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Biochemical Marker OCBs and IgG index roles in the Diagnosis of Multiple Sclerosis at Ali Omar Askar Hospital, Libya 2025

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دور المؤشرات البيوكيميائية، كالأشرطة قليلة النسيلة ومؤشر الغلوبولين المناعي جي، في تشخيص التصلب المتعدد في مستشفى علي عمر عسكر، ليبيا 2025

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Abstract:

Multiple sclerosis (MS) is a chronic autoimmune inflammatory disorder affecting the central nervous system and represents a leading cause of neurological disability in young adults. This retrospective study evaluated the diagnostic value of cerebrospinal fluid (CSF) oligoclonal bands (OCBs) and IgG index in suspected MS patients attending Ali Omar Askar Hospital, Tripoli, Libya, between January and October 2025. A total of 460 clinically suspected patients were assessed using the 2017 McDonald criteria, incorporating magnetic resonance imaging (MRI), CSF OCB analysis, and IgG index measurement. Results showed that 337 patients (73.3%) were confirmed as MS cases, while 123 patients (26.7%) were classified as non-MS neurological disorders. Positive OCBs with elevated IgG index were strongly associated with confirmed MS diagnosis. Female predominance was observed, with 253 females (75.1%) and 84 males (24.9%), giving a female-to-male ratio of approximately 3:1. Monthly variation in case distribution was statistically significant ($\chi^2 = 43.62$, $p < 0.001$). These findings support the important diagnostic role of CSF biomarkers, particularly OCBs and IgG index, when combined with MRI and clinical evaluation. The study also demonstrates that Libyan MS patients exhibit epidemiological patterns similar to global populations. Expanding access to CSF testing and MRI may improve early diagnosis and patient outcomes in Libya.

Keywords: Multiple Sclerosis, MRI, CSF biomarkers (OCBs), IgG index, Neurology, Libya.

الملخص

التصلب المتعدد (MS) هو اضطراب التهابي مزمن مناعي ذاتي يصيب الجهاز العصبي المركزي، ويمثل سببًا رئيسيًا للإعاقة العصبية لدى الشباب. هدفت هذه الدراسة الاسترجاعية إلى تقييم القيمة التشخيصية للأشرطة قليلة النسيلة (OCBs) في السائل النخاعي الشوكي (CSF) ومؤشر IgG لدى المرضى المشتبه بإصابتهم بالتصلب المتعدد والذين راجعوا مستشفى علي عمر عسكر في طرابلس، ليبيا، خلال الفترة من يناير إلى أكتوبر 2025. تم تقييم 460 مريضًا مشتبهًا بإصابتهم سريريًا باستخدام معايير ماكدونالد لعام 2017، والتي تضمنت التصوير بالرنين المغناطيسي (MRI)، وتحليل الأشرطة قليلة النسيلة في السائل النخاعي الشوكي، وقياس مؤشر IgG. أظهرت النتائج أن 337 مريضًا (73.3%) تم تأكيد إصابتهم بالتصلب المتعدد، بينما صُنِّف 123 مريضًا (26.7%) على أنهم يعانون من اضطرابات عصبية أخرى غير التصلب المتعدد. وارتبطت الأشرطة قليلة النسيلة الإيجابية مع ارتفاع مؤشر IgG ارتباطًا وثيقًا بتشخيص التصلب المتعدد المؤكد. لوحظت غلبة الإناث، حيث بلغ عدد الإناث 253 (75.1%) مقابل 84 ذكراً (24.9%)، بنسبة تقريبية 3:1. وكان التباين الشهري في توزيع الحالات ذا دلالة إحصائية ($p < 0.001$). تدعم هذه النتائج الدور التشخيصي المهم للعلامات الحيوية في السائل النخاعي، وخاصة الأشرطة قليلة النسيلة ومؤشر IgG، عند دمجها مع التصوير بالرنين المغناطيسي والتقييم السريري. كما تُظهر الدراسة أن مرضى التصلب المتعدد الليبيين يُظهرون أنماطاً وبائية مشابهة لتلك الموجودة في عموم السكان. وقد يُساهم توسيع نطاق الوصول إلى اختبارات السائل النخاعي والتصوير بالرنين المغناطيسي في تحسين التشخيص المبكر ونتائج المرضى في ليبيا.

