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The Impact of Migration on the Risk of Developing Multiple Sclerosis: A Literature Review from 1962 to 2022

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Abstract

Introduction: Multiple sclerosis is a multifactorial disease, with many factors still unknown to this day. Studies on migrants play a significant role in the epidemiological and etiological research of this condition. **Objective:** This paper aims to study the impact of migration on the risk of developing multiple sclerosis. **Methodology:** A narrative review of the literature based on 80 articles retrieved from PubMed, Web of Science, Google Scholar, and ScienceDirect databases, using the following keywords: "multiple sclerosis", "migration", "migrants," and "immigrants", published from 1962 to 2022. **Results:** This review suggests that migration is a risk factor for multiple sclerosis. It supports the existence of an "age at migration" effect and highlights the particular role of environmental factors. The trend also points to an increased risk for second-generation immigrants compared to initial studies. **Conclusion:** Concepts regarding migrants and the risk of developing multiple sclerosis have evolved significantly over the past three decades. The older theory that those migrating after age 15 retain the risk of their country of birth is now less widely accepted, especially in cases of migration to high-prevalence regions, as they may influence future disease risk even into adulthood.

Keywords

Multiple Sclerosis, Migration, Migrants

1. Introduction

Multiple sclerosis (MS) is a chronic autoimmune inflammatory demyelinating

disease of the central nervous system, affecting approximately 2.8 million people worldwide [1]. MS is an increasing condition, with global prevalence rising from 33 per 100,000 in 2013 to 36 per 100,000 in 2020 [1]. Its distribution is not uniform and is characterized by a North-South gradient, with countries farther from the equator having the highest risk (**Figure 1**). For instance, the prevalence of MS exceeds 100 per 100,000 inhabitants in North America and Europe but remains low in East Asia, the Middle East, and sub-Saharan Africa [2].

