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Multiple Sclerosis in India

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ABSTRACT : The central nervous system is affected by the inflammatory neurodegenerative illness known as multiple sclerosis. Multiple sclerosis is a great candidate for precision medicine because of its varied presentations in both clinical presentation and course. This chapter outlines our present knowledge of the genetics and genomes research environment surrounding multiple sclerosis. Approximately half of the heritability of multiple sclerosis has been characterized as a result of recent progress in mapping the genetic architecture of the disease. Significant differences have been found in the immune systems of MS patients as well as in lesions and unaffected regions by transcriptome studies..Proteomic research has also identified several clinical and exploratory biomarkers that may be useful in the creation of targeted treatments.Nonetheless, a diverse range of genes that exhibit epistatic interactions most likely mediate susceptibility.Advances in numerous fields have laid the basis for future precision medicine applications.cell-mediated autoimmune disease that is triggered by unknown exogenous agents in subjects with a specific genetic background. Genes of the major histocompatibility complex class II region are the only ones that have been consistently associated with the disease.Nonetheless, a diverse range of genes that exhibit epistatic interactions most likely mediate susceptibility. In addition, the etiology of MS has been proposed to be infectious, and the immune response against self-antigens is probably shaped by infectious pathogens. Multiple sclerosis (MS) is believed to be mediated by myelin-specific CD4 T lymphocytes that enter the central nervous system upon activation, according to data from animal models, the composition of plaques, and the response to therapy. Different patterns of tissue damage have been shown in active MS lesions, suggesting that the mechanisms of injury are probably distinct in different subgroups of patients. Heterogeneity in clinical characteristics, magnetic resonance imaging, and response to therapies support this notion. The experience gained during several pharmacological studies has improved our understanding of the pathogenesis of MS. As imaging techniques develop, new technologies like proteomics and DNA mcicroarrays for gene expression profiling may help us find susceptibility genes and disease indicators.senable us to design more effective treatments and to modify them based on various illness forms or steps.

I. INTRODUCTION

The most prevalent non-traumatic debilitating illness affecting young individuals is multiple sclerosis (MS). Both in industrialized and emerging nations, the incidence and prevalence of MS are rising, yet it is still unclear what the underlying reason is. MS is a complicated illness; in addition to a number of well-established environmental factors, such as vitamin D or ultraviolet B light (UVB) exposure, Epstein-Barr virus (EBV) infection, obesity, and smoking, several genes also slightly enhance the risk of developing the condition.Historically, multiple sclerosis has been categorized as an autoimmune illness mediated by T cells that are specific to specific organs.But the efficacy of B-cell-targeted treatments is challenging.Breaks the conventional T-cell autoimmune paradigm *4+. It is commonly thought to be a two-stage illness, with The first inflammation that causes relapses and remissions Illness and postponed neurodegeneration that results in non-Regression trajectory, that is, secondary and main Increasing MS (1)

Keywords : male and female bacound in ms; ms disease-modifying drug tolerance and safety; drug therapy for ms **Overview :**

The central nervous system (CNS) is afflicted due to potentially crippling condition known as multiple sclerosis (MS) Myelin, the protective sheath that protects nerve fibers, is attacked by the immune system in MS, which impairs brain-to-body communication. The condition may eventually result in nerve fiber degeneration or irreversible injury. Patient-to-patient variability in MS signs and symptoms is mostly dependent on the location and extent of damage to nerve fibers inside the central nervous system. A small percentage of MS patients may develop total or partial paralysis.Depending on the type of MS they have, other people might go for extended stretches of time without developing any new symptoms. Multiple Sclerosis has no known treatment option. Treatments exist, nevertheless, to slow the onset of attacks, alter the course of the illness, and control symptoms.(2)

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Symptoms :

Depending on where the damaged nerve fibers are located, the signs and symptoms of multiple sclerosis can vary significantly from person to person and throughout the disease.

Common symptoms include:

