**Conversion and reversion of JCV antibody serostatus and longitudinal evaluation in a Mexican Multiple Sclerosis population treated with natalizumab**

**Introduction.**

With the increasing availability of high efficacy pharmacological therapies used for the management of multiple sclerosis (MS) there is also a greater potential for severe adverse events.

Infection with the John Cunningham virus (JCV) among MS patients reported ranges from 50% to 70% and increases the risk of progressive multifocal leukoencephalopathy (PML) in patients undergoing treatment with some of these new drugs, particularly natalizumab. There are some other risk factors associated with the development of PML such as previous use of immunosuppressive agents and the total number of natalizumab infusions.

It is safer to use these drugs in subjects who test negative for JCV antibodies, but we must be aware of potential seroconversion in these patients at any time. Only few studies have focused on the observation for changes in JVC antibody indexes (AI) over time among MS patients.

**Material and Methods.**

Our study included 78 patients at the MS Clinic of the National Institute of Neurology and Neurosurgery Manuel Velasco Suárez (México), receiving natalizumab therapy and annual register of JCV AI in the period from January 2014 to march 2019. 52 patients meet criteria inclusion. Patient's sera were sent to Copenhagen, Denmark, where anti-JCV antibodies were tested by a two-step enzyme-linked immunosorbent assay. Qualitative (negative/positive) and quantitative results (anti-JCV antibody index) were used for statistical analyses. Then identified the rate of seroconversion and retro conversion, finally analyzed the factors associated with both outcomes.

**Results.**

In our cohort, mean age at baseline was 36 ± 11,88 years. 15 patients (28.8%) were male and 37 (71.15%), female. There was no significant difference regarding gender, EDSS change and anti-JCV antibody status or rate of serostatus change.

Of the 52 patients, 20 (38,4%) were anti-JCV antibody negative, 25 (48,7%) positive at baseline, and 7 patients (13,4%) had indeterminate status. During the study 6 of the patients converted or reverted between negative and positive serostatus, 4 (7,6%) reverted and 2 converted. Furthermore, 4 patients (7,6%) reverted from indeterminate to negative index and, 1 patient from negative to indeterminate index.

Most subjects showed stable anti-JCV antibody status over time. We did not find any sign of a higher seroconversion rate in Natalizumab-treated patients as it was described in previous studies; conversely, we found a higher rate of retro conversion in our cohort.

The great majority of anti-JCV antibody negative patients at baseline remained negative at all time points of testing, while, similarly, all highly positive patients remained on high index throughout the study.

**Conclusion.**

In our study, we were able to show that a longer-term serostatus is highly predictable by testing through time, biannual or annual; including identification of serostatus fluctuation due to assay variability without real seroconversion. Anti-JCV antibody index at baseline predicted stable negative as well as stable positive JCV serostatus over the observational period.