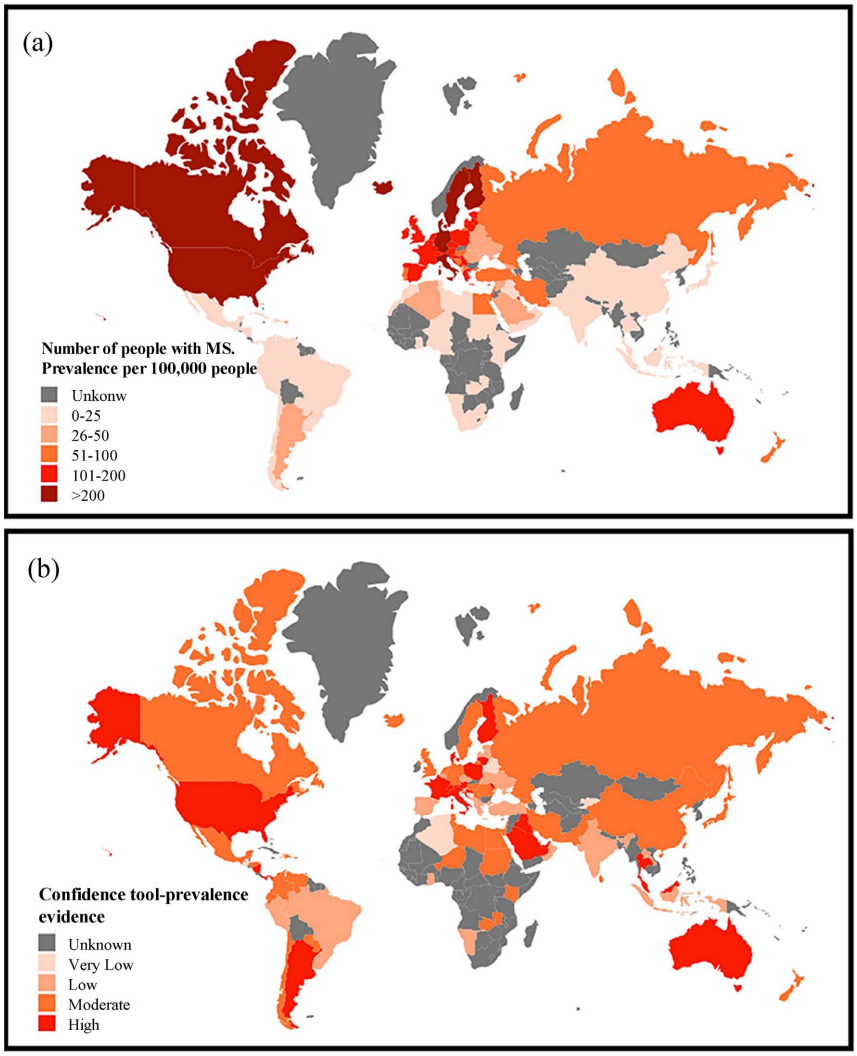

Figure 1. Map showing geographic variation in MS prevalence and in data confidence scores by country [4]. (a) MS prevalence per 100,000 population in 2020 by country shown in shades of orange and red as per the key. Countries without prevalence data are shown in grey. (b) Confidence score assigned to each country based on the prevalence data sources provided. Scores of very low, low, moderate or high are shown in shades of orange and red as per the key. Countries without prevalence data or with data but no source information provided are shown in grey.

In France, MS is estimated at 160 per 100,000 inhabitants, with a Northeast-Southwest gradient. About 5000 new cases are diagnosed each year. It is the

leading cause of non-traumatic disability in young adults [2]. MS predominantly affects women (with a sex ratio of 1:3) in its relapsing-remitting form, which accounts for 85% of patients and usually manifests between the ages of 25 and 35. The primary progressive form of the disease affects 15% of patients, with onset around age 40, similar to the age at which relapsing-remitting MS may convert to secondary progressive MS [2]. MS significantly impacts the quality of life of affected individuals and their families and has a societal impact due to its substantial cost [1].

It is widely accepted that MS has a multifactorial origin, involving interactions between exogenous environmental factors—such as sun exposure, vitamin D deficiency, viral infections, hygiene, smoking, and obesity—and endogenous genetic factors [2] [3]. However, many contributing factors remain unknown. Studies on migrants offer the opportunity to analyze the environmental and genetic contributions to the origin of diseases, making them an essential component of the epidemiological and etiological research on MS. Thus, the objective of our study was to draw up the current state of research on the impact of migration on the risk of developing MS.

2. Methodology

This study involved a narrative review of all research on multiple sclerosis (MS) and migration published between 1962 and 2022. We searched the following data sources: PubMed, Web of Science, Google Scholar, and ScienceDirect, using the keywords: "multiple sclerosis", "migration", "migrants", and "immigrants". Our eligibility criteria included studies published within the specified time frame, with no restriction on patient age, and published in English or French.

We excluded studies where full-texts were unavailable, such as conference abstracts, editorials, and short communications. Additionally, we excluded studies published in languages other than English or French, duplicates, and those that provided only general discussions on MS without presenting empirical data. Our process of inclusion of articles followed four steps:

- Step 1: All studies found after exploring the different databases using keywords were included. There were 122 of them.

- Step 2: The 122 articles obtained were exported to the Zotero bibliographic reference management software version 4.0.28.3 where we proceeded to the automatic exclusion of duplicates, 13 in number.

- Step 3: Articles were screened for eligibility based on the relevance of the title and abstract by at least three authors blinded using the Rayyan software. Those that met one of the exclusion criteria were deleted and any conflicts were resolved by consensus during a meeting at which titles and abstracts were reviewed. The remaining articles were re-examined by at least two authors and conflicts were resolved as before. When an article was not available online, a written request was made to the corresponding author in order to obtain it. During this stage, 16 articles were excluded (language: 5, off-topic: 4, full text unavailable: 7) and 93

articles remained eligible.