الكلمات المفتاحية: التصلب المتعدد، التصوير بالرنين المغناطيسي، المؤشرات الحيوية في السائل النخاعي (OCBs)، مؤشر IgG، علم الأعصاب، ليبيا.

INTRODUCTION

Multiple sclerosis (MS) is a chronic, autoimmune inflammatory disorder that damages the central nervous system (CNS), it is unpredictable disease leading to non-traumatic neurological disability in young and middle age adults between 20 and 40 years. Worldwide, MS affects approximately 2.9 million individuals with around 3-fold more females than males (Peters et al., 2025; Perdaens & van Pesch, 2021; Dobson & Giovannoni, 2019; Orton et al., 2006). Multiple sclerosis characterized by multifocal demyelination, axonal degeneration, and gliotic (scar-like lesions) that compromise the integrity of neural signal transmission between the brain and the rest of the body (Perdaens & van Pesch, 2021; Weiner, 2004). Clinically, MS exhibits a wide range of clinical symptoms that are vary between individuals, and it is including visual impairment, weakness and fatigue, loss of balance, numbness, pain, muscle spasms, bladder dysfunction, mood changes, cognitive impairment which often leads to gradual neurological deterioration and impact overall life quality (Filippi et al., 2018; Klineova and Lublin., 2018). In 1996, the U.S. National Multiple Sclerosis Society (NMSS) formally classified multiple sclerosis into four clinical phenotypes: Relapsing Remitting MS (RRMS) the most common form that affects ~ 85% of MS patients and characterized by episodic relapses followed by periods of remission, Primary Progressive MS (PPMS) affects ~ 10 - 15 % of cases, with continuous neurological decline without relapses, secondary progressive MS (SPMS), and progressive relapsing MS (PRMS) (Klineova & Lublin., 2018; Mathur et al., 2021). The early multiple sclerosis diagnosis permits an early treatment and appropriate control of MS evolution but it requires multiple evidence to confirm it (Brownlee et al., 2017). Neurologists using the McDonald criteria guideline to diagnose multiple sclerosis and rule out other neurological disorders that mimic MS symptoms, this criteria is a combination of physical examination, medical history, brain and spinal cord magnetic resonance imaging (MRI) to determine the lesions dissemination in space or DIS (2 - 5 lesions in different CNS areas including optic

