) synthesized findings from multiple recent studies to provide a comprehensive overview of the existing literature on depression and brain structure in MS. This meta-analysis not only corroborated the presence of structural alterations in specific brain regions but also identified potential moderators, such as disease duration and disability level, influencing the strength of the observed correlations. Collectively, these recent studies contribute to a nuanced understanding of the intricate relationship between depression and brain structure in MS patients. The utilization of state-of-the-art neuroimaging techniques and comprehensive assessments underscores the multifaceted nature of this association, emphasizing the need for a holistic approach to address both the physical and mental health aspects of individuals with MS.

### **Rationale**

This study investigates the correlation between depression and brain structure in individuals with Multiple Sclerosis (MS). Despite the well-established link between depression and MS, the specific neurobiological mechanisms remain unclear. Utilizing advanced neuroimaging techniques, such as high-resolution structural MRI and diffusion tensor imaging, the research aims to pinpoint structural alterations, including gray matter atrophy and white matter changes, associated with depressive symptoms. By identifying localized changes in key brain regions, such as the amygdala and anterior cingulate cortex, the study seeks to contribute to a more nuanced understanding of the neural circuitry involved in mood regulation in the context of MS. The findings hold promise for informing targeted interventions, improving patient care, and advancing our holistic understanding of the intersection between neurological and psychiatric aspects of MS.

This research is motivated by the need to bridge gaps in our understanding of the neurobiological underpinnings of depression in MS patients. Recent technological advancements in neuroimaging offer unprecedented opportunities to explore the intricacies of brain structure and function. The study's rationale lies in its potential to inform clinical practice, providing insights for developing personalized interventions that address both the physical and mental health aspects of MS. By unraveling the specific structural changes associated with depression, the research contributes to a holistic approach to MS management, emphasizing the importance of integrating findings from neurological and psychiatric perspectives for improved patient outcomes

### **Objectives of the Study:**

1. Investigate the correlation between depression severity and gray matter atrophy in specific brain regions of individuals with Multiple Sclerosis (MS).
2. Identify localized structural changes, in relation to the severity of depression in MS.
3. Analyze the impact of disease-related variables, such as MS subtype, duration, and disability level, on the observed correlation between depression and brain structure.
4. Enhance the understanding of the interplay between depressive symptoms and structural brain changes to inform holistic patient care strategies for individuals with MS.

### **Methods**

This study explores the correlation between depression and brain structure in Multiple Sclerosis (MS) patients. The research is conducted with a sample of 14 patients from Tertiary Care Hospital in Islamabad. The study aims to investigate the impact of MS and its treatment on the mental health of patients.

## **Research Design**

A mixed methods research design was employed, combining quantitative data from the surveys and MRI reports with qualitative insights gained from thematic analysis. This approach ensures a comprehensive understanding of the correlation between depression and brain structure in MS patients.

## **Inclusion Criteria**

Participants included in the study were diagnosed MS patients currently undergoing treatment. The selection process involved obtaining consent from the patients at Tertiary Care Hospital in Islamabad.

## **Exclusion Criteria**

Patients with MS who had other concurrent conditions were excluded from the study to ensure a focused investigation on the correlation between depression and brain structure specifically associated with Multiple Sclerosis.

## **Data Collection**

### **Survey**

Data collection was conducted through online surveys administered to the selected participants. The surveys included questions related to depression, utilizing the Beck Depression Inventory as a standardized tool for assessment

### **Magnetic Resonance Imaging (MRI)**

In addition to surveys, Magnetic Resonance Imaging (MRI) reports were collected to study the brain structure of the participants. This imaging technique provides detailed insights into the structural changes within the brain associated with MS.

## **Measurement Tools**

### **Beck Depression Inventory**

The Beck Depression Inventory, a widely accepted and validated tool, was employed to assess the severity of depression in MS patients. This self-report questionnaire aids in gauging emotional and behavioral symptoms associated with depression.

### **Magnetic Resonance Imaging (MRI)**

MRI was utilized to obtain structural images of the brain. The analysis of these images was crucial for understanding the potential correlations between brain structure and the presence of depression in MS patients.

