

Cerebrospinal Fluid Protein Is Higher in Males with Multiple Sclerosis: Results from an International Multicenter Cohort

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Objective

To compare the cellular, chemical, and immunological profile of CSF at the time of diagnosis in MS patients stratified by sex.

Background

Sex has a differential effect on MS disease severity. Males tend to have a more severe clinical course and a greater tendency towards primary progressive phenotype and neurodegeneration compared to females. However, little is known about differences in cerebrospinal fluid (CSF) profile.

Design/Methods

- This is a cross-sectional study analyzing data from CSF obtained at the time of MS diagnosis in patient cohorts from MCW and JUST.
- We compared nucleated cells (NCs), protein, IgG index, IgG synthesis rate, and oligoclonal band (OCBs) positivity.
- The student's t-test to compare continuous variables and chi-square to compare categorical variables; p-value was set at 0.05

Demographics of Patients

43 male patients and 89 female patients who had complete CSF profiles and were analyzed.

- Age mean(SD) was 38.4(12.1) for males and 35(13) for females, p=0.59.
- Males included 23 Caucasians (53.5%), 10 Arabs (23.3%), 8 African Americans (18.60%), 2 Hispanics (4.7%).
- Female included 50 Caucasians (56.2%), 24 Arabs (27%), 14 African Americans (15.7%), 1 Hispanic (1.1%).

Results

Nucleated Cells (NCs): Pleocytosis of >5 NCs was observed in 21/43(48.8%) of males and 39(43.8%) of females, p=0.59.

