Uric Acid Levels in Relation to Progression of Multiple Sclerosis

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ABSTRACT

Multiple sclerosis (MS) is a neurodegenerative disease caused by demyelination in the central nervous system. In previous studies, serum uric acid (UA) levels have been implied as a useful biomarker in understanding MS disease progression and development. The majority of previous studies have found MS patients have a lower UA level than healthy controls, however some studies have found higher UA levels with MS patients. Previous studies have compared UA levels between subtypes of MS, but have not produced conclusive data. To better understand the correlation between UA levels and MS patients, we compared UA levels between our set of MS patients from the Vanderbilt BioVU database, which includes the electronic health records of ~7,000 MS patients.

In 499 MS patients and 276 healthy controls with UA results, both gender and age were found to be contributing factors to UA levels (p = 5.979e-10 and p = 4.448e-5). With both age and gender as covariates, we found no significant different UA levels associated with MS patients (regression, p = 0.0838). UA levels were compared to MS subtype with no significant association (p = 0.628).

Our study failed to support previous evidence of low UA levels associated with MS patients. Gender and age were identified as contributing factors to UA level. There was no significant difference found between UA levels of different subtypes of MS.

STUDY POPULATION

BioVU is a resource of over 180,000 leftover blood samples from outpatients that have been collected and used to extract DNA, and each sample is linked to the individual’s clinical data through a “synthetic derivative” of their de-identified EMR.

Patients in BioVU are representative of all patients that come to VUMC, in that they come from diverse regions of the country, varied ethnicities and health statuses, and are of all ages. We have limited our study to patients 18 years or older. EMR usage at Vanderbilt dates back to 1997, so we have over 10 years worth of clinical information for many patients.

Most of the MS patients in our study have been seen at the Multiple Sclerosis Clinic by one of three physicians. The Vanderbilt MS Clinic was established in 1994 and up to 30 patients are seen each day. In general, patients at the MS Clinic are seen twice a year. Additionally, some patients in our study were seen at Vanderbilt in other clinics for other reasons but also have a diagnosis of MS.

The cohort for this study included all MS patients with UA values (499 individuals) and a set of healthy controls (276 individuals).

METHODS and RESULTS

Multiple Sclerosis (MS) is a neurodegenerative disease caused by demyelination in the central nervous system. In previous studies, serum uric acid (UA) levels have been implied as a useful biomarker in understanding MS disease progression and development. The majority of previous studies have found MS patients have a lower UA level than healthy controls, however some studies have found higher UA levels with MS patients. Previous studies have compared UA levels between subtypes of MS, but have not produced conclusive data. To better understand the correlation between UA levels and MS patients, we compared UA levels between our set of MS patients from the Vanderbilt BioVU database, which includes the electronic health records of ~7,000 MS patients.

Patients diagnosed with MS and had uric acid values were extracted from our parent dataset. To account for multiple testing with individuals, median uric acid values were isolated for each individual. When median value was an average between two numbers, the date associated with the closest value was chosen. When values were equivalent, the more recent date was utilized. Our cases and controls were first analyzed for normality of sampling distribution. The sampling distributions are visualized in figure 1 after removing one outlier from the cases and one from the controls. The sampling distribution was assessed to be normal.

Gender was determined to be a contributing factor with males having a significantly higher average UA level. This was confirmed through a two sample t-test comparing the median uric acid values of males to females in our entire population (p = 1.360e-18) and displayed in figure 2. Through linear regression analysis, age was also found to be a significant contributing factor to uric acid levels (p = 6.002e-6) and displayed in figure 3.

UA levels of cases and controls were compared to each other through regression analysis with age and gender included as covariates with no significant difference found (p = 0.0868). To determine whether subtype is a contributing factor in UA level, 45 Relapsing Remitting MS (RRMS) individuals were compared with 13 Primary Progressive MS (PPMS) in a regression analysis with age and gender as covariates. No significant difference was found between the two groups (figure 4).

CONCLUSIONS

Our study failed to support previously established conclusions relating uric acid levels to MS and to MS subtype. The correlation between low uric acid levels and MS diagnosis is near significance and this may be rectified through a larger sample. However, similar studies failed to include age and gender as covariates in their comparison of MS to UA levels. This points out a possible flaw that necessitates further investigation. The subtype analysis was only performed on a small fraction of our population (58 of 499). Acquiring additional subtype data would give our study greater power. Using a more specific measurement of MS progression than subtype classification would also provide more power to our study.

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