nerve location) as well as dissemination in time or DIT (new lesions over time) (Brownlee et al., 2017; Miller et al., 2008), along with laboratory biomarkers of cerebrospinal fluid (CSF) and blood which indicates CNS inflammation (Dobson et al., 2013; Brownlee et al., 2017). The most sensitive laboratory method to support MS diagnosis is the qualitative detection of oligoclonal IgG bands in cerebrospinal fluid by the isoelectric focusing electrophoresis (IEF) on agarose or polyacrylamide gels followed by immunofixation or immunoblotting, which separated IgG molecules according to their isoelectric points within pH range of 6–9, complemented by the quantitative assessment of intrathecal IgG synthesis using the immunoglobulin G index (IgG index) (Brownlee et al., 2017; Willis et al., 2023; Candeloro et al., 2025; Rommer and Zettl., 2018). In healthy individuals, intrathecal IgG synthesis is negligible, and most IgG detected in the CSF is derived from peripheral blood circulation by crossing the blood brain barrier (BBB). Therefore, its presence alone does not indicate CNS inflammation as it may reflect the serum IgG concentrations and BBB permeability rather than local immunoglobulin production (Petzold, 2013; Simonsen et al., 2020). In contrast, in neuroinflammatory disorders, particularly multiple sclerosis, clonally expanded B cells migrate from the peripheral blood into the central nervous system, where they differentiate into plasma cells and produce Immunoglobulin G locally (intrathecal IgG synthesis), contributing to inflammation and demyelination within the CNS (Simonsen et al., 2020). This process is most reliably evidenced by the presence of oligoclonal bands (OCBs) in the cerebrospinal fluid, which are detected in more than 95% of patients with multiple sclerosis (Thompson et al., 2017). These bands are typically absent in the corresponding serum, thereby constituting a robust marker of intrathecal IgG production (Boufidou et al., 2023; Ziemssen et al., 2019). Oligoclonal band (OCB) patterns are classified into five internationally recognized types based on the distribution of Immunoglobulin G bands in cerebrospinal fluid (CSF) and serum. Among these, type 2 (CSF-restricted bands) and type 3 (CSF-restricted bands with additional identical bands in serum) are indicative of intrathecal IgG synthesis and are strongly associated with Multiple sclerosis (Jin et al., 2023). The presence of two or more CSF-restricted IgG bands is considered a highly sensitive diagnostic marker with 95% sensitivity (Freedman et al., 2005; Thompson et al., 2017). In parallel, the IgG index serves as a quantitative, cost-effective biomarker for evaluating intrathecal IgG production by comparing cerebrospinal fluid (CSF) and serum IgG concentrations normalized to albumin (Willis et al., 2023). An elevated IgG index (> 0.7) reflects a disproportionate elevation of CSF IgG relative to albumin, thereby supporting intrathecal IgG synthesis rather than passive diffusion from the bloodstream; this elevation is observed in approximately 70–80% of cases (Reiber and Peter, 2001; Link and Huang, 2006; Willis et al., 2023). Collectively, OCBs and the IgG index represent a key laboratory indicator of the chronic intrathecal inflammation characteristic of MS, and their integration in the McDonald criteria has significantly improved the MS diagnostic framework for the disease (Candeloro et al., 2025; Willis et al., 2023). According to Samara & Ontaneda 2025, multiple sclerosis diagnostic criteria developed over time from 1965 (Schumacher Criteria), to 1983 (Poser Criteria), then 2001 (Original McDonald Criteria), later during 2005, 2010, and 2017 many updates were made to increase diagnosis sensitivity. The most recent update was the 2024 revision of the McDonald Criteria (published in 2025), which added the optic nerve as a 5th DIS location. All updates were done to enhance the sensitivity and specificity of multiple sclerosis diagnosis (Samara & Ontaneda, 2025; Thompson et al., 2017; Freedman et al., 2005). Recent reports from 2011 to 2021 have highlighted a significant fast increase in multiple sclerosis diagnosis and prevalence in some Libyan neighborhood countries as the Middle East and North Africa (Hassan et al., 2023; Walton et al., 2020; Yamout et al., 2013). On the other hand, despite the high diagnostic value of CSF biomarkers, their utilization in Libya is often limited by cost, technical requirements, and patient reluctance toward lumbar puncture procedures. These barriers can delay diagnosis and treatment initiation, potentially

worsening disease outcomes. Ali Omar Askar Hospital, particularly its neurology department, represents a key center for patients with suspected multiple sclerosis in Libya. Its diagnostic records provide an important resource for MRI results alongside blood and CSF analysis results, thereby improve the understanding of MS diagnosis in this local hospital.

Methods and Materials

Study design

This study was designed as retrospective study based on collected files of patients attended to Ali Omar Askar Hospital, Tripoli, Libya during January to October 2025. The study evaluated the diagnostic value of OCBs and IgG index for MS diagnosis utilizing 2017 McDonald criteria incorporating magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) analysis (oligoclonal bands and IgG index).

Study Population

The study included 460 suspected multiple sclerosis patients attended the neurology department at Ali Omar Askar Hospital, Tripoli, Libya.