- One side of your body usually experiences numbness or weakness in one or more limbs at a time.
- Pins and needles
- Feelings similar to electric shock that happen when you tilt your neck forward in particular
- Inadequate collaboration
- An unsteady gait or immobility
- Complete or partial blindness, typically affecting one eye at a time, frequently accompanied by pain when moving the eyes
- Prolonged bilateral vision
- Hazed visio
- dizziness
- Issues relating to bladder, bowel, and sexual function
- Pins and needles
- Feelings similar to electric shock that happen when you tilt your neck forward in particular
- Inadequate collaboration
- An unsteady gait or immobility
- Complete or partial blindness, typically affecting one eye at a time, frequently accompanied by pain when moving the eyes
- Prolonged bilateral vision
- Hazed vision
- dizziness
- Issues relating to bladder, bowel, and sexual function
- Fatigue
- Slurred speech
- Cognitive problems ∟ Mood disturbances
- Depending on where the damaged nerve fibers are located throughout the body, the signs and symptoms of multiple sclerosis can vary significantly between individuals and over the course of the disease.
- Typical signs consist of:
- A condition where you experience numbness or weakness in one or more limbs, usually on one side of your body at once.
- Certain neck movements, especially bending the neck forward, might cause tingling electric shock feelings
- Coordination deficit
- Gait instability or an inability to walk
- Partial or total blindness, typically affecting one eye at a time, and frequently accompanied by eye movement pain
- Persistent double vision
- Cloudy vision
- Vertigo
- Issues with digestive, sexual, and urinary function
- Chronic fatigue
- Fluent speech
- Cognitive issues
- Disorders of the mood(2,3)

Causes and risk factors :

- **Age**: Between the ages of 20 and 40, the majority of patients acquire a diagnosis.
- **Sex:** Women are twice as likely as males to develop the majority of MS variants.

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- **Genetic factors:** While environmental triggers are thought to be necessary for MS to develop, even in people with certain genetic traits, susceptibility may be inherited genetically.
- **Smoking:** MS seems to be more prone to develop in smokers. In comparison to nonsmokers, they also frequently have greater lesions and brain atrophy.
- **Infections:** Research has not conclusively linked Epstein-Barr virus (EBV) or mononucleosis exposure to an increased risk of developing multiple sclerosis (MS). Human herpes virus type 6 (HHV6) and mycoplasma are two other viruses that could be involved.(3)

What is multiple sclerosis (MS)?

The immune system is the source of MS. When you have these conditions, your immune system mistakenly attacks healthy cells. Immune system cells in the myelin, the protective layer that encases nerves in the brain and spinal cord, are targeted by MS patients' bodies .

Nerve signals traveling from the brain to other regions of the body are disrupted when the myelin sheath is damaged. Your brain, spinal cord, and eyes may be affected by the damage which might cause symptoms.

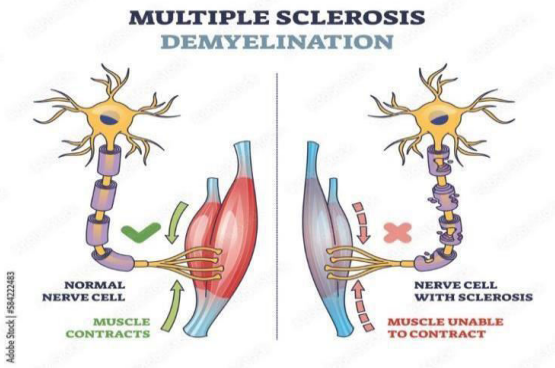

fig: multiple sclerosis demyelination(5)

History :

Any severe neurological condition characterized by motor disability is referred to as "paraplegia". The first reference of MS was recorded by Saint Lidwina of Schiedam, who resided in the Netherlands at the end of the 14th century . For 26 years, Augustus d'Este kept a journal in which he described signs of what we now know as Modes: now know to be MS got worse over time. At age 28, he first experienced a transient visual impairment, most likely causedneurites'.Heied at age 54 of motor symptoms and lower extremities that hindered his walking .Charcot's naming and framing of MS provided a framework for organizing previously unexplained discoveries and making future advances in MS. Since then, the consolidation has continued. now recognized as Over time, MS got worse. At age 28, he experienced a brief loss of vision, which was most likely the result of optic neuritis. He passed away at the age of 54 from lower extremity problems and motor symptoms . The identification and description of MS by Charcot provides a foundation for categorizing previously unrecognized future MS discoveries and advancements. Consolidation has continued ever since.The clinical signs of the illness and the pathology of the postmortem lesions were connected by Charcot's students. Plaques in the brain and spinal cord were described in Joseph Babinski's 1885 MS thesis. Peter Marie emphasized autonomic Impediments to gait and functioning in MS *. Ernst Leyden first proposed a hereditary element MS around the middle of the 19th century. Still, Curtius and other Germans didn't begin doing so until the 1930s.(6)

According to the progression of the disease, neurologists concur that patients can be divided into four main categories:

- About 85% of MS patients have the most prevalent kind, relapsing-remitting MS. It is characterized by periods of remission, when symptoms become better or go away, followed by symptom flare-ups (relapses or exacerbations).
- A small percentage of people with relapsing-remitting disease may acquire secondary progressive MS. Treatment with disease-modifying medications helps many patients halt this progression. With or without remissions or plateaus in the severity of the symptoms, the disease course continues to worsen.
- About 10% of MS patients have primary progressive MS. From the start, the symptoms steadily get worse. There are no remissions or relapses, however there could be sporadic plateaus. This type of MS is more severe.(7)

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male and female background in multiple sclerosis :

Women are around three times as likely as men to get multiple sclerosis (MS). However, a risk factor for worse impairment progression is being a man. Susceptibility has been linked to genes involved in inflammation, while the advancement of disabilities is caused by neurodegeneration. As a result, sex seems to have a different impact on neurodegeneration than it does on inflammation.

