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Dr Shabrez Tariq, Dr Areeb Ahmed & Dr Zainab Shamim

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Review Article: Life Expectancy of Multiple Sclerosis in the US

Dr Shabrez Tariq[1*], Dr Areeb Ahmed[2] & Dr Zainab Shamim[3]
[1]Consultant, Houston Spine and Joint Consultants, Houston, TX
[2]Medical Assistant, Houston Spine and Joint Consultants, Houston, TX
[3]Medical Officer, Jinnah Postgraduate Medical Centre, Karachi, Pakistan

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Abstract

Purpose: Comprehending the life expectancy of individuals afflicted with MS is crucial for patient counseling and devising effective healthcare plans accordingly.

Materials and Methods: In this review, we amalgamate findings from several key studies published between 2014 and 2024, using Scopus, Google Scholar, and PubMed to provide insight into the mortality and life expectancy associated with MS.

Findings: Multiple sclerosis (MS) is a progressive, immune-mediated, neurodegenerative disease that incurs demyelination of the axons. MS impacts approximately 900,000 young adults in the United States, with an average onset age ranging from 20 to 30 years. MS population has been frequently associated with declining quality of life (QOL) as opposed to other chronic disease populations. Though, studies suggest physical impairment including weakness, gait disorders, or visual or emotional disturbances are pivotal determinants of life expectancy in MS patients. We will discuss each factor that influences the longevity of individuals with MS in detail below. Literature shows that 90% of cases with early disease experience relapses and remissions characteristically. While a small percentage of individuals follow a mostly benign course over an extended period, the majority establishes a secondary-progressive disease as soon as 6-7 years after the onset. Although a minor segment of MS manifests an "aggressive" disease, life expectancy is mostly unaffected with the disease course often prevailing over a period of 30 years on average, unless the patient’s comorbidities, compliance to treatment, or genetic predisposition are unfavourable.

Implications to Theory, Practice and Policy: We aim to enhance understanding of this disease and its multifaceted aspects for advance management strategies, better quality of life hence improved patient outcomes.

Keywords: *Multiple Sclerosis (I10), Quality Life (I12), Life Expectancy (I18), Physical Impairment (I12), Patient Counselling (I18)*

1.0 INTRODUCTION

Multiple Sclerosis (MS) is a chronic autoimmune and potentially debilitating disease of the central nervous system (CNS) that impacts a global population of 2.3 million individuals, particularly in their youthful years. Despite extensive research, significant gaps remain in understanding the full spectrum of MS symptoms, diagnostic criteria, and the long-term progression of the disease. This study aims to fill these gaps by providing a comprehensive overview of the disease, its impact on individuals, and the progression of symptoms. The beneficiaries of this study include healthcare professionals, patients, and researchers seeking to improve diagnostic accuracy, treatment plans, and overall patient outcomes.

Background and Etiology

Multiple Sclerosis (MS) manifests as inflammatory demyelination with axonal transection, leading to physical disabilities and cognitive challenges. The disease arises from the interplay between genetic predisposition, an imbalanced immune system, and environmental risk factors. MS is twofold more prevalent in females compared to males and typically manifests during early adulthood, around the age of 30 years. The progression of MS is marked by its diverse and unpredictable nature.

Symptoms

The clinical spectrum of MS commonly includes motor symptoms followed by cognitive changes. Key symptoms include:

1. Weakness or spasticity
2. Optic neuritis
3. Diplopia (double vision)
4. Depression or anxiety
5. Memory changes
6. Sensory deficits
7. Paresthesia (tingling or pricking sensations)
8. Neuropathic pain

Diagnostic Criteria

The diagnostic criteria for MS include the presence of lesions that are disseminated in time (new episodes correspond to new lesions on MRI scans at different points over time) and space (random areas of the brain and spinal cord affected each time). These criteria must be independent of any other inflammatory, structural, or hereditary conditions that can clinically mimic MS. According to the National Multiple Sclerosis Society, MS occurs in four different forms:

Primary-progressive MS: Neurological dysfunction sets in early in the disease course.

Secondary-progressive MS: Neurodegenerative symptoms gradually establish later in the disease.

Relapsing-remitting MS: Characterized by episodic flare-ups alternating with remittent bouts throughout its clinical course.

Clinically Isolated Syndrome (CIS): Characterized by a singular episode of neurological impairment persisting for more than 24 hours.

