Alqalam Journal of Medical and Applied Sciences. 2026;9(2):336-343
https://doi.org/10.54361/ajmas.269204

Original article

Multiple Sclerosis: Molecular Pathogenesis, Prevalence, and Major Risk Factors Contributing to Its Distribution in Benghazi City

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Abstract
Multiple sclerosis (MS) is a chronic autoimmune disease affecting the central nervous system, primarily causing demyelination of neurons. It impacts around 2.8 million people globally, with higher prevalence in the USA and the Middle East and North Africa (MENA) region. MS is a multifaceted condition with an unclear causative origin, believed to arise from a combination of genetic, environmental, and lifestyle influences. Genetic factors play a crucial role in the susceptibility to MS; specific genes, such as TNFRSF1A and TNFSF13B, are associated with an elevated risk and integral to the pathogenesis of MS. Multiple sclerosis risk is also influenced by several environmental factors, including viral infections, smoking, and a deficiency in vitamin D. Highlighting the complex interplay of genetic and environmental influences that contribute to the etiology of MS disease. The study used a mixed-methods design to retrospectively analyze 128 patient records from the Benghazi Medical Centre (BMC) spanning 2021 to 2025, along with a literature review of the disease's characteristics, molecular pathogenesis, and associations with viral infection. This study on multiple sclerosis (MS) in Benghazi indicated a low prevalence of the disease generally, with the majority of cases occurring in women aged 20 to 29, who represented 69% of those diagnosed. Over the course of the study, a gradual increase in cases was observed, starting with 28 recorded instances in the first year and rising to 49 by the final year, reflecting a slight increase in the number of diagnosed MS patients in recent years. Therefore, the present study emphasizes the urgent need for increased public awareness of the risk factors associated with MS, early detection, and the implementation of stronger diagnostic strategies, particularly for viral infections, as well as the establishment of region-specific prevention programs to manage MS effectively in Libya.
Keywords. Multiple Sclerosis, Molecular Pathogenesis, Risk Factors, Viral Infection, Benghazi Medical Centre.

Introduction

Multiple sclerosis (MS) is a complex and debilitating autoimmune disorder that poses a substantial public health challenge globally. Key pathological features, including inflammation, demyelination, gliosis, and neuronal loss, characterize MS disease. Patients with MS experience a range of neurological symptoms, including visual impairment, numbness and tingling, focal weakness, bladder and bowel dysfunction, and cognitive impairment [1,2]. Clinical studies identify four primary types of multiple MS: relapsing-remitting (RRMS), primary progressive (PPMS), secondary progressive (SPMS), and progressive relapsing (PRMS), characterised by various cycles of symptom progression and recovery. Primarily affecting individuals aged 20 to 40 years, with rising incidence and prevalence rates, especially in North America and Europe [3, 4]. Approximately 2.8 million individuals worldwide are affected by the disease, with significantly higher prevalence rates observed in the USA and the Middle East and North Africa (MENA) region, where healthcare access may be poor. The incidence rates of MS vary notably among ethnic groups [5].

In the MENA region, most countries fall within the low-to-moderate prevalence zone for MS, exhibiting prevalence rates that are slightly lower than those in Southern Europe but considerably higher than in sub-Saharan Africa [6]. It is worth mentioning that the prevalence of Multiple Sclerosis (MS) has been steadily rising in the MENA region over recent decades. The clinical phenotype of MS in this region resembles that in Western populations, albeit with an earlier onset age and a more aggressive course, resulting in disabilities occurring sooner [7, 8]. As research in the MS area progresses, the intricate interplay between genetic predispositions, epigenetic mechanisms, and environmental factors is increasingly acknowledged as fundamental in elucidating the etiology of this condition. However, the molecular pathogenesis of multiple sclerosis (MS) remains poorly understood [9, 10, 11].