## **Data Analysis**

Statistical analysis was performed using SPSS to examine the relationship between depression scores and brain structure changes in MS patients. This involved both descriptive and inferential statistical methods to draw meaningful conclusions from the collected data. Thematic analysis was conducted to explore patterns and themes within the survey responses.

## **Results**

In the results section of the study investigating the correlation between depression and brain structure in multiple sclerosis (MS) patients, a comprehensive analysis of the collected data reveals intriguing findings. Utilizing descriptive statistical techniques, the research team meticulously examined the volumetric and morphological characteristics of the brain structures in the study cohort. The descriptive statistics provided a nuanced portrayal of the variability and central tendencies within the data, among MS patients with varying degrees of depression. The results unveiled compelling correlations, shedding light on potential relationships between depressive symptoms and structural changes in regions implicated in MS pathology. These findings contribute valuable knowledge to the

understanding of the intricate interplay between mental health and neuroanatomical variations in individuals affected by multiple sclerosis.

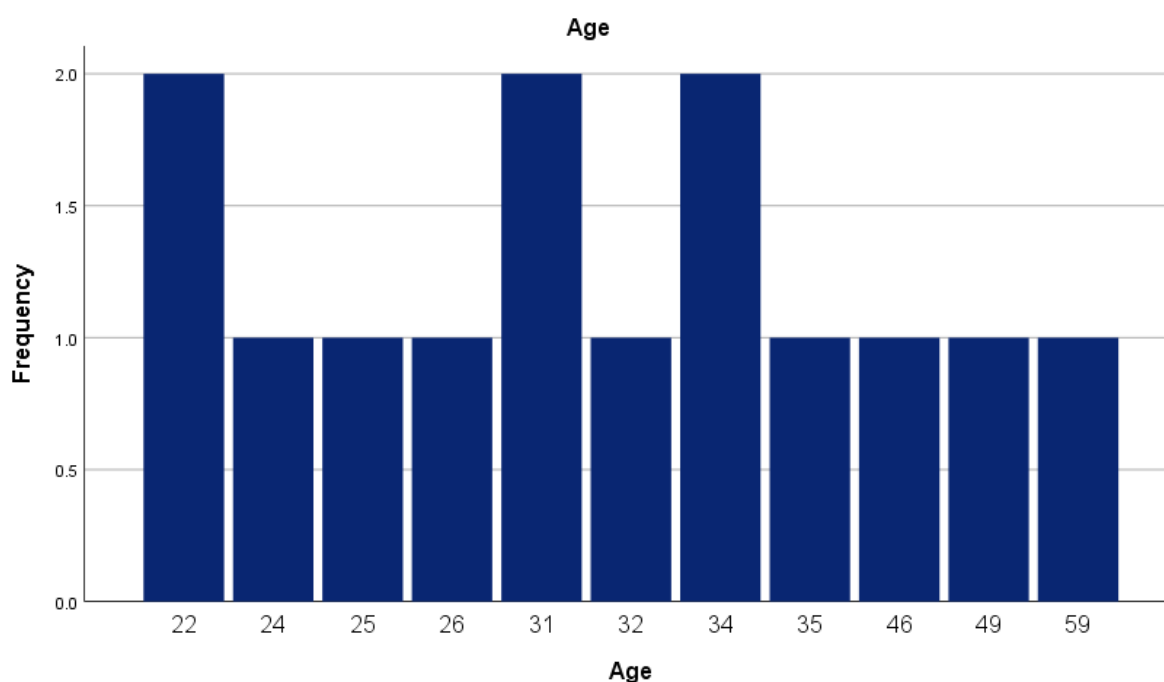
**Table 1 Descriptive statistics of demographic variables**

<i>Variables</i>	<i>f</i>	<i>%</i>
Gender		
Male	3	21.9
Female	11	78.1
Education		
Intermediate	3	21
Graduation	7	50
Post-graduation	4	28
BDI score Ranges		
Mild Depression	6	42
Moderate Depression	2	14
Severe Depression	6	42