- Step 4: After reviewing the full texts of the 93 articles, we further excluded those that presented only a general discussion on MS without providing empirical data, and therefore deemed irrelevant to our research focus. This selection process resulted in the inclusion of 80 articles.

The data collection tool was a standardised sheet, digitised on KoboCollect, which included the following information when available: publication references, sample size, age at migration, sex, country of origin, host country, MS prevalence, incidence, relative risk, EDSS score and MS-related mortality.

Data entry was carried out on the KoboToolbox platform. through the KoboCollect Android version application, then they were exported to an Excel file for cleaning. The analysis of the data collected was done with the R software version 4.2.1. The qualitative synthesis of the results was carried out as part of a narrative review.

3. Results

a) Concept of an "Age at Migration" Effect

A number of pioneering studies on migrants have suggested that the risk of developing MS is largely determined before the age of 15 [5]-[9], or at least during the first two decades of life [10]. Studies conducted by Dean and Kurtzke [8] as well as Alter [5]-[7] reported that the incidence of MS changed in individuals who migrated from a high-prevalence country to a low-risk country.

This phenomenon was first observed in South Africa, where the prevalence of MS was low among Afrikaners, higher among European immigrants, and intermediate among Anglo-South Africans [8] [11]. The population at risk, based on the age of immigration, was estimated using two indirect methods: census data from 1960 and surveys on the at-risk population in 1968-1969. Both studies suggested that the risk of developing the disease was reduced to less than one-third of the expected risk for those who immigrated before the age of 15 or 16. Indeed, immigrants from Northern Europe, where MS was common, who changed their residence before the age of 15, had a lower risk of disease, reflecting the incidence rate of South Africans born in the country. It was suggested that MS risk factors primarily exert their influence during childhood and adolescence [8] [11]. Similarly, for Jewish populations emigrating to Israel, the risk of contracting the disease was determined before the age of 15 [7].

In 1995, the systematic review by Gale and Martyn [12] identified two consistent patterns from various migrant studies: individuals who moved from a region where MS is common to a region where it is rarer showed a decrease in the disease rate. Conversely, those who migrated in the opposite direction tended to retain the low risk of their country of origin. Regarding the age of migration, they concluded that the risk of developing MS was largely determined during the first two decades of life.

Alongside these theories, other researchers such as Detels *et al.* [13], Kurtzke

and Hyllested [14] [15], Fischman [16], and later Hammond *et al.*, based on surveys from 1987 and 2000 [17] [18] concerning immigrants from the UK to Australia, hypothesized that the risk of developing MS, rather than being predominantly determined by age 15, actually spans a much broader period and is not confined solely to childhood and young adulthood.

b) Migration: A risk Factor for Multiple Sclerosis

The work of Philippe Cabre [19] [20] highlighted the role of return migration in the emergence of MS in the French Antilles, a population that includes a large number of Antilleans who returned to Guadeloupe and Martinique after emigrating to mainland France. A prospective demographic study on the prevalence and incidence of MS was conducted from January 1, 1998, to December 31, 2004, using the McDonald diagnostic criteria and examining migration as a risk factor for the disease.

The prevalence of MS among the population aged 15 to 64 as of December 31, 1999, was twice as high among migrants compared to non-migrants. Migration to mainland France before the age of 15 increased the risk of the disease fivefold compared to migration after the age of 15. Furthermore, the annual incidence from July 1997 to June 2002 was higher among migrants, and residence in mainland France before the age of 15 increased the incidence rate compared to residence that began after this age.

In 2019, Nielsen [21] examined the effects of MS among first- and second-generation immigrants in Denmark. This cohort included 9,121,187 individuals living in Denmark, of which 1,329,089 were foreign-born, including 1,176,419 with two foreign-born parents (first-generation immigrants), and 7,792,098 Danish-born individuals, 184,282 of whom had two foreign-born parents (second-generation immigrants). The study compared the relative risk of MS between first-generation immigrants, second-generation immigrants, and ethnic Danes.