Several systematic studies suggest that Multiple Sclerosis (MS) is fundamentally driven by autoimmune responses that specifically target myelin antigens. In the molecular pathogenesis of the disease, the active participation of various T cell types, including Th1, Th17, and CD8+ T cells, as well as B cells, with a significant presence of CD20+ B cells during the initial phases, plays a crucial role in MS disease [12, 13]. As the disease progresses, plasma cells become more significant, with their development being heavily influenced by cytokines. Additionally, genetic factors play a pivotal role in susceptibility to MS, with genes such as TNFRSF1A and TNFSF13B being linked to an increased risk, although the underlying mechanisms are still being explored [14,15]. Furthermore, additional genetic elements, such as the YAP/TAZ

Received*: 01-12-2025 -* ***Accepted****: 27-01-2026 -* ***Published****: 04-02-2026*

transcriptional regulators and HLA-DR15 haplotype, have also been identified as contributing factors that elevate the risk of developing MS, particularly among Caucasians [16].
Recently, genome-wide association studies (GWAS) have identified genetic risk factors for multiple sclerosis (MS) linked to variations in the major histocompatibility complex (MHC) gene cluster, with a particular focus on the HLA genes [17,18,19]. Multiple lines of evidence suggest that environmental factors, including viral infection, among them, human endogenous retroviruses (HERVs), particularly Epstein-Barr virus (EBV) infection, smoking, and low vitamin D levels, influence the risk of multiple sclerosis (MS), especially in individuals carrying the HLA-DR15 haplotype. The EBV viral infection is notably linked to increased susceptibility to MS, highlighting the importance of vaccinations for infections among MS patients, as these infections can worsen their condition [20,21]. In parallel, the emergence of new viral infections, especially COVID-19, introduces a new layer of complexities in understanding MS, prompting urgent questions about how these infections and the corresponding vaccinations may affect the progression and management of MS disease [22].
A systematic review and meta-analysis conducted to assess the overall prevalence of COVID-19 infection among MS patients found that 4% of MS patients were infected with the virus, which has heightened the risk for severe complications in MS patients [23]. Moreover, Vitamin D (Vit D) is recognized as a vital immune modulator, functioning as a steroid hormone essential for calcium and phosphate metabolism, immune homeostasis, and influencing brain development and function throughout life. Deficiency in vitamin D (hypovitaminosis D) has been linked to a variety of diseases. Several studies indicate a significant relationship between circulating Vit D levels and multiple sclerosis (MS), with findings showing that higher serum Vit D levels are associated with a 41% reduction in MS risk [24,25]. Alongside its effects on the immune system and viral infections, there is notable evidence implicating vitamin D, Epstein-Barr virus (EBV), and abnormal immune responses as significant contributors to the pathogenesis of MS [26,27,28].
In Libya, early estimates from 1984 indicated a low prevalence of multiple sclerosis (MS) in Benghazi, at about 4 cases per 100,000 people [29]. However, patient records from the Benghazi Medical Centre, covering the years 2016 to 2021, revealed a significant increase in diagnoses of Multiple Sclerosis (MS). Notably, 68% of newly diagnosed patients were female. The data also showed that the average age of onset for these patients was 28 years, while the mean age at diagnosis was 30 years. These insights implied improvements in disease recognition alongside a heightened incidence of MS among women. Another study conducted in Tobruk, eastern Libya, revealed a low level of public knowledge and awareness regarding Multiple Sclerosis (MS). There are significant gaps in understanding the disease's causes, symptoms, and management. This lack of awareness likely leads to diagnostic delays and underreporting of cases, indicating that the actual prevalence of MS in Libya, especially in Benghazi, may be higher than currently estimated [30,31].
This gap highlights an urgent need for comprehensive research to better understand the connections between MS, viral illnesses, and vaccinations. Furthermore, enhancing community education on recognizing and preventing MS is crucial to addressing these shortcomings. Given the context, this study explores the prevalence of multiple sclerosis (MS) in Benghazi, alongside clarifying the molecular pathogenesis of MS and investigating potential links to major risk factors. The study aims to increase public awareness of the risk factors associated with developing multiple sclerosis (MS) and to promote the development of effective diagnostic and management strategies suited to the Libyan healthcare system, ultimately enhancing outcomes for MS patients.

Methods

The study utilized a mixed-methods design to assess the prevalence of Multiple Sclerosis (MS) in Benghazi. It was structured as a descriptive cross-sectional study, which included the analysis of medical records of patients at the Benghazi Medical Centre. The study sample comprised 128 patient files belonging to individuals diagnosed with Multiple Sclerosis.
Data were meticulously collected from the statistics department of medical records at Benghazi Medical Centre (BMC), covering the period from 2021 to 2025. This integration of records provided a comprehensive understanding of patient demographics, gender, disease history, and prevalence rates. Additionally, it clarified the major risk factors associated with developing multiple sclerosis (MS) in the Benghazi community.