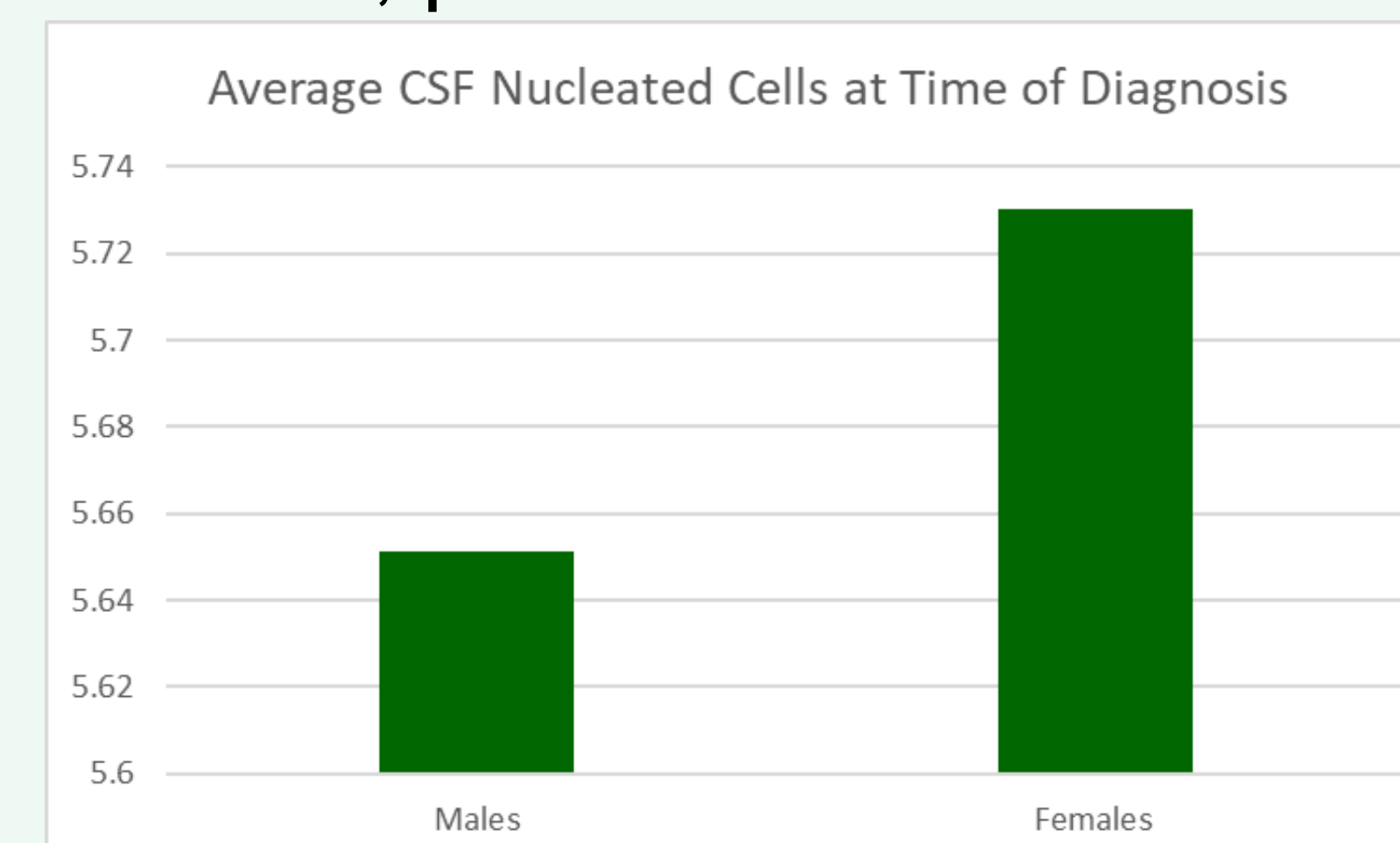


Figure 1. The mean(SD) NCs were 5.65(5.84) in males and 5.73(6.94) in females, p=0.36

Protein: Protein was greater than 45mg/mL in 19/43(44.2%) of males and 17/87(19.5%) of females, p<0.005.

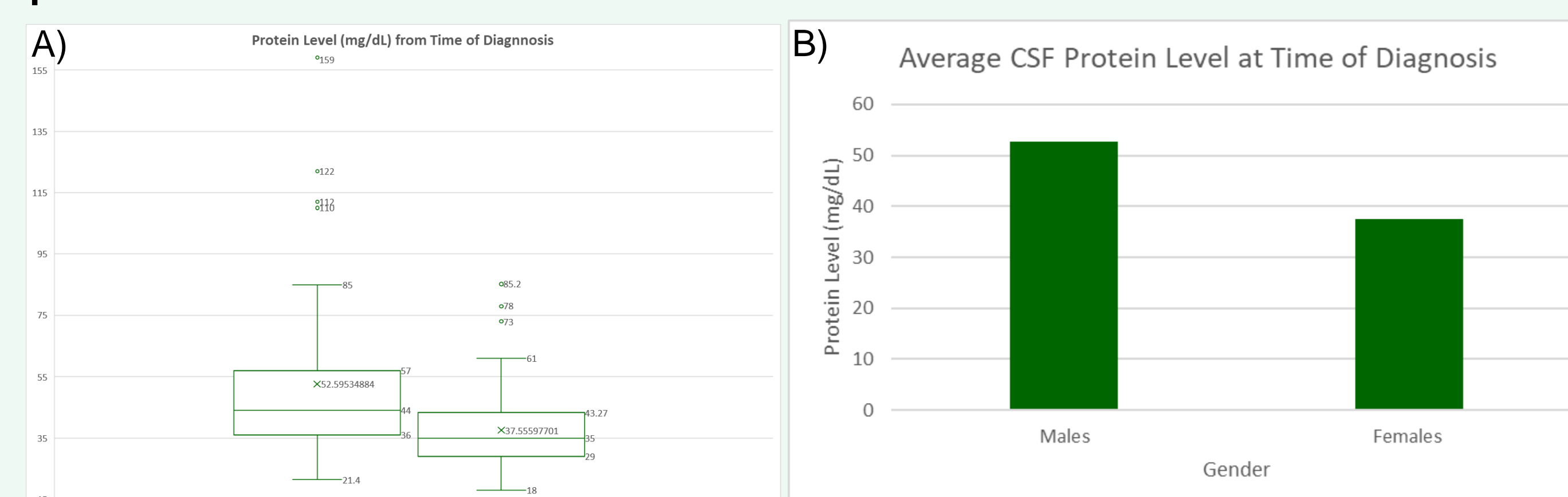


Figure 2. A) Box and whiskers diagram displaying raw protein data from males (range 21.4 to 159 mg/dL with SD 28.56) and females (range SD 18 to 85.2 mg/dL 12.39). **B)** The mean(SD) for CSF protein was 52.60(28.56) in males and 37.56(12.39) in females, p<0.005.