First-generation immigrants consistently had a higher MS risk compared to their country of origin, but this risk remained generally lower than that of ethnic Danes (RR = 0.49; 95% CI: 0.45 - 0.53). Within this group, the risk of MS was 54% higher for those who arrived in Denmark before the age of 15 compared to those who arrived at an older age (RR < 15/RR ≥ 15 = 1.54; 95% CI: 1.20 - 1.98). After adjusting for the country of birth, first-generation immigrants who arrived in Denmark before the age of 15 were 1.8 times more likely to develop MS (RR < 15/RR ≥ 15 = 1.79; 95% CI: 1.38 - 2.31).

Additionally, second-generation immigrants had a 28% higher overall risk of MS (RR = 1.28; 95% CI: 1.06 - 1.56) compared to ethnic Danes. Other studies also show an increasing trend of higher MS risk among second-generation immigrants [22] [23] compared to earlier surveys [24] [25]. The characteristics of several studies on MS and migration are summarized in **Table 1** and **Table 2**.

c) Current Concepts on Migrant Risk

Migration from a High-Risk to a Low-Risk Area

The recent re-evaluation of Australian immigration data by Hammond *et al.* in 2011 [26] and 2012 [27] aligns with the conclusions of most earlier studies.

Migrants from high-risk areas who moved to low-risk areas before the age of 15 are significantly less likely to develop multiple sclerosis (MS) compared to those who migrate at an older age. This contradicts their earlier findings [17] [18], which they now consider incorrect. Their updated results clearly show a significant reduction in MS risk for migrants arriving in Australia before the age of 15, reaffirming the concept of an "age at migration" effect, consistent with contemporary studies. Furthermore, the authors support the idea that MS is not only an acquired disease but also that for residents or migrants from high-risk areas, it is primarily acquired between the ages of 11 and 15. There is a latency period of approximately 15 to 20 years before the clinical onset of the disease [10]. This reinforces the importance of early-life environmental exposure in determining MS risk.

Table 1. Studies on multiple sclerosis and migration between countries from 1962 to 1980.

Authors	Country or region of origin	Host country	Mesure of disease frequency or disability	Rate in origin country	Rate in host country	Rate in migrants
Alter *et al.* (1962)	Northern and central Europe	Israel	Prevalence per 100,000		4	30 - 51
Alter *et al.* (1962)	Southern Europe	Israel	Prevalence per 100,000		4	9 - 18
Alter *et al.* (1962)	North Africa	Israel	Prevalence per 100,000		4	6
Sutherland *et al.* (1962)	UK and Ireland	Australia	Prevalence per 100,000	60	9 in Australian-born	15
Sutherland *et al.* (1966)	Northern Europe	Australia	Prevalence per 100,000	60		16.3
Rischbieth (1966)	UK	South Australia	Prevalence per 100,000		37.6 in Australian-born	37
Rischbieth (1966)	Southern Europe	South Australia	Prevalence per 100,000	45		17
Dean (1967)	UK	South Africa	Prevalence per 100,000	44 and 63	6.9 in SA-born whites (Age-standardised)	40.9 (Age-standardised)
Dean (1967)	UK	South Africa	Incidence per 100,000	2.8	0.4 in SA-born whites (Age-standardised)	2.8 (Age-standardised)
Dean (1967)	Europe	South Africa	Mortality per 100,000		0.2 in SA-born whites	1.7
Alter *et al.* (1971)	Northern Areas	Hawaï	Prevalence per 100,000		9.9 in whole population	17.1 in all migrants
Kurtzke *et al.* (1971)	Ireland	USA	Mortality per 100,000	2.8		2.9
Kurtzke *et al.* (1971)	Germany	USA	Mortality per 100,000	2.3		1.6
Kurtzke *et al.* (1971)	Austria	USA	Mortality per 100,000	2.2		2.3