Specimen Collection:

Specimens were obtained from the neurology department at Ali Omar Askar Hospital and subsequently transported under strictly controlled conditions to Bioscientia Medical Laboratory in Ingelheim, Germany, where all analyses were conducted in accordance with standardized diagnostic protocols. Upon completion of testing, the neurology department at Ali Omar Askar Hospital received the full set of laboratory results, which were archived for future reference and clinical evaluation. Under aseptic conditions and in line with established clinical procedures, cerebrospinal fluid (CSF) samples were collected by neurologists via lumbar puncture, concurrently with blood sampling, to ensure accurate paired analysis of CSF and serum. Immediately following collection, all specimens underwent careful visual inspection; samples exhibiting gross blood contamination were excluded, whereas clear and colorless specimens were retained for analysis. Uncontaminated samples were then transported to the Germany laboratory under controlled conditions and processed without any delay to preserve protein integrity and ensuring the reliability and validity of analytical outcomes. The gold standard qualitative method used for OCBs detection in CSF and serum samples was the IEF followed by immunofixation which separated IgG molecules and made bands on the agarose gel, this method enabled high resolution discrimination of clonally restricted bands. The quantitative method to support the OCBs results is the IgG index biomarker, this method comparing the CSF/serum IgG ratio against the albumin ratio. Together, these two complementary laboratory methods provide evidence for CNS inflammation and support the diagnosis of multiple sclerosis.

Data Analysis

Data were analyzed using Microsoft Excel 2019, z-test approximation for each month, GraphPad Prism Software with Chi-square test and all $P < 0.05$ were statistically significant. Confidence Intervals (95% CI) were calculated to reflect the precision of this data, enhancing the interpretability of the findings.

Results

From January to October 2025, a total of 460 patients with suspected multiple sclerosis (MS) were enrolled in this study. Magnetic resonance imaging (MRI), oligoclonal bands (OCBs), and IgG index results were reviewed from patients medical records. Among the 460 patients aged between 18–63 years, 73.3% showed positive OCBs (two or more bands detected in CSF compared with serum) together with an elevated IgG index (>0.7), supporting the diagnosis of MS. In contrast, 26.7% were excluded because of negative OCBs and normal IgG index values,

and were classified as having other neurological disorders with symptoms resembling MS (Figure 1).

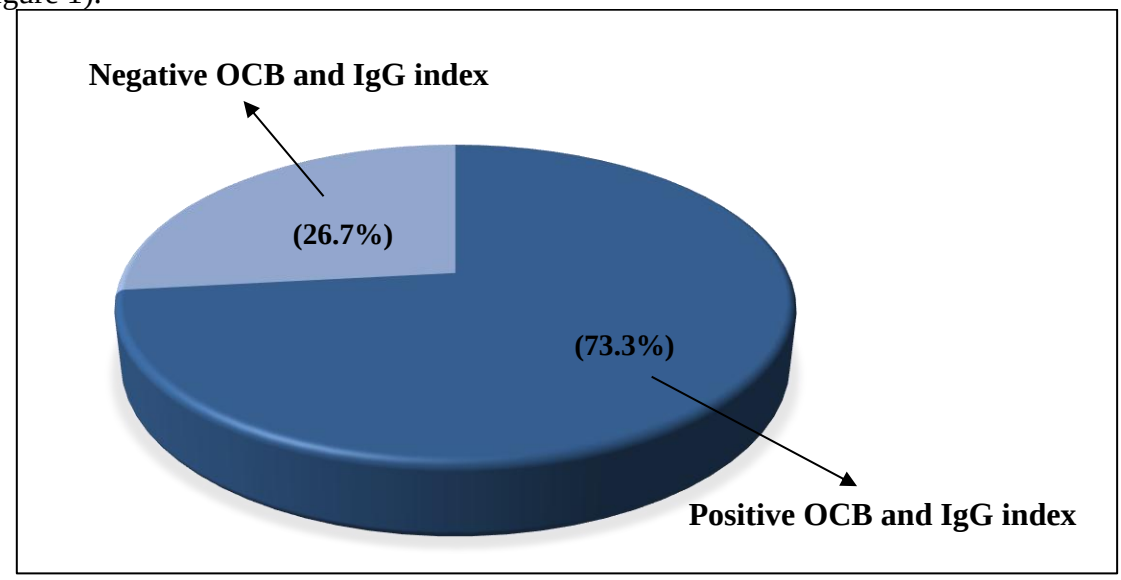

Figure 1: Positive OCB and IgG index cases vs. Negative OCB and IgG index cases.

