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Sensitivity and Specificity of Some Laboratory Diagnostic Test in Rheumatoid Arthritis

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ABSTRACT

Background and aims. *Rheumatoid Arthritis (RA)is a chronic autoimmune disease affect the joints. It is characterized by a progressive symmetric inflammation occurrence between age 65 to 80 years. Early treatment is confirmed in order to prevent and decrease its complications by different laboratory investigation of immune activation, for example erythrocyte sedimentation rate (ESR) which is a general hematology examination that might indicate and monitor an elevate in inflammatory activity inside the body. The aim of the current study was to evaluate the sensitivity and specificity of some clinical investigation for rheumatic disease to aid early detection and treatment.* **Methods**. *A total of 50 elderly individuals were screened in this study and were divided into two categories. The first category collected from departments of Rheumatology in Tripoli University Hospital and Tripoli Central Hospital, and the second category collected randomly from healthy individuals which served as control. Personal information and data relating RA diagnostic tests in patient, including erythrocytes sedimentation rate, rheumatoid factor by latex and Mindray and last test is uric acid.* **Results**. *The mean± SD of uric acid between RA cases and control, which was not significant, was 3.96 ±1.64 and 4.10 ±2.32 respectively (P=0.7); with AUC was 0.509. While the mean of other results was significant, mean± SD of ESR 62.2 ±33.3 to 37.5 ±22.1 (P=0.018); with AUC was 0.694, mean± SD of RF latex was 90.0 ±187 to 8.08 ±0.08 (P=0.011); with AUC was 0.709, RA Mindray mean ± SD 73.0 ± 130 to 4.24 ± 5.19 (P=0.006); with AUC is 0.726.* **Conclusion**. *The results showed that RF test by latex is good for the diagnosis, with more advantage such as the ease of technique used, fast and low cost.*

INTRODUCTION

Sensitivity and specificity are important indicator of test accuracy and let healthcare provider to decide the suitability of the diagnostic tool [1]. Providers must use diagnostic tests with the good level of confidence in the results derived from identified sensitivity and specificity [2]. Sensitivity is the percentage of true positives tests out of all patients with a condition [3]. In other words, it is the ability of an investigation or tool to give way a positive result for individuals that have that

disease [1]. Sensitivity does not allow provider to know those who tested positive but did not have the disease [4]. False positives are a consideration during measurement of specificity. Specificity is the proportion of true negatives out of all individuals who do not have a disease or condition [3]. In other words, it is the ability of the investigation or tool to get normal range or negative results for a someone who does not have a disease [1]. Sensitivity and specificity are inversely related: as sensitivity elevates, specificity tends to reduce, and vice versa [2,5].

Highly sensitive tests will guide to positive result for patients with a disease, while highly specific tests will show patients without a result having no disease [5]. Sensitivity and specificity must always advantage consideration together to give a general picture of a diagnostic test.

Rheumatoid arthritis (RA) is a chronic autoimmune disease affect the joints. It is characterized by a progressive symmetric inflammation of affect joints follow-on cartilage destruction, bone are affect erosion, and disability [6], it is one of the most common chronic inflammatory diseases [6], it is a disease that affects skin, kidneys, lungs, eyes, and heart [7]. According to epidemiologic data, RA is more widespread in women compared to men, with a lifetime risk of RA 3.6% in females and 1.7% in males [8]. RA risk as well increases with age, with a peak occurrence between age 65 to 80 years of age [9]. The disease, in addition to decrease in average life expectancy of patients, is connected with major morbidity. therefore that 50% of RA cases are not able to continue their jobs after ten years of sickness [10].

In recent studies, early treatment is confirmed in order to prevent and decrease its complications. In several independent studies it has been exposed that even a short delay in initial treatment can have a major effect on the disease activity in the next years [11,12], but known that today, RA is primarily diagnosed depends on clinical symptoms, and in most patients, the characteristic symptoms of disease become visible after 1-2 years of onset, early discovery of disease is not often possible. therefore, today "how to treat rheumatoid arthritis" has been shifted to "how to recognize rheumatoid arthritis rapidly and reliably" [13].