Continued

Kurtzke *et al.* (1971)	Italy	USA	Mortality per 100,000	0.7		1
Kurtzke *et al.* (1971)	Mexico	USA	Mortality per 100,000	0.1		0.5
Dean *et al.* (1976)	Europe	UK	Numbers admitted to hospital in Greater London with first diagnosis of MS		158.1 cases	152 cases
Dean *et al.* (1976)	Old Commonwealth	UK	Numbers admitted to hospital in Greater London with first diagnosis of MS		24.8 cases	17 cases
Dean *et al.* (1976)	New Commonwealth Africa	UK	Numbers admitted to hospital in Greater London with first diagnosis of MS		25.8 cases	4 cases
Dean *et al.* (1976)	New Commonwealth America	UK	Numbers admitted to hospital in Greater London with first diagnosis of MS		130 cases	16 cases
Dean *et al.* (1976)	West Indies	UK	Numbers admitted to hospital in Greater London with first diagnosis of MS		101.2 cases	11 cases
Kurtzke *et al.* (1980)	Vietnam	France	Cumulative risk per 100,000	3		74

Table 2. Studies on multiple sclerosis and migration between countries from 1987 to 2022.

Authors	Country or region of origin	Host country	Mesure of disease frequency or disability	Rate in origin country	Rate in host country	Rate in migrants
Hammond *et al.* (1987)	England	Australia	Prevalence per 100,000	127	17.8 (Queensland) and 27.6 (Perth) in Australian-born (Age-standardised)	26.1 (Queensland) and 44.1 (Perth) (Age-standardised)
Hammond *et al.* (1987)	England	Australia	Incidence per 100,000		0.9 (Queensland) in Australian-born (Age-standardised)	1.09 (Queensland) (Age - standardised)
Elian and Dean (1993)	West Indies	UK	Numbers of MS deaths and expected numbers using England and Wales rates as standard		59.2	12
Dean and Elian (1997)	India and Pakistan	England	Migrants < 15 years old with MS compared to expected		19.8	36
Hammond *et al.* (2000)	England	Australia	Prevalence per 100,000	127	27.6 (Perth) and 69.7 (Hobart) in Australian-born (Age-standardised)	44.1 (Perth) and 141.1 (Hobart) (Age-standardised)
Hammond *et al.* (2000)	Overseas-born (high risk areas of Europe)	Australia	Incidence per 100,000		1.28 (Perth) 3.6 (Hobart) and 2.38 (Newcastle) (Age-standardised)	1.54 (Perth) 4.16 (Hobart) and 1.57 (Newcastle) (Age-standardised)
Cabre *et al.* (2004)	West Indies	France	Prevalence per 100,000		14.8 (11.9 - 17.7)	36.1 (26.3 - 45.9)
Cabre *et al.* (2004)	West Indies	France	Prevalence per 100,000		14.8 (11.9 - 17.7)	95.8 (56.6–135) in migrants <15 years old
McLeod *et al.* (2011)	UK	Australia	Relative risk of MS per 100,000			22.3 (16.9 - 29.0) migrants <15 years old against 45.3 (39.2 - 52.0) for migrants >15 years old

Continued

Barnett *et al.* (2016)	UK	Australia	Prevalence per 100,000	68.21 (55.4 - 83.04) among Australian-born residents of Hobart	185.31 (113.192 - 86.19)
Nasr *et al.* (2016)	Iran	Canada	Prevalence per 100,000	240	433
Nielsen *et al.* (2019)	Overseas-born	Denmark	Relative risk of MS		RR < 15/RR ≥ 15 = 1.79
Belgin Petek *et al.* (2022)	Overseas-born migrants > 15 years old	Turkey	EDSS Score	2.07 ± 1.42	1.92 ± 1.67

4. Migration from an Intermediate-Risk Area to a High-Risk Area

A study on North African immigrants in France [28] suggested that migrants from an intermediate-risk area moving to a high-risk region for multiple sclerosis (MS) require approximately three years of exposure between the ages of 11 and 45, followed by an average interval of ten years before the clinical onset of the disease. Moreover, these migrants tend to have a significantly higher prevalence of MS compared to the native population in the high-risk region, in line with the findings of two recent surveys [22] [29]. This indicates that migration from an intermediate-risk area to a high-risk area can increase the risk of developing MS [30].

