

The Effect of Comorbid Allergies on the Physical and Psychosocial Outcomes of MS patients – a Th1/Th2 paradigm of Autoimmune Disease



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Background

Multiple sclerosis (MS) is an inflammatory and neurodegenerative disease of the Central Nervous System (CNS.) It is an autoimmune disease primarily characterized by an abnormal response of CD4+ T helper (Th1) cells against myelin self-antigen while allergies and asthma are the result of an abnormal response of the Th2 cell lineage and it's respective cytokines (Figure 1.) The beneficial therapeutic effect of several of the approved MS therapies are linked to their ability to switch from a Th1 to a Th2 milieu¹.

> Figure 1: Naïve CD4 (Th0) cell differentiating into Th1 and Th2 cells².



It has been proposed there is a decreased risk for developing MS in individuals with Th2-mediated diseases, like asthma and allergies^{3, 4}. The etiology of this association is theorized to be secondary to the underlying Th1/Th2 ratio imbalance that results in an increased frequency of one disease and decreased frequency of another. It has been shown in previous studies that Th2-mediated disorders may have a protective effect on the Th1 immune response of MS; in particular, allergic respiratory disease was associated with either lower rates of MS or decreased severity^{4,5,6}. However, this inverse association between MS and allergies is contested as alternative studies have provided conflicting results^{7,8}.

In this study, we aim to investigate if self-reported allergies may be associated with physical and psychosocial metrics in MS patients. We used the validated LIFEware[®] questionnaire to assess patient self-reported psychosocial limitations.

Objective

To compare the disability status, assessed by Kurtzke Expanded Disability Status Scale (EDSS) score, and quality of life, as measured by psychosocial questionnaire (Lifeware), between MS patients with and without allergies at enrollment and after a 5-year follow up.

Methods

We conducted a retrospective matched case-control study comparing MS patients with and without allergies using 5,096 subjects extracted from the New York State MS Consortium. The presence of allergies was determined through a self-reported questionnaire at study enrollment. The groups were matched 1:1 on sex, age, and disease duration. Chi-square tests and independent samples *t*-tests were used to analyze differences in measures between the two groups. A subsample of 1,310 subjects was analyzed to investigate group differences at 5 years after study enrollment.

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Demographic Results

There was no significant difference between the two groups in sex, race, smoking status, or DMT use. However, there was an association between allergies and education status (those with allergies were more likely to have at least a college education, 74.3% vs 66.4% in the group without allergies, p<0.001). At enrollment, the allergies group had a higher proportion of Relapsing Remitting MS (RRMS) (73.2% vs 65.6%, p<0.001) compared to subjects not reporting comorbid allergies, despite having the same disease duration (mean 10.2 [SD=9.6] vs 10.3 [SD=9.7] respectively). This difference persisted at 5 years but

was no longer statistically significant (p=0.07).				
	Table 1: Demographic Characteristics of MS patients with and without comorbid allergies			
	Demographic Characteristics, n (%)	Allergies (n=2548)	No Allergies (n=2548)	P-value
	Sex, Female	2071 (81.3%)	2071 (81.3%)	>0.999
	Race, African-American	157 (6.2%)	178 (7.0%)	0.074
	Education Level High School or Less College or greater	639 (25.7%) 1844 (74.3%)	840 (33.6%) 1657 (66.4%)	<0.001
	Smoking status, yes	292 (33.4%)	227 (36.8%)	0.177
	DMT Use at Enrollment	1192 (46.8%)	1176 (46.2%)	0.653
	MS Type at Enrollment RRMS Progressive MS	1797 (73.2%) 659 (26.8%)	1617 (65.6%) 848 (34.4%)	<0.001
	MS Type at 5 year Follow Up RRMS Progressive MS	378 (62.5%) 227 (37.5%)	393 (57.5%) 290 (42.5%)	0.071

Psychosocial Results – Enrollment &

5-year-follow-up

At enrollment, the participants with allergies reported more feelings of annoyance (38.5% vs 33.6%, p<0.001), guilt (17.7% vs 15.4%, p=0.23), panic (11.7 vs 9.9%, p=0.039), tension (46.7% vs 38.9%, p<0.001), and loneliness (17.8% vs 15.2%, p=0.012), and were more likely to report pain (53.8% vs 47.2%) p<0.001) compared to the group without allergies. However, at 5 year follow up, all differences in the perception of negative feelings between the groups lost statistical significance, except for the difference in perceived pain (56.5% in the allergies group vs 48.2% in the group without, p=0.003).



Figure 2A: Graph of participants' perceived psychosocial impairment at enrollment by whether they had comorbid allergies.

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Physical Results – Enrollment & 5-year-follow-up

At enrollment, the allergy group had lower mean EDSS scores (3.3 [SD=2.2] vs 3.6 [SD 2.2], p<0.001) and no difference in mean T25FW times (8.3 [SD 10.3] vs 8.6 [SD 10.9] seconds, p=0.293). At 5-year follow up, the difference in EDSS scores persisted (4.0 [SD 2.4] vs 4.2 [SD 2.4], p=0.17) but was no longer significant. T25FW times became significant at 5-year-follow up with the allergy group averaging 8.7 [SD 10.2] vs 10.6 [SD 14.6] seconds, p=0.015.)



Figure 3A: Graph comparing EDSS score and T25FW times at enrollment

Discussion

We found an association between reporting comorbid allergies and more psychosocial impairment at enrollment and, with a loss of significance, at follow up. For physical impairment, the allergy group had marginally better EDSS scores and T25FW times at enrollment and follow up, but EDSS differences were only statistically significant at enrollment and T25FW differences were only statistically significant at 5-year follow-up. This is mostly in agreement with a previous survey study that showed an association between asthma and psychological impairment in MS but not with physical disability⁹. We anticipate that the loss of significance may be attributed to some limitations of our study including a large loss-to-follow-up at the 5 year mark (Allergies: 2,548 to 623; No allergies: 2,548 to 687) which decreased the power of the study; and a reliance on self-reported diagnosis of allergies. However, our study also has several strengths, including: the use of a large well-established cohort of MS patients with routine clinical follow up, our ability to match the allergies and non-allergies group on several possible confounding demographic variables, and the extensive data about physical and psychosocial limitations that we had.

Of note, the increased association between comorbid allergies and having RRMS support a current hypothesis that having a history of atopic allergy reduces the risk of both development of MS and progressive MS⁶. The pathogenesis remains unclear, however, there is data to suggest that during the relapsing stage a pro-inflammatory response that involves both the adaptive and innate immune system dominates while during the progressive stage abnormalities of the innate immune system prevails¹⁰. Patients with allergies may have Th2 cells that behave in a regulatory manner to redirect the immune system away from an innate response thus delaying the onset of progressive stage of MS.

Conclusion

In conclusion, we observed a small but significant association between reporting comorbid allergies and a higher number of RRMS after 10 years and a trend after 15 years of disease duration, lower EDSS scores and a stronger association with psychosocial impairment at enrollment. More studies are required to examine the role of Th2 co-morbid disorders associated with MS for more individualized appropriate therapies.



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Figure 3B: Graph comparing EDSS score and T25FW times at follow-up



Thank you

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