Among the 337 confirmed MS patients, the highest proportion of cases was observed in 20–40 years age group, accounting for 270 patients. According to the 2017 McDonald criteria which incorporate magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) analysis, including OCBs and IgG index, 337 cases were confirmed as MS while 123 cases were non-MS based on alternative diagnostic criteria than MS during this 2025 ten months study (Table 1). The ratio of confirmed MS to non-MS cases were around 2.7:1, indicating a high proportion of MS diagnoses within this study. All confirmed MS patients 337 (100 %) underwent brain and spinal cord MRI follow up every 6 months when available to assess disease progression and confirm disseminate in space (DIS) nor in time (DIT). Overall, the proportion of confirmed MS cases was 73.3 % (95% confidence interval = 95% CI), reflecting a high MS diagnostic yield within this study.

Table 1: Total multiple sclerosis and non- multiple sclerosis cases 2025

Total suspected MS	MS cases	MS %	non-MS	non-MS %
460	337	73.3 %	123	26.7%

This statistical analysis confirmed that the distribution of MS versus non-MS cases was highly significant ($p < 0.0001$). This negligible p-value indicates that the observed diagnostic distribution is representative of the cohort's clinical characteristics and is effectively zero probability to have occurred due to stochastic variation (random chance) alone. These 337 multiple sclerosis cases showed a variable monthly distribution throughout 2025 ten months study period comparing to the other neurological conditions (non-MS), revealed substantial variability in diagnostic yield (Figure2).

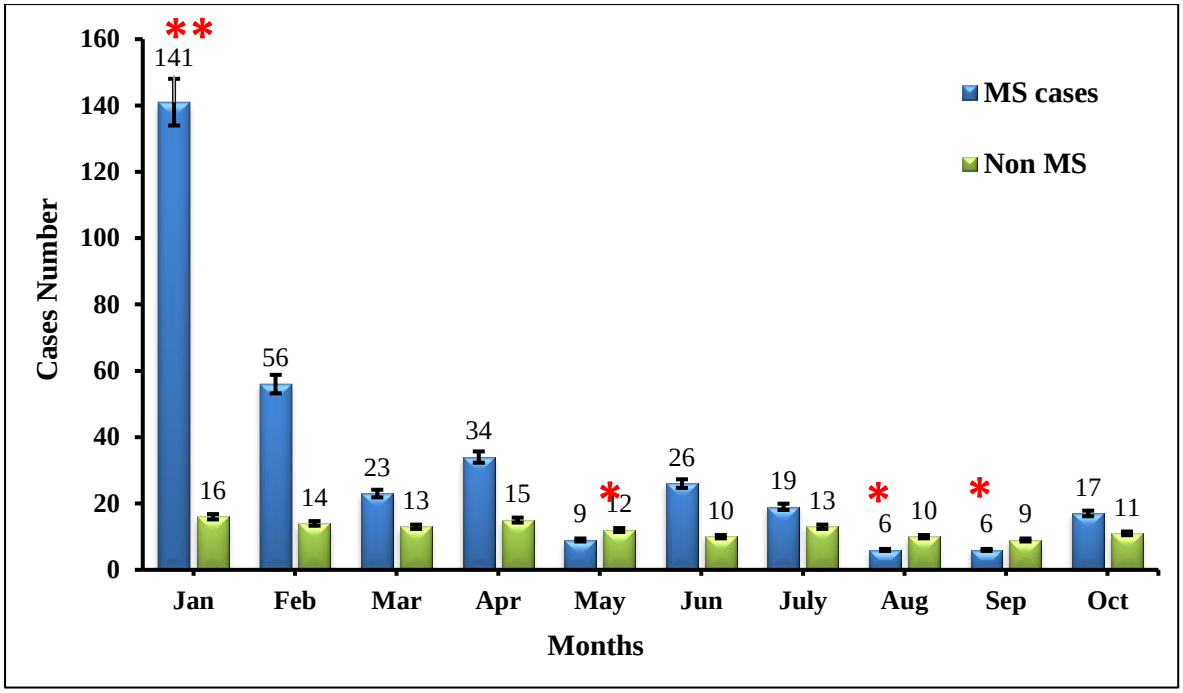

Figure 2: Monthly distribution of multiple sclerosis vs. non MS.