Ethical Considerations

Ethical approval was secured from the relevant institutional review boards before data collection for the study. Strict measures were in place to maintain the privacy and confidentiality of patient information, with only aggregate data used for analysis.

Results

Patient admission numbers

(Figure 1) showed patient admissions with MS disease in 2021; the number of patient cases was 28. In 2022 and 2023, there was an equal number of patients, with 37 cases recorded in each year, displaying a relatively

Received*: 01-12-2025 -* ***Accepted****: 27-01-2026 -* ***Published****: 04-02-2026*

stable pattern over those years. By 2024, a total of 42 cases had been documented. The number of patient cases recorded was a slight increase to 49 in 2025.

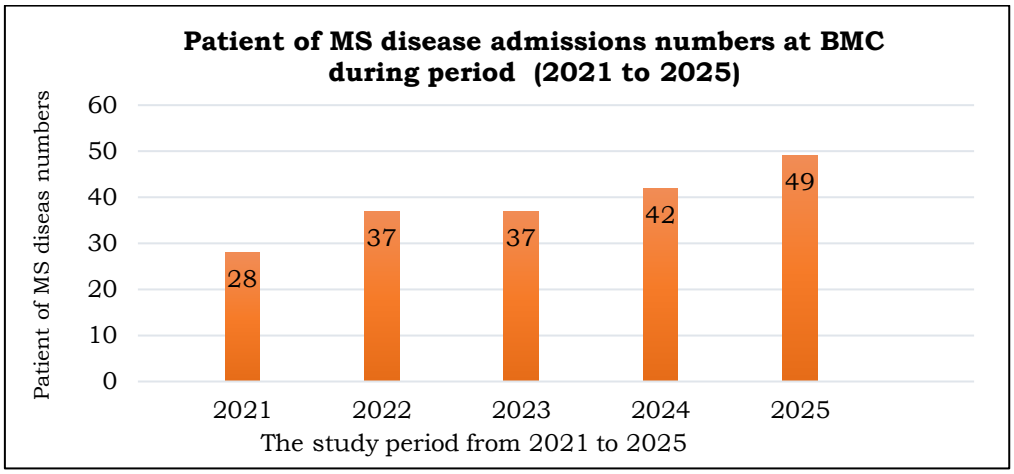

Figure 1. Patient Admissions from (2021–2025) at Benghazi Medical Center (BMC).

Age Group Distribution

Analysis of 128 patient records revealed that MS predominantly affects individuals in their twenties and thirties, as shown in Figure 2. The youngest patient in the dataset was 10 years old, while the oldest was 75 years old. The most common of MS disease at patient group (20- 29) was recorded in 40 patients. These findings align with global trends, where MS is most commonly diagnosed in young adults.

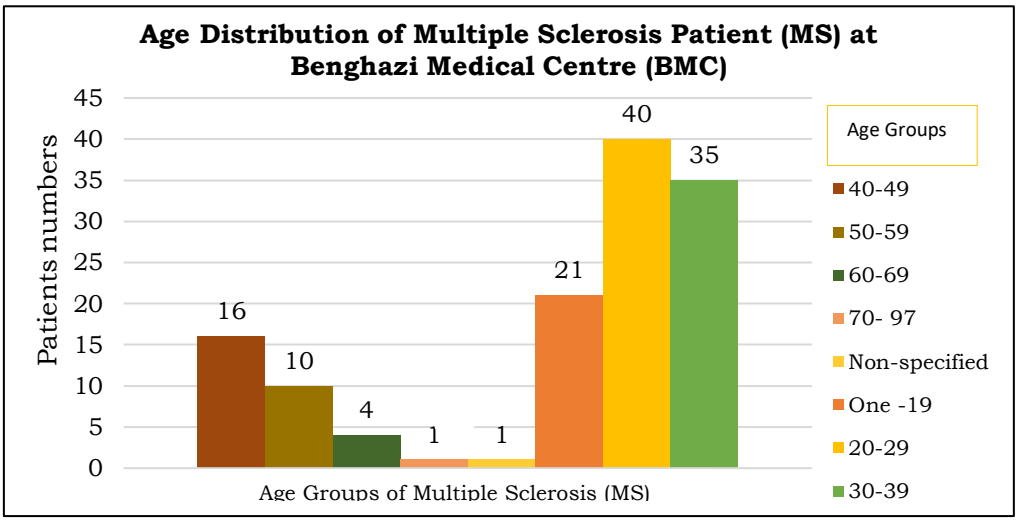

Figure 2. Age groups of MS patients at Benghazi Medical Centre.