Additionally, gray matter (GM) atrophy is not consistent throughout the brain in MS but exhibits regional variance instead. Here, we compare regional GM atrophy in a cohort of MSaffected men and women with their corresponding age- and sex-matched healthy controls in order to examine sex variations in neurodegeneration.(8)

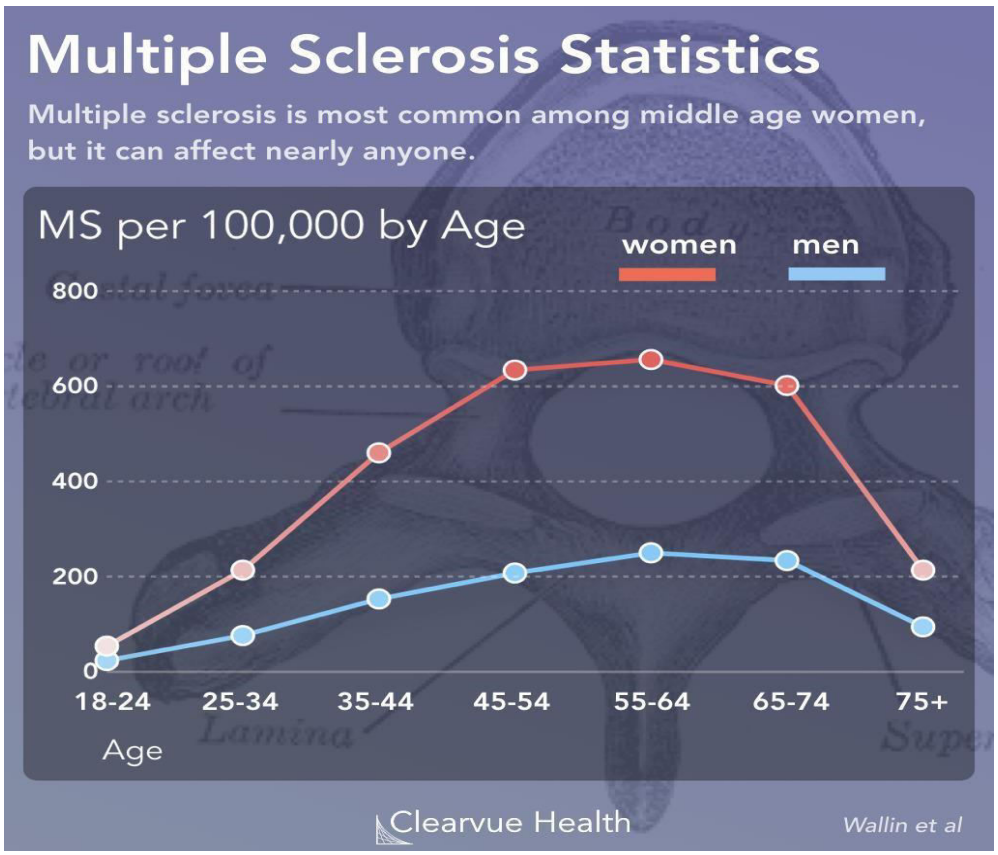

Fig : multiple sclerosis Statistics (9)

MS disease-modifying drugs: tolerance and safety :

There are two types of pharmacological treatment for MS: symptomatic therapy and symptomatic/immune-modulatory therapy. Treatments for symptoms primarily seek to Sustain function and to enhance quality of life, whereas the primary objective of disease is to Modifying drugs for multiple sclerosis (DMTs) aim to decrease recurrence rates and postpone disability with an impact on numerous magnetic resonance imaging (MRI) measurements *11+. Several Therapeutics that have been approved by the Authority Agencies can lessen the symptoms of sickness and Progression in people with secondary progressive MS and relapse types of MS; of these, Mitoxantrone, glatiramer acetate, natalizumab, fingolimod, and interferon beta-1a and beta-1b are The most popular.(10)

