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Original Article

# Rheumatoid Factor Seropositivity and its Association with ABO and Rh Blood Groups in an Elderly Population

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ABSTRACT

Introduction: Rheumatoid factor (RF) is an autoantibody commonly found in rheumatic, non-rheumatic, and infectious diseases, as well as in some healthy elderly individuals. Given the established associations between ABO/Rh blood groups and various RF-related disease conditions, exploring a possible link between these blood group phenotypes and RF seropositivityis of scientific interest.This study aims to determine the association between ABO/Rh blood groups and rheumatoid factor antibody positivity among elderly individuals. Materials and Methods: A cross-sectional study was conducted among 92 elderly individuals aged ≥60 years. RF screening was performed using a latex agglutination method, while ABO and Rh blood groups were determined using the cell-tile method. Statistical analysis was carried out using SPSS version 22.0, with significance set at $p<0.05$. Results: RF antibody was positive in 29 (31.5%) of participants. Blood group distribution among RF positive and RF negative individuals followed the pattern O>A>B>AB and Rh D positive > Rh D negative. Pearson's chi-square analysis revealed no statistically significant association between ABO or Rh blood group and RF antibody status ($p>0.05$). Conclusion: The study found no significant association between ABO or Rh blood group phenotypes and rheumatoid factor antibody positivity among the elderly population studied.Larger, more diverse studies are needed to confirm these findings and identify other factors influencing RF positivity in the elderly.

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## Introduction

Rheumatoid factors (RF) are autoantibodies primarily directed against the Fc region of immunoglobulin G (IgG), often appearing in several autoimmune and inflammatory disorders [1]. Although they are a hallmark of rheumatoid arthritis (RA), RFs are not exclusive to it and may be present in other rheumatic conditions, infectious diseases, and even in a subset of healthy individuals, especially the elderly [2]. These autoantibodies can belong to the IgM, IgG, or IgA isotype classes [3]. Their development is generally triggered by an immunogenic stimulus, often in the form of microbial antigens such as bacterial lipopolysaccharides or viruses like the Epstein-Barr virus, suggesting the role of chronic immune activation in their pathogenesis. In RA patients, RF positivity has been strongly linked with increased disease severity and poor prognosis [4]. Nonetheless, elevated RF levels are also observed in other connective tissue disorders like Sjögren's syndrome, mixed connective tissue disease, systemic lupus erythematosus, and mixed cryoglobulinemia. Additionally, non-rheumatic and infectious conditions such as hepatitis B & C virus infection, tuberculosis, subacute infective endocarditis, sarcoidosis, and certain malignancies like primary sclerosing cholangitis are known to show increased RF levels, likely due to chronic immune stimulation and inflammation [5].

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RF presence may be transient and often resolves with successful treatment of the underlying condition.Fabien et al [6] reported RF positivity in 25% of individuals with rheumatic diseases other than RA, while Shim et al [7] found RF prevalence rates of 11.8% and 10.6% in hepatitis B and C patients, respectively. Hepatitis C–associated cryoglobulinemia, in particular, may result in RF levels as high as over 60%, due to the cold-precipitating IgM antibodies against IgG that define this condition [8].

Interestingly, low-level RFs, especially of the IgM type, are sometimes detected in the healthy elderly population, possibly as a reflection of age-related immune dysregulation. In this demographic, the prevalence of RF positivity may reach up to 4%, and it appears to be evenly distributed across both genders [9]. Despite its role in autoimmune pathogenesis, RF may also exert protective effects by enhancing the clearance of immune complexes and facilitating antigen presentation, especially during infections [9].

Parallel to the relevance of RF, human blood group systems, particularly ABO and Rhplay critical roles in immunology and disease susceptibility. Of the over 38 recognized blood group systems, ABO and Rh remain the most clinically significant due to their high immunogenicity and their implications for blood transfusion compatibility [10]. However, the relevance of these blood groups extends beyond transfusion medicine. Numerous studies have demonstrated associations between ABO/Rh blood groups and the susceptibility, progression, or severity of a wide spectrum of diseases, both infectious and non-infectious.