Gender Distribution

The chart (Figure 3) illustrates the gender distribution of MS patients at BMC, indicating a notable female predominance. Women accounted for approximately 69% of the sample, while men comprised 31%. This observation is consistent with global epidemiological data, which suggests that MS is more prevalent among females, likely due to genetic and hormonal factors.

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https://doi.org/10.54361/ajmas.269204

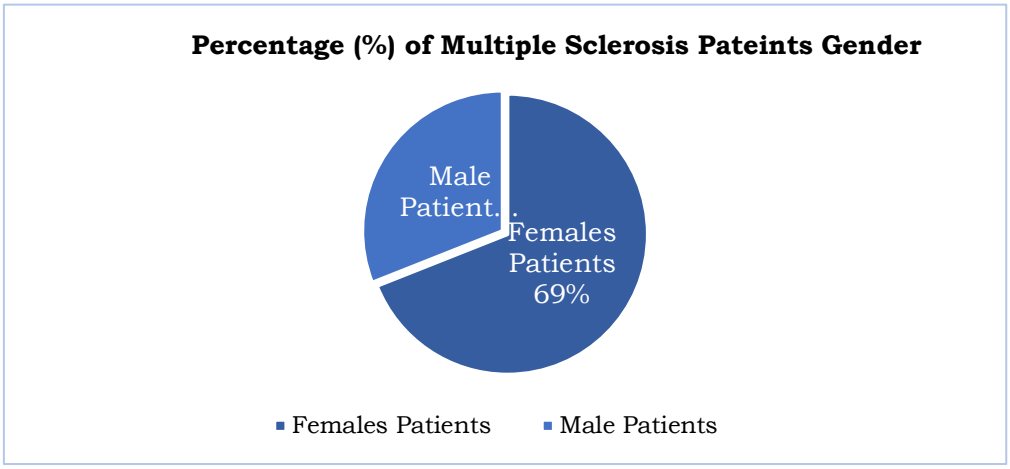

Figure 3. The Gender Distribution of MS Patients at Benghazi Medical Centre.

MS Patients Comorbidities

Among the patient cohort, comorbidities were reported in varying frequencies. The most prevalent conditions included diabetes mellitus (6 cases), respiratory tract infections (4 cases), and ischemic heart disease (4 cases). Other conditions, such as systemic lupus erythematosus (2 cases), epilepsy (2 cases), and single occurrences of sickle cell anaemia, psoriasis, Parkinson's disease, multiple myeloma, JC virus infection, hyperthyroidism, hypertension, celiac disease, and breast cancer, were also documented. However, 88 patient records did not specify the presence or absence of comorbidities (Figure 4).