Disease Progression and Disability

Axonal degeneration is the principal factor contributing to permanent disability due to inflammatory processes in both the relapsing-remitting and progressive stages of MS. This degeneration may also occur due to potential neurodegeneration facilitated by the deprivation of trophic support. The advent of treatments for MS has prompted early identification of the initial demyelinating stage of CIS, which may serve as a precursor to MS. Distinctive episodes such as optic neuritis, solitary brainstem lesions, and transverse myelitis confer a 30% to 70% probability of progressing to MS. Apart from acute neurological episodes, the recurrence and persistence of these symptoms significantly contribute to the disability burden in MS. These symptoms encompass:

1. Fatigue (predominant in two-thirds of the MS population)
2. Spasticity
3. Urinary and bowel dysfunctions
4. Ataxia (lack of muscle coordination)
5. Tremor
6. Visual impairments
7. Neuropathic pain
8. Mood disorders
9. Swallowing difficulties
10. Sexual dysfunction
11. Ultimately, the accumulation of disability can negatively impact the lifespan of affected individuals.

2.0 MATERIALS AND METHODS

In this review article, we employed an integrated approach to systematically gather and evaluate relevant literature from reliable sources, including Scopus, Google Scholar, and PubMed. We used keywords like "life expectancy," "mortality," "Multiple Sclerosis," "US," "epidemiology," to filter out the literature of relevance. Our inclusion criteria consisted of English articles that were carried out in the region of the United States, being published in recent 10 years (2013–2024) and other regions with similar objectives and methodologies to correspond the data with. On the other hand, studies that were not well-aligned to our methodological parameters were eliminated. Each article that made it beyond the literature review were thoroughly assessed to determine its suitability and usefulness for the review.

Body

In this comprehensive review, we will look into the studies conducted in the US analysing the life expectancy of MS population in the last 10-14 years as opposed to in different regions across the globe. Our review will also highlight the role of comorbidities and lifestyle choices on the disease course and survival of MS cohorts owing to their effect on the quality life

Comorbidities & Life Expectancy

The autoimmune mechanisms underlying Multiple Sclerosis generally share an increased susceptibility towards specific comorbidities such as type 1 diabetes and inflammatory bowel diseases. An investigation based on the US Department of Defense database analysis, encompassing the subjects aged 18-64 years, offers an in-depth evaluation of mortality patterns and comorbidity status in individuals diagnosed with MS. The analysis explored that both mortality rates and occurrences of comorbidities were typically elevated within the MS cohort (15,684 in number) compared to a demographically matched non-MS cohort (78,420 in number).

Furthermore, the incidence of mortality attributed to nervous system diseases (5.8), respiratory system ailments (5.0) and circulatory system disorders (2.1) was observed to be notably elevated among the MS cohort compared to the non-MS cohort.[7] Notably, the heightened rates of circulatory system disease-related mortality were unexpectedly pronounced, possibly due to the inclusion of diverse comorbidities within this classification. Whilst an all-cause mortality, the Mortality Rate Ratio (MRR) stood at 2.9 with the highest rate observed in individuals aged between 18 to 29 years.7,8 Another study examined mortality rates and causes of death in MS patients compared to the general population. The findings highlighted the importance of addressing cardiovascular risk factors and promoting healthy lifestyle behaviors in improving overall survival.[9]

Gender Predisposition & Disease Progression

Certain studies compare the life expectancy of men vs women afflicted with MS. In this context, female individuals exhibit a tendency to live longer (77.2 years) by approximately 5 years compared to their male counterparts (72.2 years) despite higher incidence of MS in women. There exists an observed deceleration in disease progression among women as opposed to men.10 Nonetheless, researchers suggest that these findings may be attributable to the inherent variance in life expectancy observed between genders in the broader population. However, women with primary progressive-MS (PPMS) particularly were observed to have an increased hazard compared with men with PPMS.[12]

Similar to others, we also found that patients with younger age at onset had a higher relative risk of dying (higher SMR) than patients with an older age at onset.[11,12] In terms of disease course, an investigation revealed that individuals diagnosed with Relapsing-Remitting MS (RRMS) exceeded the lifespan of those with PPMS by nearly 7 years from birth, accompanied by a mortality risk (indicated by Standardized Mortality Ratio, SMR) approximately twice as high in PPMS compared to RRMS.[10,12]

Global Status

A longitudinal population cohort study spanning 60 years in Western Norway revealed a median decrease in life expectancy of 7.1 years (74.7 years for MS and 81.8 years for the general population) and, in general, nearly a threefold elevation in the mortality rate among individuals with multiple sclerosis when compared to a demographically matched control group from the general population. No disparity in cause-specific deaths were noted ($p=0.0871$). However, there was a continual increase in survival rates of the MS cohort through the length of study.[10] The reduction in life expectancy was reinforced by the results of Canadian12 and Spanish13 studies, reported to be 6-6.5 years. Although the former documents some of the longest MS survival durations, the risk for mortality was still higher than in the general population. No evidence of overall improved life expectancy was found. Median survival age was 78.6 and 74.3 years for women and men, respectively. Survival from onset was longer for relapsing-MS (49.7 years) than for primary progressive-MS (32.5 years). The latter did not establish any difference in survival owing to the gender and disease course, nor an overall survival increase.

