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ORIGINAL ARTICLE

Finding the Role of Elevated Antinuclear Antibodies (ANA) in Diagnosis and Treatment of Medically Critically Ill Patients

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ABSTRACT

Introduction: Antinuclear antibody (ANA) testing is an important screening tool for autoimmune conditions, such as systemic lupus erythematosus (SLE) and scleroderma.

Objectives: Finding the role of elevated antinuclear antibodies (ANA) in diagnosis and treatment of medically critically ill patients.

Material and methods: This cross sectional study was conducted THQ Hospital, Muree during July 2021 to November 2021. The data was collected from 600 patients of different diseases. In patient with multiple hospitalizations, the most recent one was considered for the study.

Results: The data was collected from 600 patients had their ANA levels drawn, out of which 78 were positive and 522 were negative. Out of the ANA positive patients, 14 (17 percent) had the values to 1:40, 29 (35 percent) had values to 1:80, 14 (17 percent) had values to 1:160, 8 (9.7 percent) had values to 1: 320, 11 (13.2 percent) had values to 1:640, 4 (4.8 percent) had values to 1:1280, 2 (2.4 percent) had values greater than >1:1280.

Conclusion: It is concluded that in patients with RA, important differences exist between those who are ANA-positive and ANA-negative in terms of time to fulfillment of RA criteria and time to DMARD initiation as well as choice of initial pharmacotherapy.

Keywords: ANA, Patients, Medically, Diagnosis

INTRODUCTION

Antinuclear antibody (ANA) testing is an important screening tool for autoimmune conditions, such as systemic lupus erythematosus (SLE) and scleroderma. Large population analyses, such as the Dallas Regional Autoimmune Disease Registry, have estimated that the ANA positivity rate is between 20% and 30% of the healthy general population. Antinuclear antibodies (ANA) and a type of antibodies that are produced against macromolecules in cell nuclei or the cytoplasm. Indirect immunofluorescence is the most widely method to detect ANA with additional solid phase assays also being available [1].

ANA autoantibodies are most commonly used to diagnose connective tissue diseases like SLE, systemic sclerosis and Sjogren's syndrome with their sensitivity varying with dilution. They are for instance 100 percent sensitive for Systemic sclerosis at a dilution of 1:40 and 87 percent sensitive at a dilution of 1:160. At the same time, they can be detected in 32 percent of normal population at a dilution of 1:40, with their prevalence dropping to 5 percent at 1:160 [2].

Anti nuclear antibodies can also be elevated in a number of other causes other than rheumatological illnesses like other autoimmune diseases (hashimoto thyroiditis, autoimmune hepatitis, primary biliary cirrhosis), infections like EBV, HIC, HCV, syphilis and lymphoproliferative malignancies. In addition, some medications like procainamide, hydralazine can also elevate ANA levels [3].

Although ANA are studies extensively for their utility in diagnosis of rheumatological illnesses and their presence in other clinical scenarios listed above, there is a very limited date on their significance when elevated in critically ill patients [4]. The purpose of our study is to see what is the prevalence and common probable causes for elevated ANA in critically ill patients and if there is any difference in their interpretation in critically ill patients. The primary outcome was hospital mortality, and secondary outcomes included duration of mechanical ventilation and MICU length of stay [5].

Objectives: The basic aim of the study is to find role of elevated antinuclear antibodies (ANA) in diagnosis and treatment of medically critically ill patients.

MATERIAL AND METHODS

This cross sectional study was conducted in THQ Hospital, Muree during July 2021 to November 2021. The data was collected from 600 patients of different diseases. In patient with multiple hospitalizations, the most recent one was considered for the study. ANA levels were detected using immunofluorescence assay technique. Patient with multiple ANA levels during the same admission, the highest value was recorded for the study.

Data collection: Baseline demographics (age, race and gender), WBC count, neutrophil percentage, hemoglobin level, platelet count. Manual chart review was formed to collect date on the presence of medical comorbid illnesses including acquired immune deficiency syndrome/human immune deficiency virus (AIDS/HIV) infection, hypertension (HTN), diabetes mellitus (DM), obstructive airway disease (OAD), chronic liver disease (CLD), congestive heart failure (CHF), coronary heart disease (CAD), chronic kidney disease (CKD), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), other rheumatological diagnosis. The admitting diagnosis of the patients were also recorded and were classified into Cardiac, GI, metabolic, neurological, pulmonary, obstructive airway disease, pulmonary, renal, sepsis/septic shock, and hematological.

Additional data collected included further testing of done for anti double-stranded DNA antibodies (anti-DsDNA), anti-smith antibodies, anti-U1-RNP antibodies, anti-Ro antibodies, anti-La antibodies, ant ribosomal P antibodies, antitopoisomerase-1, anticentromere antibodies, anti-jo-1 antibodies, Rheumatoid factor, Anti-cyclic citrullinated peptide antibodies and anti histone antibodies.

Statistical analyses were performed using IBM SPSS Statistic Version 21 (IBM Corp and others, 1989, 2013). Continuous normally distributed variables were reported using means and standard deviation.