Oligoclonal Bands: Unique Oligoclonal bands were specimens that contained 2 or greater in CSF than serum

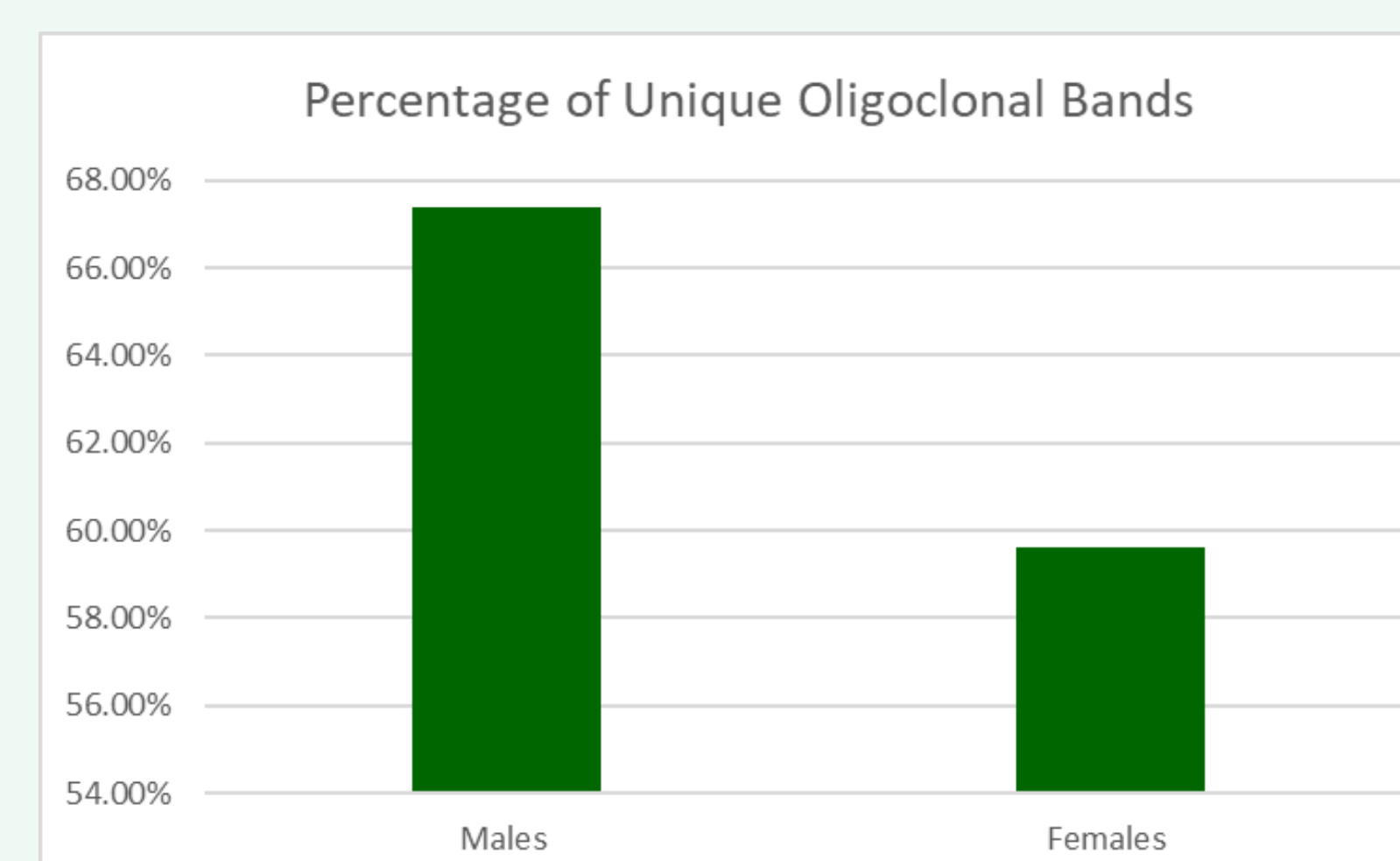


Figure 3. OCBs were present in 67.4% of males and 59.6% of females, p=0.38.