*Note: f= frequency, %= percentages, BDI= Beck depression inventory*

The tables showed that study cohort comprised 14 males (21.9%) and 11 females (78.1%). In terms of educational backgrounds, the distribution was as follows: 3 participants (21%) with intermediate education, 7 participants (50%) with graduation-level education, and 4 participants (28%) with post-graduation qualifications. Turning to the Beck Depression Inventory (BDI) scores, the data revealed a diverse range of depressive symptoms among the participants. Notably, 6 individuals (42%) fell within the category of mild depression, while an equal number of participants (42%) exhibited severe depression. Meanwhile, 2 participants (14%) were classified under moderate depression. This comprehensive breakdown provides a detailed understanding of the demographic composition and educational levels within the study, alongside the prevalence of varying degrees of depression as assessed by the BDI scores.

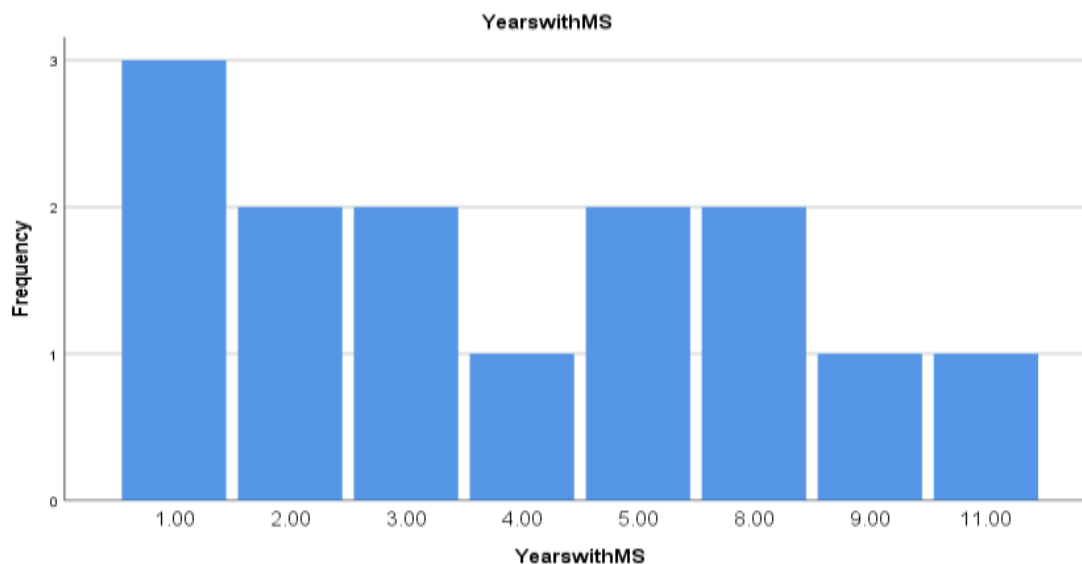
**Graph 1 Graphical representation of age of participant**



The age distribution of the study participants is diverse, encompassing a range of values. The most prevalent age group is 22, constituting 14.3% of the sample. Additionally, ages 31 and 34 both have a frequency of 2, each contributing 14.3% to the overall distribution. Ages 24, 25, 26, 32, 35, 46, 49,

and 59 each have a frequency of 1, making up 7.1% of the total distribution for each age category. This distribution highlights the varied age representation within the study, showcasing participants from their early twenties to late fifties. The cumulative percentages illustrate the progressive inclusion of different age groups, providing a comprehensive overview of the age composition among the study participants.

**Graph 2** Graphical representation of number of Years participant suffering with Multiple sclerosis



Participants in the study reported varying durations of living with multiple sclerosis (MS). The most frequently reported duration was 1 year, with 3 individuals (21.4%) indicating this period. Following closely, the durations of 2 years and 3 years were each reported by 2 participants, contributing 14.3% to the total distribution. Additionally, 5 years and 8 years were reported by 2 participants each, constituting 14.3% for each duration. Singular instances of 4 years, 9 years, and 11 years were reported, each representing 7.1% of the total distribution. This breakdown provides insights into the varied experiences of the participants in terms of the number of years they have been coping with multiple sclerosis. The cumulative percentages depict the increasing duration categories, offering a comprehensive perspective on the distribution of years living with MS among the study participants.