Disease activity in rheumatoid arthritis is related to examining symptoms of inflammatory joint disease, functional status and different laboratory investigation of immune activation, for example erythrocyte sedimentation rate (ESR)" [14]. The Erythrocyte Sedimentation is a general hematology examination that might indicate and monitor an elevate in inflammatory activity inside the body caused by one or more conditions such as autoimmune disease, it is not specific for any disease but is used in combination with additional tests to decide the presence of increased inflammatory activity." [15]. It is clear that a sensitive and specific serologic investigation is needed for diagnosing the disease in early-stages [16].

Rheumatoid factors are antibodies with different isotypes and affinities, directed against the Fc portion of immunoglobulin G. The usually mentioned rheumatoid factor is an IgM RF, although other immunoglobulin types, including IgG and IgA, are rarely found [17]. IgM isotype of rheumatoid factor, conducted as serological analysis in laboratories today, is not helpful and specific for the diagnosis of RA due to the low prognostic value [18, 10].

Many years have passed since rheumatoid factor (RF) was exposed to be related with rheumatoid arthritis, and later with confirm other autoimmune diseases; so, the functions of rheumatoid factor and its position in the development of autoimmune disease stay a mystery. many studies of the specificity and properties of rheumatoid factor have exposed that rheumatoid factor is a group of antibodies that is heterogeneous in specificity and properties [19-22]. The Latex agglutination assay (LAT) is a fast, simple, instrumentation-less and easy to understand technique, helpful for the discovery of the Rheumatoid Factor (RF) [23], which is an autoantibody targeting IgG [24] and one of the serologic measures to diagnose Rheumatoid Arthritis (RA) [25]. Latex reagents consist of antibodies or antigens coupled to polystyrene latex spherical particles [26]. The aim of our study was to assess the sensitivity and specificity of some clinical investigation of for rheumatic disease to aid early detection and treatment.

METHODS

A total of 50 elderly individuals was screened in this study. The subjects were divided into two categories. the first category collected from departments of Rheumatology in Tripoli University Hospital and Tripoli Central Hospital, and the second category collected randomly from healthy individuals which served as control. Personal information and data relating RA diagnostic tests in patient, including erythrocytes sedimentation rate (ESR) by semiplastic Westergren method measures the distance (in millimeters per hour), and rheumatoid factor in two method; agglutination RF by latex is qualitative slide test which diluted to semi-quantitative test, and the other method is photometer RF Mindray device use antigen-antibody reaction that occurs between RF and IgG result agglutination which detected as an absorbance, and last test is uric acid that measured via same device use enzymatic, colorimetric method. All these investigations have done in privet Lab.

After recording the data, it was imported into excel 2007 and finally the results of this survey were reported. investigate this further and verify if such changes in the values between the two groups were statistically significant or not, the means were compared via applying independent-test using SPSS-16 program.

RESULTS

The analysis showed that the values of parameters used in this study were statistically significant higher in RA cases subjects ($P < 0.05$) than controls except uric acid.

Compare the mean of uric acid between RA cases and control shows non-significant results, with mean ± SD 3.96 ± 1.64 and 4.10 ± 2.32 respectively (P=0.7), shown in Figure 1.
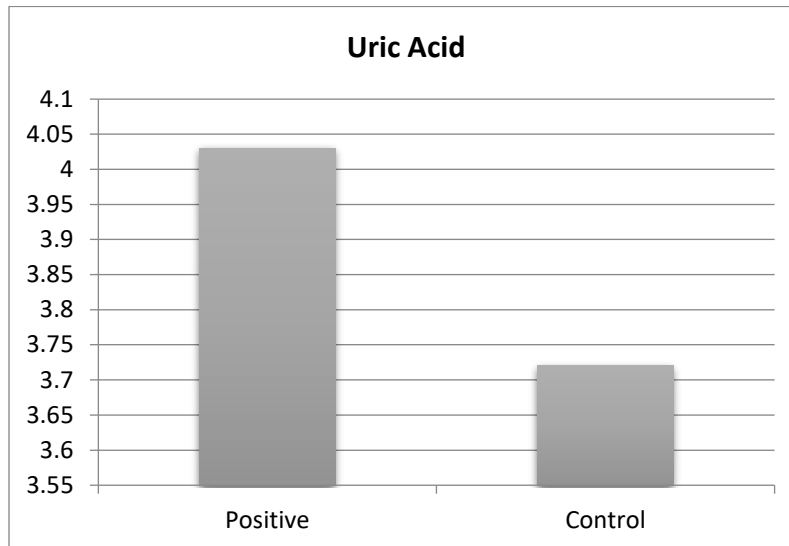

Figure 1. The mean of uric acid between RA cases and control.