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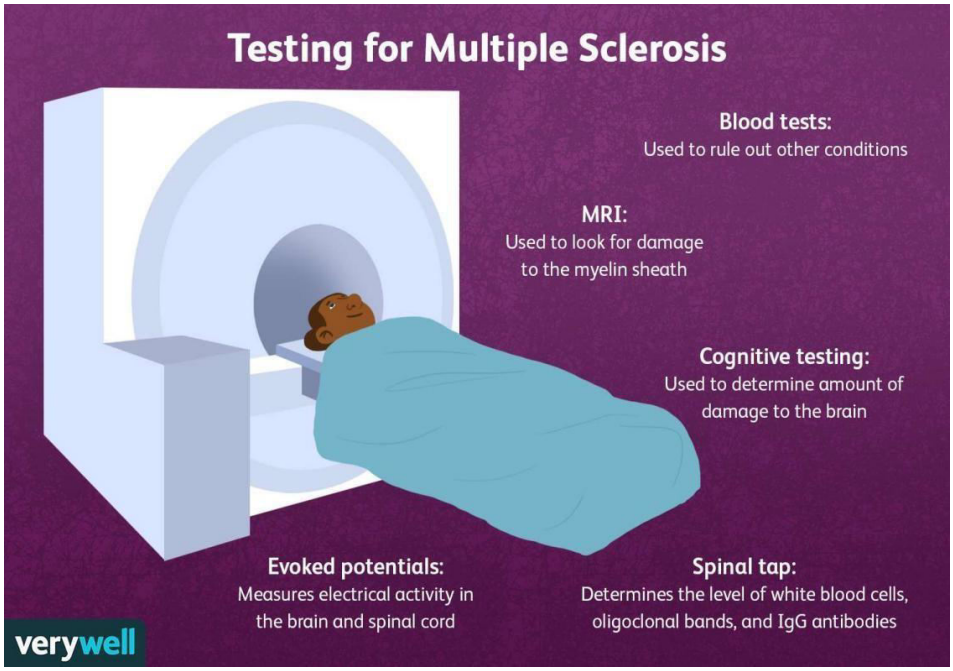

Fig3: multiple sclerosis diagnostic criteria (11)

DIAGNOSIS OF MULTIPLE SCLEROSIS:

MS is a CNS neuroinflammatory and neurodegenerative illness that is immune-mediated. Clinical and neuroimaging studies should, by definition, demonstrate the spread of the illness process both spatially and temporally within the central nervous system. Neuroimaging (MRI) or clinical evidence showing multifocal involvement of the CNS at the indicated sites should be used to confirm dissemination in space (DIS) The presence of recurring attacks or a continuous progression, as well as neuroimaging that demonstrates asymptomatic enhanced lesions on the initial scan or the emergence of additional lesions on follow-up scans, are clinical requirements for dissemination in time (DIT) fulfillment. Lastly, there shouldn't be a more appropriate explanation (no alternative neurologic condition) for the symptoms, signs, and MRI results. When a patient is brought with a suspected MS diagnosis or when imaging or clinical abnormalities raise suspicions about MS in the differential, the first step in diagnosing MS is to get a thorough medical and neurologic history and examination. (12)

Drug therapy for MS:

Dimethyl fumarate and teriflunomide are two novel therapies that are being studied. When dimethyl fumarate is present, proinflammatory Tion of cytokines and the induction of antioxidant Mechanism as a reaction to the cytotoxic impacts of Oxidative damage. A phase III study found that dimethyl Treatment with fumarate decreased MRI activity and the Rate of relapse 11 .Alleged negative consequences Consist of digestive issues, flushing, Hepatic disease with lymphopenia. A mitochondrial enzyme necessary f"r pyrimidine production is reversibly inhibited by teriflunomide, preventing the activation and growth of stimulants.Lymphocytes in latency. In a trial using a placebo control-In a domized experiment, its ability to reduce inflammation was Verified by a lower incidence of recurrence and the Quantity of lesions that enhance contrast in the treated.Hair thinning, nausea, raised liver enzyme levels, and diarrhea are side effects. The primary issue with using teriflunomide is a terato-Genic impact observed in various animal taxa. Women who are of childbearing age must therefore be Prior to use, employ a dependable technique of contraception.Pregnancy attempts should be preceded by a washout period Must be followed for a minimum of six months, or a pro-The expedited drug elimination procedure needs to be Cholestyramine or activated charcoal first Pulverized.(13)

II. CONCLUSION

Over the past few decades, the objectives of treatment for multiple sclerosis (MS) have changed significantly. According to the initial natural history of MS cohorts reported in Lyon, France, and Olmsted County, Minnesota, MS patients become handicapped at roughly the same age regardless of treatment.1-2 As a result, the idea of medical

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futility persisted in the field even after the development of disease-modifying treatments (DMTs)(14).Ms is a chronic neurologic, demyelinating disease that Causes a great amount of disability in those patients Diagnosed with the disease. It typically presents between 20 and 40 years of age and affects a greater number of Women than men. However, 2% to 10% are diagnosed after 50 years of age.(15)

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