Anti-cyclic citrullinated peptide (anti-CCP) antibodies are used as highly specific and sensitive markers in the diagnosis of rheumatoid arthritis (RA), in recent years. The aim of this prospective and cross-sectional study was to measure the levels of anti-CCP and rheumatoid factor (RF) in patients with RA and osteoarthritis, and healthy volunteers to evaluate the specificity and possible diagnostic value of anti-CCP and RF, as well as their correlations with parameters of disease activity. Thirty-four patients with RA (mean age: 53.8 +/- 8.6; 29 female), 32 patients with osteoarthritis (mean age: 53.1 +/- 8.1; 26 female) and 32 healthy controls (mean age: 49.6 +/- 6.7; 24 female) were evaluated between July 2004-July 2005. RA diagnosis was done on the basis of criteria recommended by American College of Rheumatology (ACR). Clinical parameters, including disease activity score (DAS28) and health assessment questionnaire (HAQ) indices for physical capacity were detected for RA patients. As a result, 25 (73.5%) of the patients with RA were found positive for anti-CCP (mean value: 74.6 +/- 64.9 RU/ml), while 24 (70.6%) were positive for RF (mean value: 62.6 +/- 84.8 IU/ml). Serum levels of anti-CCP and RF showed statistically significant increase in patients with RA in comparison with osteoarthritis patients (all were negative for anti-CCP; 6.2% were positive for Rf) and healthy controls (all were negative for anti-CCP anf RF) (p < 0.001). Twenty-two of the RA patients (64.7%) yielded positive results for both anti-CCP and RF, while seven (20.6%) were negative for both of the parameters. The sensitivity and specificity of anti-CCP reactivity for RA patients diagnosed based on ACR criteria were detected as 73.5% and 100%, respectively; the corresponding results for RF were 70.6% sensitivity and 96.8% specificity. The mean DAS28 and HAQ scores of RA patients with anti-CCP and RF were higher than the patients without anti-CCP and RF, however these differences were not statistically significant (p > 0.05). Furthermore, a correlation between serum anti-CCP levels and HAQ score was determined, while there was no correlation between DAS28 and anti-CCP levels. In conclusion, antibodies against CCP were thought to be more specific than RF for RA, and the determination of anti-CCP in addition to RF could be helpful in serological diagnosis and monitorization of patients with RA.