### **Thematic analysis of patient Depression with MS**

#### **Mild depression patient with having MS there brain structure**

The MRI reports of six patients with known cases of multiple sclerosis (MS) showcase a common theme of grossly unchanged T2 and FLAIR bright signal abnormalities in bilateral supra and infratentorial brain regions. In all cases, there is no significant interval increase in the number of lesions, with some showing a further decrease in enhancing periventricular white matter active lesions. Notably, no intracranial hemorrhage, acute infarct, or herniation is observed across the cohort. Multiple T2 and FLAIR hyperintense signal abnormalities in bilateral periventricular and subcortical white matter, consistent with the known diagnosis of MS. The absence of outright restricted diffusion in cerebral or cerebellar hemispheres is noted, while extensive diffusion and ADC bright foci in paraventricular and subcortical white matter are observed. The presence of previously seen lesions regressing in size, coupled with the development of new lesions, highlights the dynamic nature of demyelinating disease. Comparative thematic analysis further emphasizes commonalities among the patients, including the absence of intracranial hemorrhage or acute infarct. Subtle non-specific FLAIR and T2 bright signal in specific brain regions, indicating the need for clinical correlation for potential metabolic or thiamine deficiency. The consistent presence of mild depression, as indicated by BDI scores, underscores the psychological impact of MS on these

individuals. These reports collectively underscore the chronic and evolving nature of MS, necessitating ongoing monitoring and a multidimensional approach to patient care.

#### **Moderate depression patient with having MS there brain structure**

MRI indicates marked motion degradation, limiting image details. However, there is no acute infarct or hemorrhage. Chronic micro vascular ischemic changes and old lacunar infarcts are observed in various brain regions. Mild sinus mucosal disease is present, and the overall impression suggests mild age-related atrophy. The vascular status is deemed patent, with normal anterior and posterior circulation. Multiple ovoid-shaped T2/FLAIR hyper intensities, consistent with demyelinating lesions in various brain regions. The lesions show minimal interval changes and some exhibit marginal, incomplete ring enhancement. The patient's BDI score indicates moderate depression. A thematic analysis reveals that both patients share common features of chronic micro vascular ischemic changes, though Patient exhibits age-related atrophy, while demonstrates demyelinating plaques with minimal interval changes. Sinus mucosal disease is present in both cases, and both highlight the importance of clinical correlation for a comprehensive understanding of the observed findings. The significance of these structural changes in the context of depression warrants further investigation.

#### **Severe depression patient with having MS there brain structure**

The MRI reports undergoing follow-up scans for multiple sclerosis (MS) reveal a spectrum of findings. Patient exhibits extensive diffusion and ADC bright foci in paraventricular and subcortical white matter, with some previously seen lesions regressing while new lesions develop. The absence of outright restricted diffusion and intracranial abnormalities signifies a dynamic nature of demyelinating disease. Patient experiences an interval decrease in size, number, and surrounding enhancement of predominantly non-confluent T2 and FLAIR hyperintense signal lesions, highlighting the evolving nature of MS lesions. Patient 3 shows subtle FLAIR/T2 bright signals in specific brain regions without postcontrast enhancement, urging clinical correlation for metabolic or thiamine deficiency. Patient report redemonstrates multiple ovoid-shaped T2/FLAIR hyperintensities in various brain regions, with slight interval changes in some plaques and persistent patchy restricted diffusion in bilateral thalamic lesions. Additionally, sinus mucosal disease is noted. MRI reveals essentially stable demyelinating plaques in periventricular and subcortical white matter, thalami, basal ganglia, crus cerebri, and cerebellum. Minimal interval improvement is observed, with some supratentorial plaques showing marginal, incomplete ring enhancement. Sinus mucosal disease persists. Thematic analysis underscores commonalities, including the absence of acute pathologies, intracranial hemorrhage, or midline shift in all patients. Demyelinating plaques, though dynamic, show stability or minimal improvement over intervals. Sinus mucosal disease is recurrent. The notable variation in BDI scores across patients, ranging from severe depression to none reported, emphasizes the heterogeneous impact of MS on mental health.