5. Migration from a Low-Risk Area to a High-Risk Area

The systematic review by Gale and Martyn [12], which suggested that individuals migrating from a low-risk MS region to a high-risk area tend to retain the low risk of their country of origin—contrary to their children, who adopt the higher risk of the host country—new concepts have emerged. Contemporary studies [21] [31] report that migrants from low-risk areas to high-risk areas exhibit a higher prevalence of MS than in their country of origin, but still lower or equal to that of the host country. Second-generation immigrants typically reach a risk level similar to or even higher than that of the native population in the high-risk area.

Ahlgren *et al.* [31] compared MS prevalence among immigrants in Sweden to that of their countries of origin and found that immigrants from India, China, and Romania had a higher prevalence of MS than in their home countries, though still lower or comparable to that in Sweden.

6. Comments

Our study has some limitations, as we are analyzing results from various works that may be subject to information, selection, or sampling biases. Nevertheless, this review allows us to assert that migration is a risk factor for multiple sclerosis (MS). Migration, whether from a low-risk area to a high-risk area or vice versa, generally involves transitioning from one environment to another. Not only does the geographical location change, but the social and cultural context is often

significantly different from that of the country of origin. This shift can alter the exposure status of first- and second-generation immigrants to certain environmental factors considered relevant to the risk of MS [21].

The review supports the existence of an "age at migration" effect on the risk of developing MS, with the critical age being around 15 years [5]-[9]. Populations migrating before the age of 15 from high-risk areas tend to acquire the low-risk status of the country to which they migrate, while those migrating after the age of 15 tend to retain their high-risk status [18]. Conversely, migrants younger than 15 moving from a low-risk region to a high-risk region tend to acquire the higher risk of developing MS compared to those who migrate at an older age [9].

This evidence highlights the complex interaction between environmental factors, age, and migration, reinforcing the idea that early-life exposure plays a crucial role in determining the long-term risk of MS. Further studies are needed to explore the underlying mechanisms and to clarify the specific environmental triggers involved in this process.

We therefore support the theory that individuals migrating after the age of 15 tend to retain the risk level of their country of birth, whereas those migrating before this age acquire the risk level of their host country, particularly when moving from a high-risk area for MS to a low-risk area. The "age at migration" effect in the opposite direction—migration to a high-risk region—is more debatable, especially for those migrating after the age of 15. Danish [21] and Canadian [32] studies have shown that migration from a low-risk country to one with a high prevalence of MS can influence the future risk of the disease even into adulthood, although the change in risk is more pronounced during childhood.

This is corroborated by recent studies in Norway, another high-prevalence country, which report that some groups of first-generation immigrants from non-Western countries had a higher risk of MS than in their countries of origin, even though most immigrants moved to Norway after the age of 15 [22] [33].

The impact of migration on the risk of developing MS has been extensively studied in the literature. In general, migration from high-risk regions to low-risk regions reduces the overall risk of MS in individuals under the age of 15, but the effect on prevalence is less consistent when migrating from low-risk to high-risk areas [34].

As for second-generation immigrants, study of Nielsen [21] reported that they had an overall risk of MS that was 28% higher than ethnic Danes. These immigrants had two foreign-born parents in countries where the prevalence of MS was low (≤5 per 100,000), intermediate (>5 - 60 per 100,000) and high (>60 per 100,000). The increased risk in this group could be explained by the fact that the children of migrants were born locally and grew up in Denmark, a country at high risk of MS, coupled with their parents' age at immigration and individual genetic susceptibility.