RESULTS

The data was collected from 600 patients had their ANA levels drawn, out of which 78 were positive and 522 were negative. Out of the ANA positive patients, 14 (17 percent) had the values to 1:40, 29 (35 percent) had values to 1:80, 14 (17 percent) had values to 1:160, 8 (9.7 percent) had values to 1: 320, 11 (13.2 percent) had values to 1:640, 4 (4.8 percent) had values to 1:1280, 2 (2.4 percent) had values greater than >1:1280. Baseline demographics and clinical characteristics are given in Table 1.

Table 01. Baseline demographic, clinical and laboratory variables comparison with respect to ANA Group.

Table 1:

	High n=37	Low N=41	ANA - (n= 522)	P-value
Age ,Median (IQR)	57 (46.5- 66.5)	56 (45.5-66.5)	56 (42 – 67)	0.972
Sex (Females), n(%)	27 (73%)	25 (61%)	253 (48%)	0.006
AIDS/HIV	1 (3%)	6 (14%)	83 (16%)	0.094
HTN	23 (62%)	21 (51%)	299 (57%)	0.615
DM	14 (38%)	12 (29%)	142 (27%)	0.373
OAD	10 (27%)	13 (32%)	136 (26%)	0.730
CLD	71 (12%)	7 (9%)	64 (12%)	0.402
CHF	3 (8%)	4 (10%)	78 (15%)	0.686
CAD	6 (16%)	3 (7%)	57 (11%)	0.449
CKD	6 (16%)	6 (14%)	94 (18%)	0.838
SLE	9 (24%)	1 (2%)	4 (1%)	<0.001
RA	3 (8%)	2 (5%)	3 (1%)	<0.001
Other Rheum	3 (8%)	1 (2%)	9 (2%)	0.036
HB	10.5 (9.05 -12.6)	11.6 (10.5 -12.95	11.7 (9.1-13.45)	0.181
Platelet count	228.5 (111.75-299.5)	257 (157-313.5)	195.5 (132 -274.75)	0.132
Albumin, serum	3.5 (2.7- 3.8)	3.7 (3-4.2)	3.6 (3-4.1)	0.250
Lymphocyte (count in blood)	12.5 (6.85-24.1)	11.8 (8.25-21.8)	13.2 (7.2 - 22.73)	0.983
Serum Creatinine	1.3 (0.85-2.65)	1.2 (0.8-1.7)	1.1 (0.8- 2.2)	0.648
Baseline Comorbidities/Risk factors, N (%)				

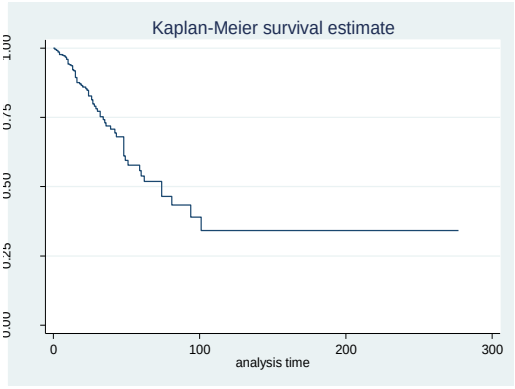

Figure 1: Survival curve for all patients

DISCUSSION

There is limited evidence that suggests that the presence of ANA antibodies in general population is not associated with an increased risk of cancer or mortality [6]. A study consulted by Selmi et al. looking at randomly selected 2828 subjects from a norther Italian region found that while the patients with positive ANA levels were more likely to develop connective tissue disorders, there was no increases risk of mortality or development of cancer in the patients with elevated ANA levels [7]. To our knowledge here has not been any studies looking at the hospital or ICU outcomes in patients based on their ANA Levels. A metanalysis of case reports and case series conducted by Quintero et al. on patients with autoimmune disease admitted to the ICU, found the mortality to range from 17 to 55 percent in patients with all autoimmune diseases [8]. They found that the studies looking on the patients with specific autoimmune illnesses, like SLE, mortality was as high as 79 percent. High APACHE score, multi-organ dysfunction, older age and cytopenia were the most reported variables associated with increased mortality [9].

A number of studies have looked at the frequency of positive ANA tests in "healthy" individuals. A study by Arroyave et al. in 1988 [3] screened sera from 241 "normal" children, testing for only IgG ANA, using both mouse kidney and human epithelial cells (HEp-2 cells). The study found a maximum positivity rate of only 2.0% at the lowest dilutions. However, data from adult studies have found much higher rates. In an adult study from 15 international laboratories using HEp-2 cells as substrate [10], ANA positive tests occurred in 31.7% of a putatively normal population at a serum dilution of 1:40. Even at a dilution of 1:320, 3.3% of the sera were positive. Interestingly the ANA frequency did not differ significantly across the age range of 20-60 years [11]. The rate of ANA positivity among blood donors in Holland was also quite high at 12.7%, with titers greater than 1:80 occurring in over 4% [12].

CONCLUSION

It is concluded that in patients with RA, important differences exist between those who are ANA-positive and ANA-negative in terms of time to fulfillment of RA criteria and time to DMARD initiation as well as choice of initial pharmacotherapy.

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