The monthly distribution of cases among patients with Multiple Sclerosis demonstrated variability in diagnostic proportions when compared to the overall MS prevalence of 73.3%. January showed a significantly higher proportion of MS cases (89.8%, $p < 0.00001$), representing the peak diagnostic period. In contrast, significantly lower proportions were observed in May (42.9%, $p = 0.0017$), August (37.5%, $p = 0.0012$), and September (40.0%, $p = 0.0036$). Other months, including February, March, April, June, July, and October, did not show statistically significant deviations from the overall rate ($p > 0.05$). Overall, despite these temporal fluctuations, the dataset maintained a high MS burden with a ratio of approximately 2.7:1 (MS to non-MS). Additionally, the overall distribution across months remained statistically significant ($\chi^2 = 43.62$, $p < 0.001$), indicating a non-random temporal variation in MS diagnosis (Table 2).

Table 2: Distribution of MS and non-MS cases from Jan to Oct 2025

Month	Total	MS cases	Non-MS	MS %	p-value	Significant
Jan	157	141	16	89.8%	$p < 0.00001$	Highly significant **
Feb	70	56	14	80.0%	$p \approx 0.20$	Not significant
Mar	36	23	13	63.9%	$p \approx 0.20$	Not significant
Apr	49	34	15	69.4%	$p \approx 0.54$	Not significant
May	21	9	12	42.9%	$p \approx 0.0017$	Significant *
Jun	36	26	10	72.2%	$p \approx 0.89$	Not significant
July	32	19	13	59.4%	$p \approx 0.076$	Borderline
Aug	16	6	10	37.5%	$p \approx 0.0012$	Significant *

Sep	15	6	9	40.0%	$p \approx 0.0036$	Significant *
Oct	28	17	11	60.7%	$p \approx 0.13$	Not significant
Total	460	337	123	73.3 %	-	-

Gender distribution analysis revealed a clear predominance of females among multiple sclerosis patients with female to male ratio of approximately 3:1, where was among the 337 patients with multiple sclerosis showed that 253 (75.1%) were females and 84 (24.9%) were males. This difference was statistically highly significant ($\chi^2 = 84.8$, $p < 0.0001$), indicating a strong female predominance (Figure 3).

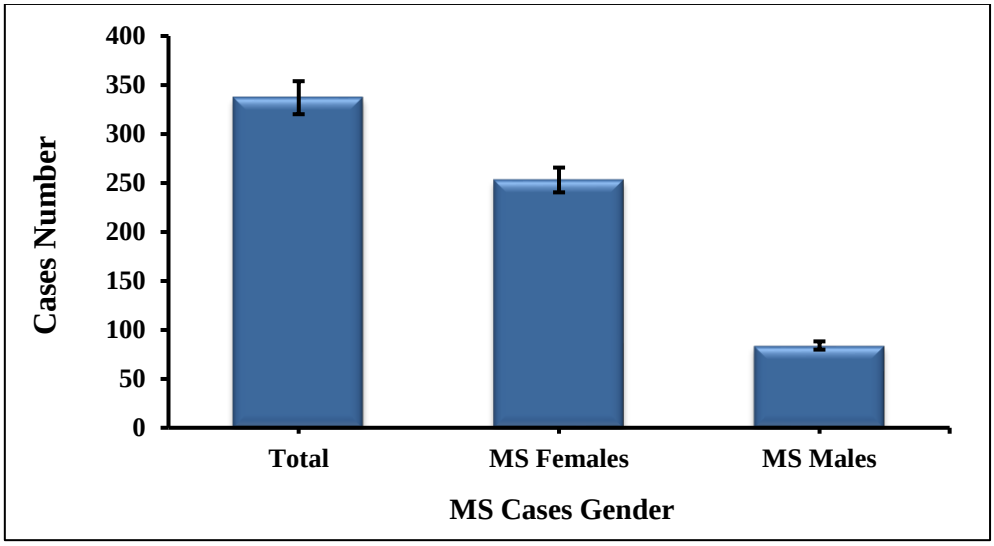

Figure 3: Multiple sclerosis females and males 2025.