For instance, variations in blood group antigens have been linked to conditions such as diabetes mellitus, malaria, HumanImmunodeficiencyVirus (HIV) infection, certain cancers, and rheumatic diseases [11-15]. These associations are thought to arise from the interaction of blood group antigens with host immunity, microbial adhesion, and inflammatory pathways.Given the documented associations between ABO/Rh blood group phenotypes and various RF-associated disease conditions, it is scientifically plausible to investigate a potential relationship between ABO/Rh blood groups and the presence of rheumatoid factor antibodies.

Despite numerous studies on the distribution of ABO/Rh blood groups and the prevalence of RF in various conditions, limited data exist on whether a specific association exists between RF positivity and blood group types in elderly populations. As both RF levels and immune responses may be altered by aging, exploring this relationship could provide new insights into age-related autoimmunity and inform clinical decision-making.This study aims to determine the association between rheumatoid factor positivity and ABO and Rh blood group types among elderly individuals.

## Materials and Methods

### Ethics approval and consent to participate

Approval to carry out this study was obtained from the Research and Ethics Committee of Obafemi Awolowo University Teaching Hospital, Ile-Ife, Osun State, assigned number ERC/2023/12/17. Written informed consent was obtained from all participants.

### Study Population

The study comprised of 92 elderly individuals aged 60 years and above, attending geriatric clinics at Obafemi Awolowo University, Osun State, Nigeria.

### Inclusion Criteria

Individuals that were aged 60 years and above, and gave consent to participate in the study were included. Individuals below age 60 years and those who did not give informed consent were excluded.

### Sample Size Estimation

This was done using the Leslie Fischer method N=(Z^2 pq)/d^2 , with the prevalence of rheumatoid arthritis in elderly of 5% [16]. The estimated sample size was 72, however, 92 participants were recruited for this study.

### Sample Collection and Handling

2 mL of whole blood was collected aseptically from the antecubital vein of the study participants into a plain sample bottle. The blood samples were allowed to clot, and serum was separated. All samples were appropriately labelled for proper identification.

### Laboratory Analysis

### Rheumatoid Factor Screening

A latex agglutination slide technique was used, using the Precision®Rheumatoid Factor Latex Kit. 25µl of patient serum was placed intoseparate circles on a clean glass slide; a drop ofrheumatoid factor latex reagent was added on eachcircle of test sample and controls. It was mixed and spread to cover about 3cm diameter. It was observed for agglutination while tilting back and forth.

### ABO and Rh Blood Group Determination

Blood group was determined using cell grouping technique to detect red cell antigens using commercially prepared anti-sera. A drop of Anti-A, Anti-B, Anti-A+B and Anti-D sera were added to a drop of participants' red cell suspension on a white tile. It was mixed, tilted back and forth and observed for agglutination.

### Statistical Analysis

Data was analysed using Statistical Package for Social Sciences (SPSS) version 22.0. Descriptive statistics was expressed in frequency and percentage. Pearson's chi-square test was carried out to test for association between variables. Differences were considered significant at P-value<0.05

## RESULTS

The mean age of the study participants was 71.07±7.08. A larger proportion of the participants 63(68.5%) were negative for rheumatoid factor antibody. 29(31.5%) were rheumatoid factor positive as shown in Table 1.

**Table 1: Rheumatoid Factor Profile of Participants**

| | Frequency (N=92) | Percentage (%) |
|---|---|---|
| **RF Positive** | 29 | 31.5 |
| **RF Negative** | 63 | 68.5 |

Results in Table 2 revealed that there was no significant association between the sociodemographic of the participants and their RF status (p>0.05). However, there were more RF positive males 19(20.7%) compared to females 10(10.9%). The study population was dominated with married individuals 77(83.7%) while 7(7.7%) and 8(8.6%) were divorced and widowed respectively. Most of the study participants had secondary level of education 42(45.6%), followed by primary level of education 24(26.1%). There were also more self-employed 44(47.8%) and retired 31(33.7%) individuals among the study participants. 61(66.3%) carried out light and normal nature of work and 31(33.7%) had exhaustive jobs.