Compares the mean of ESR between RA cases and control which show increased in total ESR values, the mean ± SD ESR of RA patients was 62.2 ± 33.3 compared with control group with mean ± SD 37.5 ± 22.1 (P=0.018), as shown in Figure 2.
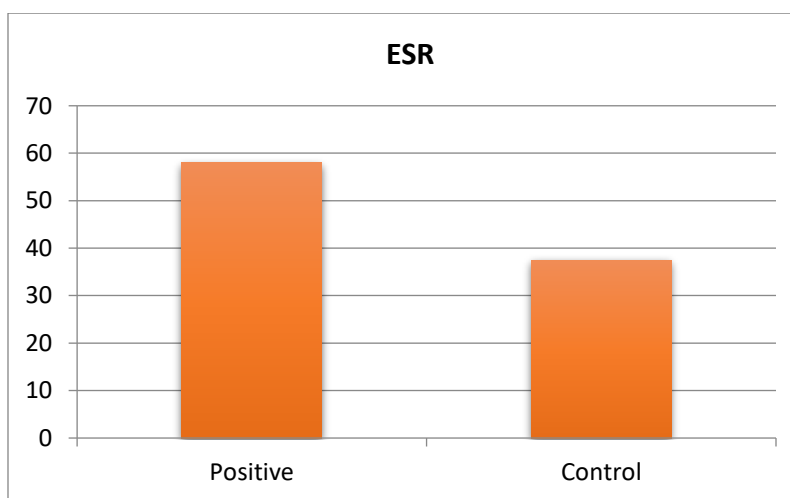

Figure 2. The mean of ESR among RA cases and control

On the other hand, compares the mean of RF latex between RA cases and control group which was the high with mean ± SD 90.0 ± 187 compared with control group with mean $8.08 \pm SD$ 0.08 (P=0.011), as shown in Figure 3.
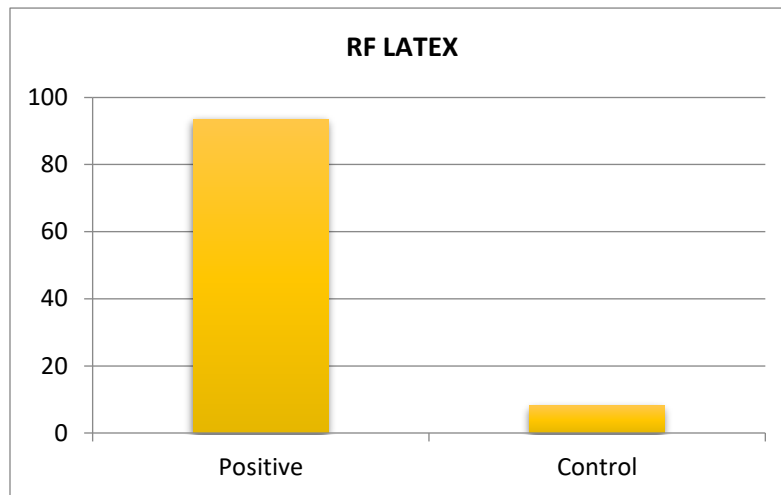
Figure 3. The mean of RF latex between RA cases and control

Similarly, the mean values of RF Mindray were also increase in RA cases compared to controls was higher in RA cases with mean ± SD 73.0 ± 130 in contrast to mean ± SD 4.24 ± 5.19 (P=0.006), as shown Figure 4.
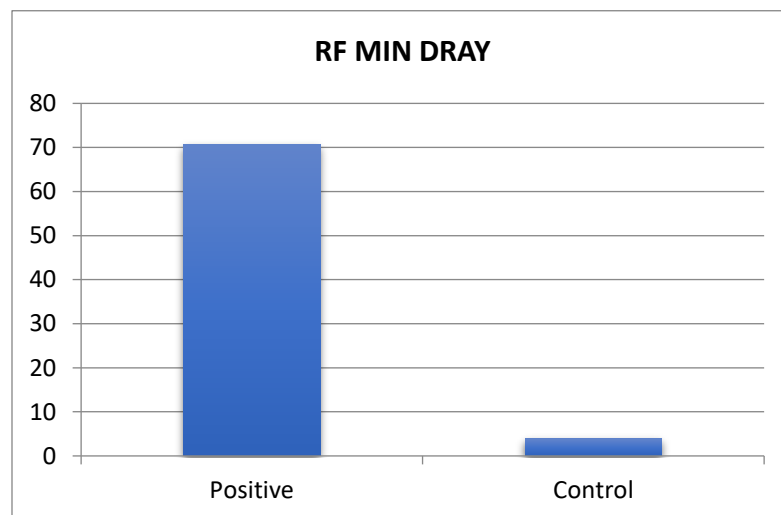