Figure 4 shows the highest numbers of confirmed cases for both sexes were observed during the early months of the study, particularly in January, February, and April, where females consistently representing higher case numbers than males during these peak periods. A gradual decline in total case numbers was noted toward the later months; however, female predominance remained stable throughout the ten-month study period, even during months with reduced diagnostic activity such as June and August.

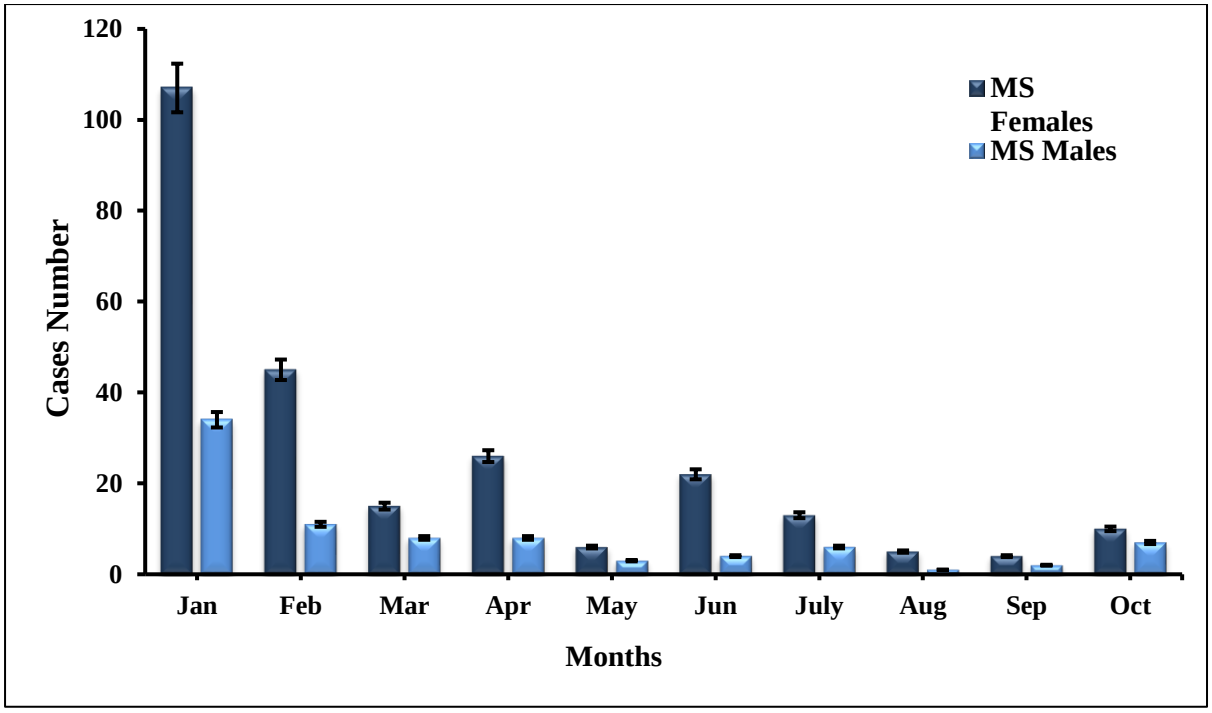

Figure 4: Monthly multiple sclerosis females and males.

Table 3 demonstrated that the sustained female to male disparity across all months is consistent with the global epidemiological patterns of multiple sclerosis with predominant women than men.