**Table 2: Sociodemographics of Study Participants**

| | RF Positive | RF Negative | x2 | df | P-value |
|---|---|---|---|---|---|
| **Gender** | | | | | |
| Male | 38 (20.7%) | 62 (33.7%) | 0.312 | 1 | 0.144 |
| Female | 20 (10.9%) | 64 (34.7%) | | | |
| **Marital Status** | | | | | |
| Married | 48 (26.1%) | 106 (57.6%) | 3.534 | 2 | 0.327 |
| Divorced | 2 (1.1%) | 12 (6.6%) | | | |
| Widowed | 8 (4.3%) | 8 (4.3%) | | | |
| **Educational Level** | | | | | |
| Uneducated | 4 (2.2%) | 8 (4.3%) | 0.845 | 3 | 0.544 |
| Primary | 10 (5.4%) | 38 (20.7%) | | | |
| Secondary | 32 (17.4%) | 52 (28.2%) | | | |
| Tertiary | 12 (6.6%) | 28 (15.2%) | | | |
| **Employment Status** | | | | | |
| Unemployed | 4 (2.2%) | 12 (6.6%) | 0.798 | 3 | 0.159 |
| Employed | 0 (0%) | 18 (9.7%) | | | |
| Self-employed | 30 (16.3%) | 58 (31.5%) | | | |
| Retired | 24 (13%) | 38 (20.7%) | | | |
| **Nature of Work** | | | | | |
| Light & Normal | 34 (18.5%) | 88 (47.8%) | 0.340 | 1 | 0.290 |
| Exhaustive | 24 (13%) | 38 (20.7%) | | | |

The ABO blood group distribution of the population followed O>A>B>AB. Among RF positive individuals, the majority had blood group O (17.4%), followed by group A (9.8%), group B (3.2%), and group AB (1.1%). Similarly, among RF negative individuals, blood group O was also the most common (37%), followed by group A (16.3%), group B (14.1%), and group AB (1.1%). Pearson's chi-square test revealed no significant association

between ABO blood group and RF status (x2=1.928; p = 0.587), as summarized in Table 3.

**Table 3: ABO Blood Group Distribution**

| | RF Positive | RF Negative | x2 | df | P-value |
|---|---|---|---|---|---|
| A | 9 (9.8%) | 15 (16.3%) | 1.928 | 3 | 0.587 |
| B | 3 (3.2%) | 13 (14.1%) | | | |
| AB | 1 (1.1%) | 1 (1.1%) | | | |
| O | 16 (17.4%) | 34 (37%) | | | |

Table 4 shows that 27 (29.3%) of the RF positive individuals were Rh 'D' positive, while 2 (2.2%) were Rh 'D' negative. In contrast, among RF negative individuals, 60 (65.2%) were Rh 'D' positive, and 3 (3.3%) were Rh 'D' negative. Pearson's chi-square test showed no significant association between Rh blood group and RF status (x2= 0.176; P = 0.675).

**Table 4: Rh Blood Group Distribution**

| | RF Positive | RF Negative | x2 | df | P-value |
|---|---|---|---|---|---|
| Rh 'D' Positive | 27 (29.3%) | 60 (65.2%) | 0.176 | 1 | 0.675 |
| Rh 'D' Negative | 2 (2.2%) | 3 (3.3%) | | | |

The most prevalent blood group was O Rh 'D' positive 48(52.2%), followed by A Rh 'D' positive 22(23.8%). Other blood groups had relatively lower frequencies, such as B Rh 'D' positive 15(16.3%), O Rh 'D' negative 2(2.2%), A Rh 'D' negative 2(2.2%), B Rh 'D' negative 1(1.1%), and AB Rh 'D' positive 2(2.2%). No cases of AB Rh 'D' negative was observed. There is no significant association between ABO/Rh blood group distribution and RF seropositivity (x2= 6.337; p=0.387), as shown in Table 5.

**Table 5: ABO/Rh Blood Group Distribution**

| | RF Positive | RF Negative | x2 | df | P-value |
|---|---|---|---|---|---|
| A Rh 'D' Positive | 8 (8.6%) | 14 (15.2%) | 6.337 | 6 | 0.387 |
| A Rh 'D' Negative | 1 (1.1%) | 1 (1.1%) | | | |
| B Rh 'D' Positive | 2 (2.2%) | 13 (14.1%) | | | |
| B Rh 'D' Negative | 1 (1.1%) | 0 (0%) | | | |
| AB Rh 'D' Positive | 1 (1.1%) | 1 (1.1%) | | | |
| AB Rh 'D' Negative | 0 (0%) | 0 (0%) | | | |
| O Rh 'D' Positive | 16 (17.4%) | 32 (34.8%) | | | |
| O Rh 'D' Negative | 0 (0%) | 2 (2.2%) | | | |