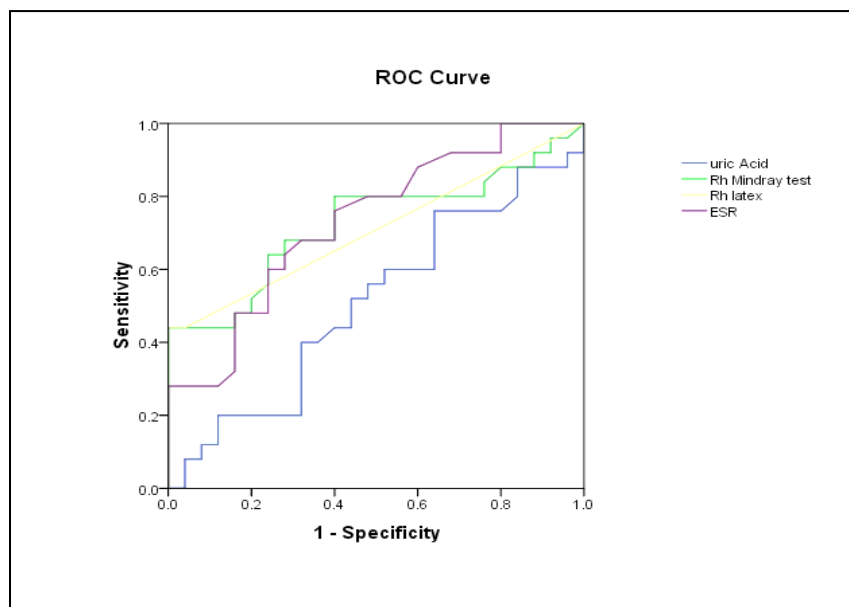**Figure 4. The mean of RF Mindray among RA cases and control.**

Figure 5. Roc curve explain the sensitivity and the specify of Rheumatoid Arthritis

The Roc Curve showed the Aria Under the Curve (AUC) of uric acid is 0.509, if more than 0.672 that is mean excellent and if less than 0.346 is unaccepted as shown in curve, Figure 5. ESR show the AUC is 0.694 that leading to cut off = 36, if AUC more than 0.841 considered good and less than 0.548 is rejected while RF Latex which show that AUC is 0.709 with cut off = 9.0, if upper value of AUC is 0.856 acceptable and the lower value is 0.562 unacceptable, finally, RF Mindray leads to cut off=2.65, the AUC is 0.726 if more than 0.871 is excellent while if less than 0.580 is unaccepted.

DISCUSSION

Identification of rheumatoid arthritis at initial appearance and treatment at earlier stage can affect illness course, prevent the progress of joint erosions or retard progression of erosive disease [27, 28]. Early diagnosis and treatment may have an effect on disease becomes to reduction state [29, 30]. For this reason, the study was designed to compare the sensitivity and the specify of some Lab diagnostic test in rheumatoid arthritis. The major focus was on ESR, RF latex, RF Mindray and uric acid. The results of our finding showed the values of such parameter were significantly larger in RA cases than control group.

The current study presented the uric acid result, which was done to avoid misdiagnosis because the symptoms between the gout and RA are very similar, and that is why all results of RA cases and control group are in normal values, Therefore, the sensitivity and specificity to RA is low according to Roc Curve, Figure 5. The ESR test is not specific for any disease but is helpful in combination with other tests to determine the presence of elevated inflammatory activity [31]. To confirm that, figure 2 show high values in two group (RA cases and control group) which means that ESR test has high sensitivity and low specificity as shown in figure 5.