Table 3: Monthly gender distribution among total confirmed MS cases

Month	MS cases	MS Females	MS Males
Jan	141	107	34
Feb	56	45	11
Mar	23	15	8
Apr	34	26	8
May	9	6	3
Jun	26	22	4
July	19	13	6
Aug	6	5	1
Sep	6	4	2
Oct	17	10	7
Total	337	253	84

Overall, the findings suggested that Libyan MS cases demonstrate epidemiological characteristics similar to those observed in other regions around the world. Therefore, this study offers important implications for multiple sclerosis, and indicates the need for more awareness raising, early detection of MS, and establish support services for women since they form the majority of the MS patient.

Discussion

The present study evaluated the diagnostic utility of cerebrospinal fluid (CSF) biomarkers, specifically oligoclonal bands (OCBs) and IgG index, in patients with suspected multiple

sclerosis (MS) attending Ali Omar Askar Hospital, Tripoli, Libya. Using the 2017 McDonald criteria in conjunction with clinical assessment, magnetic resonance imaging (MRI), and laboratory findings, 337 of 460 suspected cases (73.3%) were confirmed as MS. These findings support the continued value of integrating radiological and immunological evidence in the diagnostic workup of patients presenting with demyelinating disease (Thompson et al., 2017; Brownlee et al., 2017). The high proportion of confirmed MS cases with positive OCBs and elevated IgG index is consistent with the established role of intrathecal immunoglobulin G synthesis in MS pathogenesis. OCBs remain one of the most sensitive supportive biomarkers for MS and are very useful when MRI findings are equivocal or when dissemination in time is not demonstrated. Likewise, the IgG index provides quantitative evidence of the central nervous system immune activation and may strengthen diagnostic confidence when interpreted alongside OCB results. Previous studies have shown that combining qualitative and quantitative CSF markers can improve the overall MS diagnosis, especially during early disease stages (Link & Huang, 2006; Simonsen et al., 2020; Willis et al., 2023). A total of 123 patients (26.7%) were classified as non-MS cases, highlighting the importance of differential diagnosis in patients with neurological symptoms similar to MS, because several neurological disorders may mimic MS symptoms, including inflammatory, vascular, infectious, metabolic, and autoimmune disorders. Therefore, careful use of McDonald diagnostic criteria is essential to reduce misdiagnosis and avoid the long-term immunomodulatory therapy (Solomon et al., 2016; Dobson & Giovannoni, 2019). An important age observation in this study was that 80% of the affected patients were 20 - 40 years. This age distribution is consistent with the recognized epidemiology of MS as a disorder that most commonly affects young adults during their economically and socially productive years. Early disease within this age group causes long-term implications for quality of life, employment status, family responsibilities. Therefore, timely diagnosis and early therapeutic intervention are particularly important in this population (Dobson & Giovannoni, 2019; Peters et al., 2025). Monthly analysis showed significant variation in confirmed MS diagnoses during the study period. January recorded the highest number of confirmed cases, whereas lower rates were observed in May, August, and September. These differences may be related to seasonal healthcare attendance, referral patterns, environmental influences, vitamin D status, or infection-related relapse activity. Similar seasonal trends have been reported in previous MS studies (Simpson et al., 2011; Ascherio & Munger, 2016). Female predominance was clearly observed, with women representing 75.1% of confirmed cases and a female to male ratio of approximately 3:1. This result is consistent with international epidemiological data showing that MS affects females more frequently than males. Hormonal factors, immune response differences, and genetic susceptibility may contribute to this pattern (Harbo et al., 2013; Wallin et al., 2019). This study at Ali Omar Askar Hospital, neurology department is important because Libyan MS data is limited. The current findings suggest that Libyan MS patients share similar clinical and demographic characteristics (age, gender) with patients reported worldwide. This highlights the need for greater awareness, earlier diagnosis, and improved the hospitals radiology and laboratory systems. In conclusion, OCBs and IgG index are valuable biomarkers that significantly support MS diagnosis when combined with MRI and clinical assessment. Expanding access to these diagnostic tools may improve early detection, treatment decisions, and patient outcomes in Libya.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

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