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ORIGINAL ARTICLE

Diagnostic value of serological tests (IgA, IgG, IgM) against A-60 antigen in tuberculosis

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ABSTRACT

Background: Tuberculosis (TB) is a common infectious disease worldwide especially in developing countries. Diagnosis of TB is difficult and often needs paraclinical studies. Measuring immunoglobulin's against A-60 antigen of TB microorganism has been reported as a useful technique. The aim of the present study was to evaluate the diagnostic value of serologic test (IgA, IgM, IgG) against A-60 antigen in tuberculosis.

Patients and methods: For this case-control study, 176 TB patients (124 patients with smear-positive pulmonary TB and 52 patients with extra pulmonary TB) and 283 healthy controls were enrolled. Then, all subjects were tested for IgM, IgA and IgG against A-60 antigen using ELISA technique.

Results: Sensitivities of IgM, IgG and IgA test were 15%, 25% and 40%, respectively while the following specificities were also reported 100%, 75% and 90%, respectively. Positive predictive values (PPV) were 100%, 57% and 72%, however, negative predictive values (NPV) were 65%, 72% and 70%, respectively. Combination of immunoglobulins' results increased sensitivity, for which the most sensitivity was observed in combination of IgG and IgA results.

Conclusion: Our results revealed the usefulness of serologic testing in TB diagnosis. Although its sensitivity is not high enough, combination of immunoglobulin results may improve the sensitivity.

Keywords: *Tuberculosis, A-60 antigen, Serology*.
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INTRODUCTION

Tuberculosis (TB) is one of the most common infectious disease that infected about two milliard people of the world and is one the three important infectious diseases that cause mortality and morbidity (1,2). TB is divided to two major groups: pulmonary and extrapulmonary. Pulmonary TB included smear negative and smear-positive cases. The gold standard of TB diagnosis is isolating organism from sputum or other body fluids and finding organism in acid fast smear or pathologic samples.

In some cases such as pediatric and geriatric patients providing sputum smear tests is a problem because of inadequate accessible samples, therefore TB could be misdiagnosed or mistreated (1,2). Recently, further efforts for TB diagnosis have been achieved including PCR and serology. Serologic tests with acceptable diagnostic value are suitable because of simplicity, quickly perform ability and cost effectiveness. Several serologic tests have been proposed among which measuring IgM, IgG and IgA against A-60 antigen of mycobacterium tuberculosis by ELISA have

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received further attention. The A-60 antigenic complex is a major mycobacterial antigen that is composed of protein, carbohydrate and lipid. This complex induces antibody production in infected subjects and may be helpful for diagnosis of active and latent TB.

Serologic tests have controversial results in different studies (3-5). The present study was conducted to evaluate the diagnostic value of serologic tests against A-60 antigen in TB infected patients.

PATIENTS and METHODS

It was a case-control study. TB infected patients were defined as patients with two positive sputum smear or one positive sputum smear plus one positive sputum culture or one positive sputum smear plus compatible radiological findings and clinical criteria compatible with pulmonary TB. For extrapulmonary tuberculosis diagnosis was made by biopsy or culture in combination with compatible clinical findings. All patients were referred to TB Center of Kermanshah University of Medical Sciences. Meanwhile, 283 socioeconomic-matched healthy controls were enrolled. All patients and controls had been received BCG vaccine at birth.

Serum samples were obtained from healthy controls and TB patients before therapy commencement, then, transported to laboratory under cold chain condition. IgM, IgG and IgA were measured by Anda TB France ELISA kit according to manufacture's guidelines. Laboratory personnel were blind to case or control groups. The following cut-off points were assigned according to the manufacture's instructions: 1, 225, and 300U for IgM, IgG and IgA, respectively.

RESULTS

The case group included 124 smear-positive pulmonary and 52 extrapulmonary TB patients with the mean age of 44 and 40 years, respectively. The mean age of controls was 36 years. Totally, 58% of smear-positive and 36% of extrapulmonary patients were male. Results of performed seologic tests are presented below:

IgM: Of 176 TB patients, 27 (15.3%) were IgM-positive, however, none of the controls revealed to be IgM-positive. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy for IgM were 15%, 100%, 100%, 65% and 67%, respectively. Of 27 IgM-positive cases, 19 were smear-positive and 8 had extrapulmonary TB. Sensitivity, specificity, PPV, NPV and accuracy in pulmonary TB patients were 15%, 100%, 100%, 86%, and 86%, respectively, versus 15%, 100%, 100%, 73%, and 74% of extra pulmonary patients.

IgG: Of 176 TB patients, 94 (53.4%) were IgG-positive, however, IgG was positive in 70 controls (24.7%). Of 94 IgG-positive patients, 75 were smear-positive and 19 had extrapulmonary TB. Sensitivity, specificity, PPV, NPV and accuracy for IgG were 53%, 75%, 57%, 72%, and 66%, respectively. These figures were 60%, 75%, 52%, 81% and 70% in smear-positive and 36%, 75%, 21%, 86%, and 69% in extrapulmonary TB patients, respectively.

IgA: Totally, 70 (39.8%) TB patients and 27 (9.5%) controls had positive IgA results. Positive results were reported in 51 and 19 smear-positive and extrapulmonary TB patients, respectively. Sensitivity, specificity, PPV, NPV and accuracy for IgA were 40%, 90%, 72%, 70%, and 71%, respectively. These figures were 41%, 90%, 65%, 78%, and 75% in smear-positive and 36%, 90%, 46%, 88%, and 82% in extrapulmonary TB patients, respectively.

When we considered the combination of immunoglobulins' results, the sensitivity was improved. This improvement was more significant in combination of IgG and IgA results. Figures 1-3 show the mean sensitivities of IgG, IgA, IgM, and different combinations in varus groups.