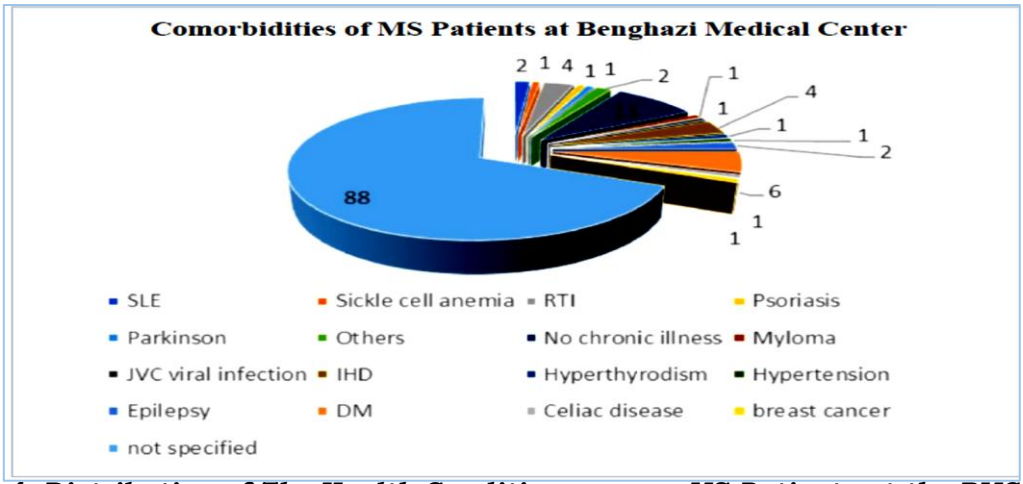

Figure 4. Distribution of The Health Conditions among MS Patients at the BMC Centre

PCR Utilization for MS Disease

Polymerase chain reaction (PCR) testing for MS follow-up was conducted in only 12 out of 128 cases, representing approximately 9.4% of the sample, as shown in Figure 5.

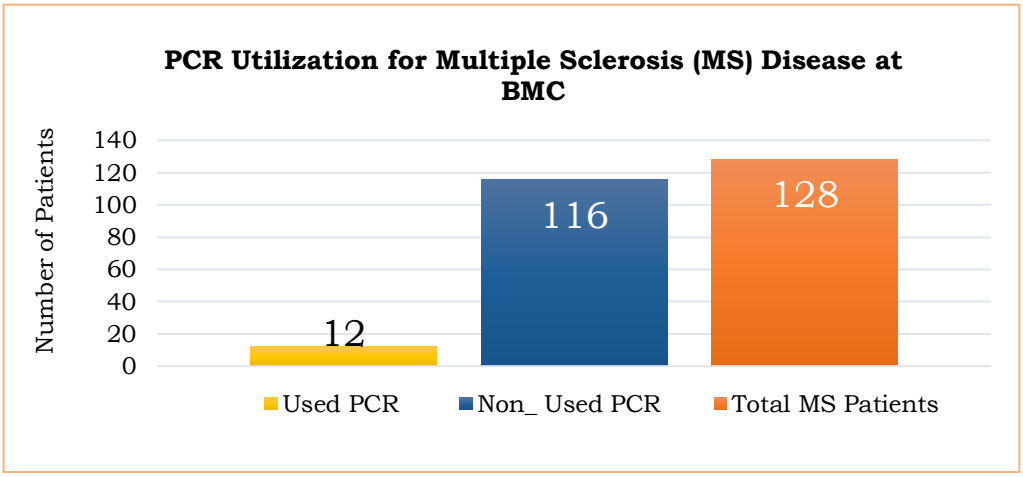

Figure 5. Frequency of PCR Utilization for MS Patients at Benghazi Medical Centre.

Received*: 01-12-2025 -* ***Accepted****: 27-01-2026 -* ***Published****: 04-02-2026*

The majority of patients (116 cases) did not undergo PCR-based monitoring, indicating limited use of advanced molecular diagnostic techniques for MS management in the study population.

Occupational Status of MS Patients

Analysis of occupational roles showed (Figure 6) that 32.8% of MS patients were housewives, followed by students (18.75%). Additionally, 12.5% of participants did not disclose their occupation. The remaining individuals were distributed across various other professions, reflecting a diverse employment background among MS patients.

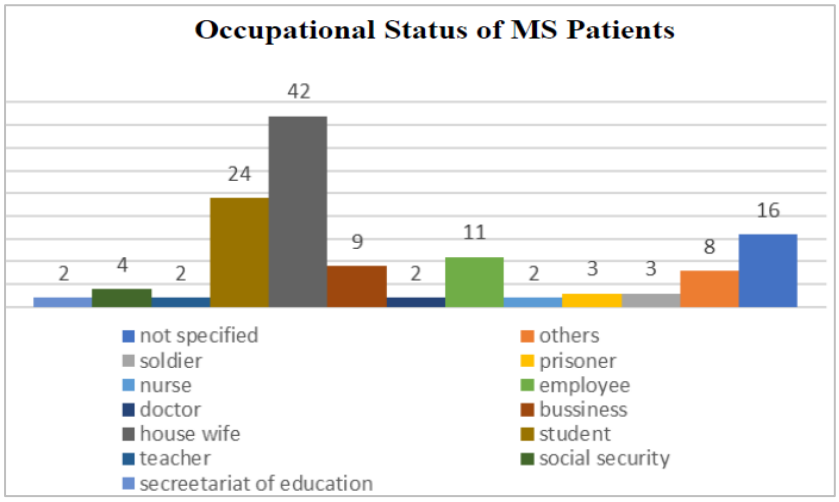

Figure 6. Employment Status and Occupational Roles of MS Patients at BMC.