In all cases, these studies point to the particular role of several environmental factors—whether protective or harmful—that influence the risk of MS, with a

stronger effect before the age of 15. Philippe Cabre observed that local environmental changes and lifestyle alterations have led to underexposure of populations in the Antilles to factors that could potentially prevent MS [35]. This further emphasizes the importance of early-life environmental exposure in modulating disease risk.

a) Low Sun Exposure and Vitamin D Deficiency

The example of the French Antilles demonstrates that younger generations are less exposed to the sun due to recent phenomena such as urbanization, the gradual abandonment of traditional housing, and the shift from an agricultural economy to a service-based one [35]. Regarding the role of vitamin D, an inverse association has been found between neonatal 25(OH)D concentrations and the risk of multiple sclerosis (MS) [36]. Neonatal vitamin D levels below 30 nmol/L are associated with an increased risk of MS, and a 25 nmol/L increase in neonatal 25(OH)D reduces the risk of the disease by 30%, suggesting that in utero vitamin D deficiency may be relevant to MS risk [36], underscoring the importance of supplementation during pregnancy.

The reduction in disease risk for individuals with 25(OH)D levels ≥ 100 nmol/L is significantly stronger before the age of 20 than in those aged 20 or older [37]. Therefore, a combination of low sun exposure, pigmented skin [38], and certain lifestyle factors—such as wearing long-sleeved clothing in summer and low consumption of fatty fish [39]—may increase the risk of vitamin D deficiency among non-Western immigrants in Nordic countries, potentially altering their risk of developing MS.

b) Hygiene

The hygiene hypothesis suggests that an infectious agent acquired during childhood may have a protective role against autoimmune diseases such as MS [40] [41], and conversely, that this agent becomes a risk factor if contracted in adulthood. This theory may explain the apparent protection against MS observed in individuals born in low-prevalence areas [42], the tendency for MS patients to experience childhood viral infections later in life compared to healthy controls [43], and the lower risk of MS in individuals exposed to younger siblings early in life [44]. It may also account for the higher incidence rate of MS among individuals with higher socio-economic status [19] [45], though there is some controversy surrounding this association [46].

In this context, improvements in hygiene in recent years and the lack of exposure to certain pathogens during childhood could explain the increased immune reactions to benign allergens later in life, as well as the rising frequency of allergies and autoimmune diseases. This idea supports the notion that early-life microbial exposure plays a crucial role in the development of the immune system and the prevention of autoimmune conditions such as MS [2].

c) Eradication of Intestinal Parasites

The protective role of parasites is suggested by several studies [47]-[49], including research by Cabre, which reports that the eradication of helminth

infections—through targeted anti-vector measures and improved hygiene, such as access to clean water—coincided with the emergence of MS in the French Antilles. This region had previously been endemic for intestinal multiparasitism, particularly schistosomiasis, among children under 15 years of age [20] [35]. The decline of parasitic infections may have disrupted the immune-regulatory benefits these infections provided, contributing to the rise of autoimmune diseases like MS in this population.

