

## Association between Chronic Inflammatory Conditions and Anti Cyclic Citrullinated Peptide Antibodies in Patients with Early Rheumatoid Arthritis

Marino L<sup>1</sup>, Secco A<sup>1</sup>, Catalán Pellet A<sup>1</sup>, Mamani M<sup>1</sup>, Dal Pra F<sup>2</sup>, Citera G<sup>2</sup>, Landi M<sup>2</sup>, Cerda O<sup>2</sup>, Martínez Muñoz A<sup>3</sup>, Chaparro del Moral R<sup>3</sup>, Rillo O<sup>3</sup>, Colombres F<sup>4</sup>, Berman A<sup>4</sup>, Berman H<sup>4</sup>, Marcos J<sup>5</sup>, García MA<sup>5</sup>, Salas A<sup>5</sup>, Caeiro F<sup>6</sup>, Alvarez AC<sup>6</sup>, Haye Salinas MJ<sup>6</sup>, Benzaquen N<sup>6</sup>, Rosa J<sup>7</sup>, Bertiller E<sup>7</sup>, Soriano ER<sup>7</sup>, Ceccato F<sup>8</sup>, Paira S<sup>8</sup>, Ledesma C<sup>9</sup>, Salvatierra G<sup>9</sup>, Leal M<sup>10</sup>, Juarez V<sup>11</sup>, Crespo M<sup>11</sup>, Velozo EJ<sup>12</sup>, Sacnún M<sup>14</sup>, Quintana R<sup>14</sup>, Abdala M

<sup>1</sup>Hospital Bernardino Rivadavia, <sup>2</sup>Instituto De Rehabilitación Psicofísica, <sup>3</sup>Hospital General De Agudos "dr. E. Tornu", <sup>4</sup>Centro Medico Privado De Reumatología, <sup>5</sup>HIGA San Martin La Plata, <sup>6</sup>Hospital Privado Centro Medico De Córdoba, <sup>7</sup>Hospital Italiano Buenos Aires, <sup>8</sup>Hospital Dr. José Maria Cullen, <sup>9</sup>Instituto Provincial De Rehabilitación Integral, <sup>10</sup>Centro Integral De Reumatología, <sup>11</sup>Hospital Señor Del Milagro, <sup>12</sup>Sanatorio y Universidad Adventista Del Plata, <sup>14</sup>Hospital Provincial De Rosario. Hospital Provincial del Centenario

**Background/Purpose:** Increased citrullination process and anti-CCP production are not restricted to rheumatoid arthritis (RA). Other inflammatory processes could develop citrullinated proteins which may contribute to the production of such antibodies. The aim of our study was to analyze whether patients with anti-CCP positive early rheumatoid arthritis have higher frequency of previous history of chronic inflammatory conditions than anti-CCP negative patients at the time of diagnosis.

**Methods:** We included patients with early RA according to ACR/EULAR classification criteria, belonging to a prospective cohort of patients with early arthritis (<2 years of disease duration). Data from the first visit were collected. We studied the relationship between anti-CCP antibodies with the previous history of chronic inflammatory conditions (ischemic heart disease, peripheral vascular disease, ischemic or hemorrhagic stroke, hypertension, dyslipidemia, asthma, chronic obstructive pulmonary disease (COPD), diabetes mellitus, hypothyroidism, tuberculosis, alcohol and smoking). The association between anti-CCP status and the presence of inflammatory processes were assessed using univariate and multivariate models.

**Results:** We included 557 patients with early rheumatoid arthritis. We found positive anti-CCP antibodies ( $\geq 25$  UI/ml) in 396 patients and negative anti-CCP antibodies in 161. There were no differences between anti-CCP negative and anti-CCP positive patients regarding to age ( $51 \pm 14$  vs  $50 \pm 14$  years;  $p=0,76$ ) and female gender (83% vs 80%;  $p=0,42$ ). When evaluating the association between anti-CCP positivity and presence of inflammatory conditions, patients with negative anti-CCP antibodies experienced significantly higher frequency of dyslipidemia (14% vs 5%;  $p < 0,01$ ) and alcohol intake (7% vs 3%;  $p=0,03$ ). No association was found between anti-CCP status and ischemic heart disease, peripheral vascular disease, ischemic or hemorrhagic stroke, hypertension, chronic respiratory diseases including asthma and COPD, diabetes mellitus, hypothyroidism, tuberculosis and smoking. Multivariate logistic regression analysis with anti-CCP as dependent variable, showed that dyslipidemia [OR=0,39 (0,17- 0,89);  $p=0,03$ ] and alcoholism [OR= 0,29 (0,15- 0,55);  $p < 0,01$ ] were independently associated with negative anti-CCP antibodies.

**Conclusion:** In this cohort with early rheumatoid arthritis, we did not found higher frequency of previous chronic inflammatory conditions in patients with positive anti-CCP antibodies. Nevertheless, negative anti-CCP antibodies were significantly and independently associated with previous history of dyslipidemia and alcoholism.