Results Continued

Immunoglobulin Index and Synthesis Rate: Elevated IgG index >0.85 was observed in 10/36(27.8%) of males and 31/67(46.3%) of females, p=0.068. IgG synthesis rate was >12 mg/24hrs in 7/30(23.3%) of males and 19/54(35.2%) of females, p=0.26

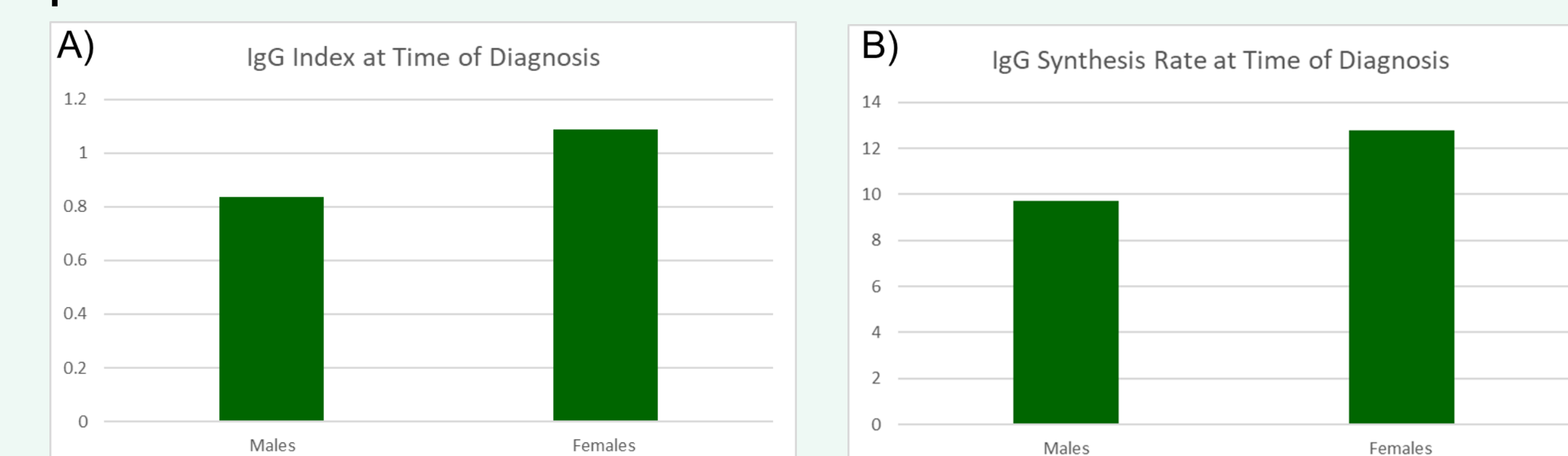


Figure 4. A) IgG index mean(SD) was 0.83(0.45) in males and 1.09(0.86) for females, p=0.11. **B)** The mean(SD) of IgG synthesis rate was 9.69(7.49) in males and 12.77(17.73) in females, p=0.37.

Discussion/Future Directions

In a multi-ethnic cohort of MS patients, males had significantly higher CSF protein than females. This may imply a sex difference in the blood-brain barrier (BBB) function. Other traditional CSF values (nucleated cells) as well as biomarkers (oligoclonal bands, IgG Index, and IgG Synthesis) did not display a sex difference.

Future studies are needed to investigate sex differences in biomarkers of BBB permeability in MS and their association with the observed sex differences in clinical parameters.

Contact/Acknowledgment

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