d) Epstein-Barr Virus Infection

The hypothesis of a transmissible factor was first proposed by Kurtzke [14] in the Faroe Islands, where the first MS epidemic in 1943 was observed in an isolated population previously free of the disease, following contact with British occupation forces during World War II. Post-war events were seen as subsequent transmissions to consecutive cohorts of Faroese people. The pathogen, introduced by the British troops, was believed to cause a "primary MS infection", a widespread and persistent infection that rarely leads to clinical disease until years later [50]. This condition could be similar to "the multiple sclerosis trait", later described by Charles Poser, and which would occur either from viral infections or from certain antiviral vaccinations [51]. Similarly, Philippe Cabre suggested that return migration may have introduced environmental infectious factors acquired in France to the Antilles, contributing to the acquisition of MS, particularly before the age of 15 [19] [20]. Return migrants may have allowed the disease to emerge in the non-migrant population through contamination, as seen in the Faroe Islands model. As for the nature of this pathogen, Ascherio *et al.* [42] speculated that the Faroese were likely infected with Epstein-Barr Virus (EBV) before 1940, but it is possible that the British troops introduced a new strain of EBV linked to MS. Similarities between the epidemiology of MS and mononucleosis have been noted for decades. Both diseases primarily affect young adults, follow a similar latitude gradient, and are rare in populations where children are infected with EBV at an early age [52]. MS and mononucleosis tend to occur earlier in life among women than men, are more common among individuals of higher socioeconomic status [19] [45], and are less frequent among Black and Asian populations compared to White populations [42]. The apparent protection of individuals born in low-prevalence areas may be explained by early acquisition of EBV, leading to a lower risk of infectious mononucleosis and MS. Conversely, late EBV infection is more common in high-prevalence MS countries, such as Denmark [53], potentially contributing to the elevated risk of MS in these regions. Thus, early migration to a country with a high prevalence of MS may delay primary infection with EBV, leading to a higher risk of developing the disease [42]. These findings partly support the hygiene hypothesis, but with a limitation : the "EBV paradox". This paradox is characterized by the fact that individuals who are seronegative for EBV have an extremely low risk of developing MS. Having escaped EBV infection during childhood, these individuals likely experienced a more "hygienic" upbringing compared to their EBV-positive peers, yet their risk of MS is much lower [44].

Ascherio *et al.* [42] have thus referred to this as the "EBV variant" of the hygiene hypothesis. For decades, it has been suggested that MS might result from an infectious insult during childhood or adolescence.

However, its incidence has not been reduced by large-scale vaccinations against viral infections, nor by the decrease in common bacterial infections in countries with well-developed healthcare systems [54]. This underscores the complexity of MS etiology, where multiple environmental, genetic, and possibly infectious factors interplay, particularly in early life, to influence disease onset.

7. Conclusions

This literature review on the impact of migration on the risk of developing multiple sclerosis (MS) highlights the significant role of environmental factors that primarily influence individuals during childhood and adolescence, with the critical age for disease acquisition being around 15 years. Over the past three decades, concepts regarding migrants and MS risk have evolved substantially. The earlier theory, which suggested that individuals migrating after the age of 15 tend to retain the risk of their country of birth, is now less widely accepted, particularly for those migrating to regions with a high prevalence of MS since these regions can influence the future risk of the disease even into adulthood, but also because of the gradual disappearance of protective factors in areas previously spared from the disease. Additionally, in the current context of increasing migratory flows, with a clear predominance toward high-prevalence MS regions, migration is likely to contribute to the globalization of the disease. This phenomenon underlines the need for further study on the interplay between migration, environmental factors, and MS, to better understand and potentially mitigate future disease risks globally.

Also, healthcare systems must allow better control of environmental factors that increase susceptibility to MS, by promoting smoking control, the adoption of a Mediterranean-type diet and the practice of preventive behaviours in the face of viral infections. Furthermore, emphasis must be on epidemiological surveillance, the use of new treatment regimens (early treatment, induction) and the search for new therapies, several trials of which are currently underway (Burton Tyrosine Kinase inhibitor, remyelination, ceramide C16 inhibition, EBV vaccines). In view of the major challenge posed by MS, further research is needed despite the expensive cost involved, including the development of a new drug, analysis of its beneficial effects and potential toxicity.

Authors' Contributions

Chermine Mboumba Mboumba, Grass Mambila Matsalou and Pupchen Gnigone drafted this paper.

Laurent Magy and Aurélie Ruet supervised the writing of the thesis topic "The effect of migrations on the risk of developing multiple sclerosis" for the obtaining of the IUD in inflammatory demyelinating pathology of the nervous system, awarded to Dr Mboumba Mboumba and from which this article is based.

Michel-Arnaud Saphou-Damon, Jennifer Nyangui Mapaga and Nelly Diouf Mbourou translated into English.

Annick Nsounda, Ibrahima Camara and Philomène Kouna Ndouongo made corrections.

Conflicts of Interest

The authors do not declare any conflict of interest.

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