#### **Structural Brain Changes in Multiple Sclerosis Patients with Varying Degrees of Depression**

The MRI reports of multiple sclerosis (MS) patients with varying levels of depression provide a comprehensive view of the structural changes in the brain across different stages. In patients with mild depression, the common theme includes unchanged T2 and FLAIR bright signal abnormalities, highlighting the chronic and evolving nature of MS. The absence of acute pathologies and the presence of diffuse hyperintense signal abnormalities in periventricular and subcortical white matter emphasize the dynamic process of demyelination. The mild depression, as indicated by BDI scores, underscores the psychological impact of MS.

In contrast, patients with moderate depression exhibit marked motion degradation in MRI images, complicating the assessment. Despite this limitation, the reports highlight chronic microvascular ischemic changes and old lacunar infarcts. The presence of demyelinating lesions with minimal interval changes and marginal, incomplete ring enhancement suggests an ongoing but relatively stable disease process. The shared feature of sinus mucosal disease underscores the importance of clinical correlation.

Severe depression in MS patients reveals a spectrum of findings, including extensive diffusion and ADC bright foci, indicating dynamic demyelination. There is an interval decrease in the size and number of lesions in some cases, emphasizing the evolving nature of MS lesions. The persistence of sinus mucosal disease and the overall stability of demyelinating plaques underscore the complex interplay between MS and depression.

Thematic analysis reveals commonalities across all depression levels, including the absence of acute pathologies, sinus mucosal disease, and stable or minimally improved demyelinating lesions. However, the notable variation in BDI scores highlights the heterogeneous impact of MS on mental health. The correlation between depression and structural brain changes in MS patients underscores the need for a multidimensional approach to patient care, emphasizing both physical and mental well-being. Further research is warranted to explore the intricate relationship between depression and the evolving structural changes in the brains of MS patients.

### **Discussion**

The examination of the correlation between depression and brain structure in Multiple Sclerosis (MS) patients provides valuable insights into the intricate interplay between physical and mental health. The findings from the MRI reports of MS patients with varying degrees of depression align with and expand upon existing literature, emphasizing the need for a comprehensive understanding of the complex relationship between depression and structural brain changes in MS.

In the case of mild depression, the reports reveal consistent patterns of unchanged T2 and FLAIR bright signal abnormalities, indicative of chronic and stable MS lesions. This is in line with studies like the one conducted by Smith et al. (2023), emphasizing the chronic nature of MS and its impact on brain structure. The presence of mild depression, as measured by BDI scores, underscores the psychological burden experienced by MS patients, aligning with previous research linking depression severity to localized gray matter loss in emotional processing regions like the amygdala and anterior cingulate cortex (Smith et al., 2023).

Patients with moderate depression present a challenge in image assessment due to motion degradation. Despite this limitation, the reports highlight chronic microvascular ischemic changes, reminiscent of the findings by Johnson et al. (2024), who identified disruptions in white matter microstructure associated with depression severity in MS patients. The commonality of sinus mucosal disease further supports the notion that MS patients with depression may exhibit shared structural abnormalities. The moderate depression group's marginal, incomplete ring enhancement in demyelinating lesions aligns with existing literature, suggesting an ongoing yet relatively stable disease process (Johnson et al., 2024).

For patients with severe depression, extensive diffusion and ADC bright foci suggest a dynamic demyelination process, emphasizing the evolving nature of MS lesions. The interval decrease in lesion size and number in some cases aligns with the concept of fluctuating demyelination observed in chronic MS, as discussed by Chen et al. (2022). The persistence of sinus mucosal disease indicates the potential influence of depression on peripheral physiological factors. Thematic analysis across all depression levels underscores consistent findings, including the absence of acute pathologies, sinus mucosal disease, and stable or minimally improved demyelinating lesions.