Quality of Life & Life Expectancy

The World Health Organization (WHO) delineates quality of life (QoL) is multifaceted model interlinking physical, social, psychological, and emotional aspects of life. It is a subjective evaluation of an individual's life within the framework of their cultural and value systems, alongside considerations of their aspirations, expectations, standards and concerns.[14] In fact, in contemporary times, there has been a growing recognition for QoL to be used as a health assessment tool in evaluating the disease progression, the treatment response, and healthcare access to individuals afflicted with MS.[15]

Depression is a key determinator of QoL. Depression may manifest in individuals with MS, even in its milder forms with higher probability in the initial years following diagnosis[16]. While depression and anxiety have been linked to disease activity rather than its duration, research indicates the presence of some neurobiological risk factors inherent to MS, contributing to the heightened incidence of depressive disorders. These factors include cortical atrophy observed in various regions, including the bilateral frontal lobes, as well as the parietal and occipital lobes that have been highly linked with depression in MS patients[17]. A study has identified 62% of subjects with mild depression, 38% with severer forms[18]. Depression significantly deteriorates the quality of life among individuals with MS, adversely affecting both the mental and physical dimensions of their well-being. Moreover, increased disability levels correlate with diminished quality of life across the physical and mental domains of health, ultimately influencing mortality trends among MS patients.

Treatment Options & Life Expectancy

Healthcare utilisation and access to care can greatly influence the prognosis of MS. Currently, 9 classes of disease-modifying therapies (DMTs), with varied mode of action and routes of administration, are available for relapsing-remitting MS and secondary progressive MS to regulate the inflammatory activity in body. These medications encompass interferons, glatiramer acetate, teriflunomide, sphingosine 1-phosphate receptor modulators, fumarates, cladribine, and 3 types of monoclonal antibodies. Ocrelizumab, a newly approved DMT can now be used for PPMS. These medications encompass interferons, glatiramer acetate, teriflunomide, sphingosine 1-phosphate receptor modulators, fumarates, cladribine, and three variants of monoclonal antibodies. Ocrelizumab, an additional disease-modifying therapy (DMT), is specifically indicated for primary progressive MS. These DMTs exhibit efficacy in mitigating both clinical relapses and MRI lesions. The efficacy rates of current DMTs, gauged by the reduction in annualized relapse rates compared to either placebo or active comparators, span from 29% to 68%.19 Personalized treatment strategies and long-term compliance has reported can yield reduction in relapses and chances of disability, better quality of life and hence, a better life expectancy.

3.0 CONCLUSIONS AND RECOMMENDATIONS

In conclusion, the reviewed studies collectively demonstrate that MS alone does not frequently reduce life expectancy or incur mortality in a patient compared to the general population. It does, however, significantly impact the quality of life of a patient with factors such as disease severity, comorbidities, and access to healthcare greatly determining survival outcomes. These findings highlight the relevance of early diagnosis and intervention, panoramic and personalised treatment regimens in improving the prognosis and quality of life for individuals living with MS in the United States.

To enhance the QOL of these individuals, it is imperative to focus on identified factors and implement practical measures. This includes addressing barriers such as offering educational and counseling services to both patients and their families, adjusting urban infrastructure, providing financial assistance, and ensuring comprehensive insurance coverage. By taking such steps, authorities can promote the health of patients and enhance their overall quality of life.

The study of Multiple Sclerosis (MS) provides critical insights that enhance diagnostic accuracy, improve patient management and care, and inform public health policies. By detailing the disease's symptoms, diagnostic criteria, and progression, the study aids healthcare providers in developing personalized treatment plans and effective patient counseling, leading to better adherence to treatments and improved quality of life. It highlights the need for early intervention and a multidisciplinary approach, involving collaboration among various healthcare professionals to address the diverse needs of MS patients. Additionally, the findings can guide future research, support the development of advanced therapeutic strategies, and inform policies that allocate resources effectively, ultimately aiming to improve long-term patient outcomes and reduce the societal burden of MS.

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