## DISCUSSION

This study revealed a rheumatoid factor antibody prevalence of 31.5% among elderly individuals, a value significantly higher than the 5% and 6% reported in a similar study conducted inElele and Port Harcourt, Rivers State, located in Nigeria's south-south region [16,17]. The disparity in prevalence rates could be attributed to methodological differences, as the Port Harcourt study utilized a convenience sampling approach, which may have underrepresented individuals with RF positivity while our study utilized purposive and simple-random sampling of individuals in a geriatric clinic. The Elele study also excluded individuals with infectious, cardiovascular and other autoimmune diseases apart from RA, while this study did not. Geographic and regional health disparities may also explain the observed variation.

Notably, the southwest region, where the current study was conducted, is documented to have a higher burden of certain infectious diseases, such as hepatitis B [18], which has been shown to contribute to elevated RF levels. Additionally, the prevalence of rheumatoid arthritis which is closely associated with RF positivityis reportedly high in the southwest, with studies indicating RA prevalence rates of 10.6% and 12.3% [19,20], while there is paucity of data in the south-south region for comparison.

These epidemiological differences suggest that comorbidities, chronic infections, and inflammatory conditions prevalent in the study region may have contributed to the elevated RF antibody prevalence observed. Interestingly, although no statistically significant association was identified, RF antibodies were more frequently detected in males than females in this study, aligning with findings from a systematic review and meta-analysis by Hadwen et al [21], which reported that while RA is more prevalent in females, RF seropositivity tends to be higher among males. Furthermore, the fact that about 13% of participants reported engaging in physically exhaustive work may have also influenced the observed RF positivity rate, as chronic stress and physical strain have been implicated in immune dysregulation and the potential triggering of autoimmune responses [22].

This study found no statistically significant association between rheumatoid factor antibody positivity and ABO or Rh blood group phenotypes distribution among elderly individuals. Despite numerous reports highlighting associations between ABO/Rh blood groups and a range of autoimmune, rheumatic, infectious, and non-communicable diseasessuch as rheumatoid arthritis, systemic lupus erythematosus, hepatitis B and C infections, HIV, and certain cancers [11-15] the present findings suggest that RF antibody presence may not be influenced by ABO or Rh blood type. The distribution pattern of ABO and Rh blood groups among both RF-positive and RF-negative individuals in this study mirrored the general blood group distribution reported in Nigeria and other African population, typically following the order O > A > B > AB and Rh D positive > Rh D negative [23-25].

This consistency may indicate that the distribution of ABO and Rh blood groups among RF-positive individuals reflects population-level norms rather than any disease-specific predisposition. Contrary to prior studies that reported associations between rheumatic diseases and specific ABO/Rh blood types [15,26,27], the lack of association in this study implies that such links, where they exist, may not be mediated by RF antibody production. Therefore, it may be inferred that the immunological mechanisms driving ABO/Rh associations in autoimmune diseases do not directly involve the RF autoantibody, at least in the context of the elderly population assessed in this study.

This study is not without limitations. The relatively small sample size of 92 participants may limit the statistical power to detect subtle associations between ABO/Rh blood groups and rheumatoid factor positivity, especially for less common blood group phenotypes. Additionally, the study was conducted at a single centre in southwestern Nigeria, which may affect the generalizability of the findings to broader populations with different genetic, environmental, or epidemiological backgrounds. The use of a latex agglutination method for RF detection, while suitable for screening, may lack the sensitivity and specificity of more advanced techniques such as Enzyme-Linked Immunosorbent Assay or nephelometry, potentially leading to under- or overestimation of RF positivity.

## CONCLUSION

This study found no significant association between ABO and Rh blood group types and rheumatoid factor positivity among elderly individuals. Although several studies have linked blood group phenotypes with various rheumatic, infectious, and non-communicable diseases, the findings from this research suggest that ABO and Rh blood groups may not serve as useful indicators for rheumatoid factor status in the elderly. Further studies with larger and more diverse populations are recommended to validate these findings and explore other possible determinants of rheumatoid factor positivity in aging individuals.

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