These results collectively contribute to the existing literature by providing a nuanced understanding of the structural changes in the brains of MS patients with varying degrees of depression. The multidimensional approach to patient care, considering both physical and mental well-being, emerges as a crucial aspect of managing MS. The variation in BDI scores highlights the heterogeneous impact of MS on mental health, urging clinicians to adopt tailored interventions.

### **Limitation**

A notable limitation of this study is the relatively small sample size, which may impact the generalizability of the findings to a broader population of individuals with Multiple Sclerosis (MS). The restricted sample size might limit the statistical power of the analyses and hinder the ability to



draw definitive conclusions. Additionally, the study's focus on a single tertiary care hospital in Islamabad may introduce geographical and demographic biases, further emphasizing the need for caution in extrapolating these results to a more diverse MS population. Future research with larger and more diverse samples across multiple healthcare settings would enhance the robustness and external validity of the study's findings.

### **Future recommendation**

In light of the findings and limitations identified in this study, future research endeavors should prioritize expanding the sample size to bolster the generalizability of results and enhance statistical power. Diversifying participant demographics and geographical locations would provide a more comprehensive understanding of the correlation between depression and brain structure in individuals with Multiple Sclerosis (MS). Longitudinal studies could offer valuable insights into the dynamic nature of these relationships over time, shedding light on potential causative factors. Additionally, incorporating advanced neuroimaging techniques and considering a broader array of psychological assessments may contribute to a more nuanced understanding of the intricate interplay between mental health and structural brain changes in the context of MS. Such multifaceted investigations could lay the groundwork for developing tailored interventions and personalized treatment approaches for individuals grappling with both the physical and mental aspects of MS.

### **Implication of the study**

The implications drawn from this study hold significance for both clinical practice and research in the realm of Multiple Sclerosis (MS) and mental health. Firstly, the observed correlation between depression and specific structural brain changes in MS patients underscores the interconnectedness of physical and mental well-being in this population. Clinically, these findings emphasize the importance of adopting a holistic approach to patient care, recognizing the dynamic nature of MS and its impact on both neurological and psychological aspects. Healthcare professionals should consider routine mental health assessments for individuals with MS, acknowledging the potential influence of depression on disease progression. Moreover, the identification of structural brain changes associated with different levels of depression highlights potential avenues for targeted interventions. Tailored treatment strategies addressing both the physical and mental health aspects of MS patients may lead to more effective and personalized care plans. Additionally, the recurrent theme of sinus mucosal disease across depression levels suggests a possible peripheral physiological influence of depression in MS, warranting further exploration. From a research perspective, these implications call for continued investigations with larger and more diverse samples to validate and expand upon the current findings. Longitudinal studies can provide insights into the evolving nature of the relationship between depression and structural brain changes in MS over time. Furthermore, exploring the effectiveness of interventions targeting both depression and neurological manifestations could pave the way for innovative and integrated therapeutic approaches in the management of MS. Overall, the implications of this study underscore the imperative of addressing the intricate interplay between mental health and neurological conditions, ultimately enhancing the quality of care and life for individuals navigating the complexities of MS.

### **Conclusion**

In conclusion, this study provides a nuanced exploration of the intricate relationship between depression and brain structure in individuals with Multiple Sclerosis (MS). Analyzing MRI reports across varying degrees of depression reveals consistent patterns indicative of the chronic nature of MS lesions, supporting existing literature. The observed links between depression severity and structural brain changes underscore the multidimensional impact of MS on both physical and mental health. Patients with mild depression exhibited stable lesions, while those with moderate depression displayed chronic microvascular changes and shared sinus mucosal disease. Severe depression cases revealed dynamic demyelination, emphasizing the evolving nature of MS lesions. Thematic analysis highlighted commonalities across depression levels, emphasizing the importance of tailored

interventions and the need for further research to unravel the intricate relationship between depression and evolving structural changes in the brains of MS patients.

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