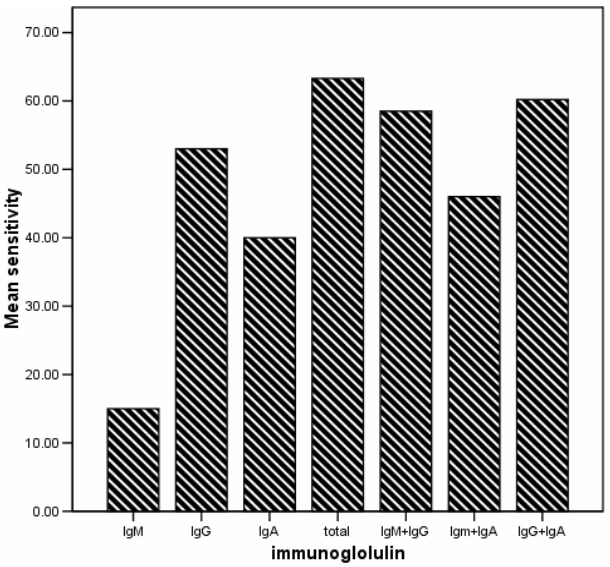

Figure 1. Mean sensitivity of IgA, IgG, IgM, and different combinations in tuberculosis patients

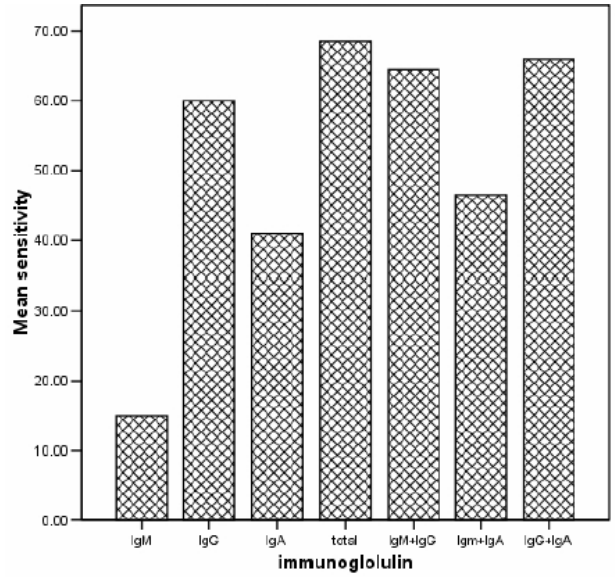

Figure 2. Mean sensitivity of IgA, IgG, IgM, and different combinations in smear-positive tuberculosis patients

DISCUSSION

This study revealed that serologic test against A-60 antigen of M. tuberculosis is a useful technique for TB diagnosis despite its rather low sensitivity. Prior investigators reported different diagnostic accuracies for ELISA test against A-60 antigen. Van der Warf, Tuneer and Simonneyn reported limited accuracies in this regards (3,4,7).

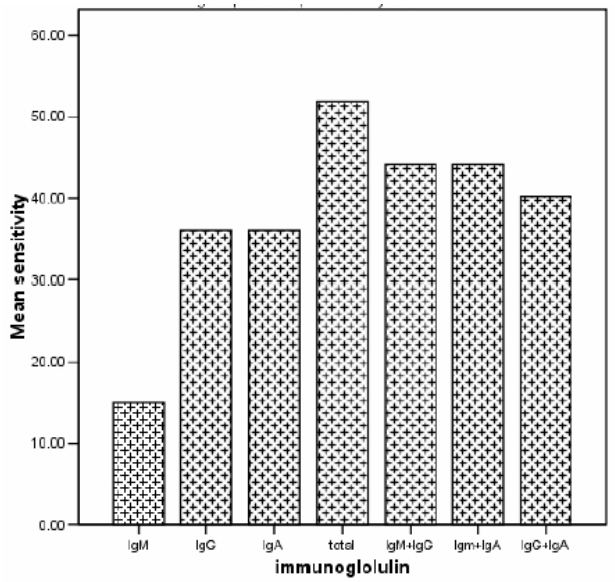

Figure 3. Mean sensitivity of IgA, IgG, IgM, and different combinations in extrapulmonary tuberculosis patients

In our study, IgG was the most sensitive test (53%), however, in smear-positive pulmonary TB cases the sensitivity of IgG, IgA and IgM were 60%, 41% and 15%, respectively. The most specific test was IgM, while PPV was highest for IgM.

In Pouthier et al study, 36.5% of TB patients who were co-infected with HIV and 69.5% of HIV-free TB-infected patients had positive IgG against A-60 antigen (6). However, Banica stated, in contrary to ours, a sensitivity of 74-90% for serologic tests against A-60 antigen, among which IgA was the most sensitive (8). Although in Sieminsko study in 1998 TB was not associated with IgG level (9), other studies in India, Spain, China, and Poland demonstrated usefulness of serologic tests in pediatric and adult TB cases with an estimated sensitivity of 75-92% in India (10-13). In a study in Saudi Arabia, sensitivity and specificity of a modified Anda–TB ELISA test for TB detection were 87% and 95%, respectively (14).

Zielonka study in 2002 in Poland was in agreement with ours. They reported nearly similar sensitivities and specificities, however,

combination of tests improved the indices, for instance, higher sensitivities were seen in combination of IgG and IgA (13). Similarly, in Alifiano study in Italia, the combination of IgG and IgA showed higher sensitivity and specificity (89% and 82.3%, respectively) (5).

In conclusion, serologic ELISA methods against A-60 antigen of M. tuberculosis can be useful for TB detection, although its sensitivity is rather low. The combination of results (i.e., IgA and IgG) may improve the sensitivity.

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