On other hand, for rheumatoid factors are not usually detectable in the blood flow without an immunogenic stimulus [32], and RF has a group of immunoglobulins (IgS) that have different isotypes and affinities [33]. In our study, there are two RF test have done by two methods, first of them is RF Latex which was the highest value in RA cases compared to control group (Figure 3) and was signified has high sensitivity to RA because in roc curve, show in figure 5.

While it is not much different from the second test, which was RF Mindray that have similar results to Latex but this test still more sensitivity as shown in curve by according roc curve Mindray presented AUC if more than 0.871. Some tests related to the disease ESR, RF latex, RF Mindray and uric acid, and it turned out that the most sensitive test to the rheumatoid arthritis is RF by Mindray device may because measuring IgG and IgM together while RF latex ranks the second highest sensitivity which measure only IgG followed by ESR general indicator and good as screening test and have high sensitivity to rheumatoid arthritis, the last test is uric acid which do not have any sensitivity to rheumatoid arthritis and it was done only to confirm the diagnosis of disease to RA patients and made no misdiagnosis with gout that have similar symptoms, therefore, according our study if ESR found high with RA symptoms.

CONCLUSION

RF test by latex is good for diagnosis, with more advantage such as the ease of technique used, fast and low cost. However, due to time constraints, we could not measure rheumatoid factor using other techniques. We hope that future studies will rely on measuring the rheumatoid factor in other ways and take a larger number of cases, and we recommended to do RA test by Mindray device to confirm the disease.

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حساسية ونوعية بعض الاختبارات التشخيصية المخبرية في التهاب المفاصل الروماتويدي

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المستخلص

الخلفية والأهداف. التهاب المفاصل الروماتويدي (RA) هو مرض مناعي ذاتي مزمن يؤثر على المفاصل. ويتميز التهاب متناظر تدريجي بين سن 65 إلى 80 عامًا. يتم تأكيد العلاج المبكر من أجل منع وتقليل مضاعفاته عن طريق الفحوصات المخبرية المختلفة لتنشيط المناعة، على سبيل المثال معدل ترسيب كرات الدم الحمراء (ESR) وهو فحص عام لأمراض الدم قد يشير ويراقب ارتفاع النشاط الالتهابي داخل الجسم. كان الهدف من الدراسة الحالية هو تقييم حساسية ونوعية بعض التحقيقات السريرية لمرض الروماتيزم للمساعدة في الكشف المبكر والعلاج. **طُرق الدراسة**. تم فحص ما مجموعه 50 من كبار السن في هذه الدراسة وتم تقسيمهم إلى فئتين. تم جمع الفئة الأولى من أقسام أمراض الروماتيزم في مستشفى طرابلس الجامعي ومستشفى طرابلس المركزي، والفئة الثانية تم جمعها عشوائياً من الأفراد الأصحاء وكانت بمثابة السيطرة. المعلومات الشخصية والبيانات المتعلقة باختبارات تشخيص التهاب المفاصل الروماتويدي لدى المريض، بما في ذلك معدل ترسيب كرات الدم الحمراء، وعامل الروماتويد بواسطة اللاتكس وميندراي، والاختبار الأخير هو حمض البوليك. **النتائج**. كان متوسط SD ± لحمض البوليك بين حالات التهاب المفاصل الروماتويدي والسيطرة عليه، والذي لم يكن مهمًا، 3.96 ± 1.64 و4.10 ± 2.32 على التوالي(0.7 = P) ؛ مع AUC كان 0.509. بينما كان متوسط النتائج الأخرى مهمًا، كان متوسط SD ± لـ 33.3 ± 62.2 ESR إلى 37.5 ± 22.1(0.018 = P) ؛ مع AUC كان 0.694، وكان متوسط SD ± من اللاتكس 187 ± 90.0 RF إلى 8.08 ± 0.08(0.011 = P) ؛ مع AUC كان 0.709 ، يعني SD ± RA Mindray 130 ± 73.0إلى 4.24 ± 5.19 (0.006 = P) ؛ مع AUC هو 0.726. **الخاتمة**. أظهرت النتائج أن اختبار RF بواسطة مادة اللاتكس مفيد للتشخيص، مع ميزات أكثر مثل سهولة التقنية المستخدمة وسرعة ومنخفضة التكلفة. **الكلمات الدالة**. الحساسية والنوعية والاختبار التشخيصي والتهاب المفاصل الروماتويدي.