Discussion

Multiple Sclerosis (MS) is a chronic autoimmune disease affecting the central nervous system, leading to progressive neurological impairments. The findings from this study provide valuable insights into the prevalence and epidemiology of MS patients at Benghazi Medical Center (BMC). Previous studies on multiple sclerosis (MS) have shown that its prevalence in Benghazi is relatively low compared to other autoimmune diseases. However, a different study revealed a significant increase in MS diagnoses, especially among newly diagnosed female patients. Moreover, the data indicated that the average age of onset for these patients is 28 years [32]. These findings align completely with the results of the current study. The data collected indicated that the annual incidence of multiple sclerosis (MS) cases has remained relatively low throughout the study period. The prevalence rates were estimated at 3.70% in 2021, with a slight increase projected from 2022 to 2025. Over the course of the study, there was a gradual rise in cases, starting with 28 recorded instances in the first year and increasing to 49 by the final year. This reflects a slight rise in the number of diagnosed MS patients in recent years. (as shown in Figure 1). Additionally, the majority of recorded diagnosed cases were among females aged 20 to 29, accounting for 69% of the total diagnosed cases (as shown in Figure 3). These findings are consistent with global trends, where MS is most commonly diagnosed in young adults. Nevertheless, given the limited sample size, these rates should be interpreted with caution, as they may not accurately represent the overall burden of MS in the region. Although the age distribution of MS patients in the present study is consistent with global epidemiological data, it mainly affects young adults aged 20– 40 years. However, the presence of a 10-year-old patient highlights the need for specialized attention to pediatric MS, which is less commonly reported but requires unique diagnostic and management strategies.

The predominance of female patients (69%) in this study aligns with well-established global trends, as MS is known to affect women two to three times more frequently than men, potentially due to hormonal, genetic, and immunological factors. While MS is more prevalent in females, several studies suggest that the severity of the disease may be greater in males [33, 34]. Notable findings of the present study were the presence of comorbidities in MS patients, with diabetes mellitus, respiratory tract infections, and ischemic heart disease being the most common. Systemic lupus erythematosus was identified in two cases, aligning with prior research suggesting a potential overlap between autoimmune disorders. Additionally, other conditions such as hyperthyroidism and psoriasis have been observed in BMC patients. These conditions have also been associated with multiple sclerosis (MS) in previous studies, possibly due to shared immunological mechanisms [35, 36].

Despite growing evidence supporting PCR-based diagnostics in monitoring MS progression, this study found that only 9.4% of patients underwent PCR testing. Previous studies have demonstrated the potential of PCR in detecting demethylated myelin oligodendrocyte glycoprotein (MOG) cell-free DNA, a biomarker of active disease [37, 38]. The limited utilization of PCR in this study suggests a gap in the adoption of advanced

Received*: 01-12-2025 -* ***Accepted****: 27-01-2026 -* ***Published****: 04-02-2026*

molecular techniques for the accurate diagnosis of MS in Benghazi city, highlighting the need for integrating such diagnostics into routine MS practices to enhance early diagnosis and management. The occupational analysis of the study sample revealed that a significant proportion of MS patients were housewives, followed by students. The socioeconomic impact of MS is profound, with many individuals experiencing unemployment or underemployment due to disability-related challenges, underscoring the importance of social and economic support for those living with MS.

Regarding risk factors, extensive evidence demonstrated that the risk is significantly increased by age, gender, family history, and certain infections. Furthermore, the most prominent factors in multiple sclerosis (MS) disease include vitamin D deficiency, obesity, certain autoimmune diseases, and smoking behaviour. Notably, smoking has been associated with increased disease severity and faster progression, reinforcing the need for targeted smoking cessation programs for individuals at risk of or diagnosed with MS. Statistical analysis of the present study indicates that the most significant risk factor elevating the probability of multiple sclerosis is gender, followed by smoking behavior and infections. Statistical analysis from this study indicates that the most significant risk factor elevating the probability of developing multiple sclerosis is gender, followed by smoking behavior and infections [39,40]. This finding aligns with substantial evidence in the field. The study acknowledged the role of vitamin D deficiency as a contributing factor, consistent with global research indicating a link between lower vitamin D levels and an increased risk of multiple sclerosis (MS). However, the statistical analysis in this study did not clearly define the extent of this risk factor.

Recent evidence suggests a strong link between Epstein-Barr virus (EBV) infection and MS, indicating a 32-fold increase in risk among individuals with prior EBV exposure that causes infectious mononucleosis. Nowadays, the global picture of MS is further complicated by external influences such as the COVID-19 pandemic, which has heightened the risk for severe complications in MS patients [41,42]. Several studies demonstrated that COVID-19 can potentially disrupt the immune system, increasing the likelihood of autoimmune responses and possibly exacerbating MS. Additionally, concerns have been raised about possible impacts on MS progression and vaccine safety. Though rare, some MS patients have experienced symptom relapses post-COVID-19 vaccination [43,44]. The reported cases of MS showed a temporal association with SARS-CoV-2 infection and related vaccines. The onset of MS appears to be more commonly linked to viral or vaccine exposure than disease reactivation, likely due to disease-modifying therapies offering a protective effect in individuals with established MS [45].

The study acknowledged the role of vitamin D deficiency as a contributing factor, consistent with global research indicating a link between lower vitamin D levels and an increased risk of multiple sclerosis (MS). However, the statistical analysis in this study did not clearly define the extent of this risk factor. In contrast, the study data reported cases of conditions like sickle cell anaemia, psoriasis, Parkinson's disease, multiple myeloma, JCV infection, hyperthyroidism, hypertension, celiac disease, and breast cancer. In addition to four cases each of respiratory tract infections and ischemic heart disease were noted, and six cases of diabetes mellitus, which have a potential link with MS. Besides a few cases of systemic lupus erythematosus (SLE) and other autoimmune conditions were also observed, suggesting a possible overlap between immune-mediated diseases.

Beyond clinical findings, this study also assessed public awareness of MS through a community survey (data have not been published). Results indicated a moderate level of knowledge, with significant gaps in understanding the genetic and gender-related aspects of MS disease. These findings emphasize the importance of targeted health education initiatives to improve public awareness, which could facilitate earlier diagnosis and better disease management. Given the relatively small sample size and the single-centre nature of this study, the findings may not be fully generalizable to the broader Libyan population. Therefore, larger-scale, multi-centre studies are recommended to provide a more comprehensive epidemiological understanding of MS in the region. Additionally, efforts should be made to integrate advanced diagnostic tools, such as PCR-based biomarkers, into routine MS management to enhance disease monitoring and treatment outcomes.

Conclusion

Multiple sclerosis (MS) is a complex autoimmune disorder that poses a significant public health challenge worldwide. The findings from this study provide critical insights into the prevalence, demographics, and risk factors associated with MS in Benghazi city. The study observed a stable incidence of MS cases over the years, with a predominance of young adults, particularly individuals in their twenties and thirties. Consistent with global trends, the majority of MS patients in this cohort were female, further supporting the well-documented gender disparity in MS prevalence. Comorbidities such as diabetes mellitus, ischemic heart disease, and respiratory tract infections were commonly observed among the study sample of MS patients,

In conclusion, the study underscores the necessity for a multidisciplinary approach to managing MS in Libya, encompassing enhanced diagnostic strategies, public health education initiatives, and targeted interventions to address modifiable risk factors. Strengthening healthcare infrastructure, increasing access to advanced diagnostic techniques, and promoting MS awareness can collectively contribute to better patient outcomes and improved quality of life for individuals living with MS in the region.

Received: *01-12-2025* - ***Accepted***: *27-01-2026* - ***Published***: *04-02-2026*

Acknowledgments
The authors gratefully acknowledge the Neurology Department at the Benghazi Medical Centre (BMC) for their cooperation and for providing the data essential to this research.

Conflicts of Interest
Nil

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Received*: 01-12-2025 -* ***Accepted****: 27-01-2026 -* ***Published****: 04-02-2026*