Original Article

Awareness and Frequency of Encounter With Subjects With Antiphospholipid Syndrome by Medical Practitioners in Tertiary and Some Other Health Institutions in Southeast Nigeria

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Abstract

Background: Antiphospholipid syndrome (APS) is an autoimmune multisystem disorder. There has been a limited number of reported cases from Nigeria. **Objectives**: To determine the awareness and frequency of encounters with APS cases by medical practitioners in health institutions in South East Nigeria. **Materials and Methods**: It was a descriptive cross-sectional study. All medical doctors met in the clinics who were willing to participate in the study were recruited during the period of the study. Statistical Package for Social Sciences was used for data entry, validation, and analysis. **Results**: A total of 581 study questionnaires were distributed to medical doctors met at the clinics and clinical meetings of five hospitals in Southeast Nigeria however, 581 were approximately filled and retrieved, giving an response rate of 94.84%. Males were 383 (69.5%) and females were 168 (30.5%). A total of 445 (80.8%) were unaware of the autoimmune multisystemic nature of APS. Of the 551 respondents, 348 (63.2%) were aware that Rheumatologist is the primary care physician for APS, 290 (52.6%) reported rarity of APS, and 366 (66.4%) had up to 50% overall knowledge of APS. Respondents' encounters with unexplained thrombotic events and unexplained stroke in the young were limited. A total of 62 (11.3%) were aware of the international classification criteria for APS. **Conclusion**: The authors conclude that APS awareness among medical practitioners in South East Nigeria is suboptimal.

Keywords: *Antiphospholipid antibody, antiphospholipid syndrome, autoimmune, medical practitioners*

Introduction

Antiphospholipid syndrome (APS) is an autoimmune multisystem disorder characterized by the existence of a heterogeneous group of autoantibodies called the antiphospholipid antibodies, which target a wide range of antigens on phospholipids and clinically presents with hypercoagulability and thrombosis in virtually all vessels of the body. The origins of the syndrome date back to the discoveries of the lupus anticoagulant by Conley and Hartmann in 1953 and, the recognition of the association between the biological false positive test for syphilis and autoimmune diseases by Moore and Mohr in the 1950s. Subsequent discovery as a disease entity and further work were between 1980

Submission: 17-May-2024, **First revision:** 12-Jun-2024, **Accepted:** 12-Aug-2024, **Published:** 18-Sep-2024.

Access this article online

Quick Response Code:

Website: www.ijmhdev.com

DOI: 10.4103/ijmh.ijmh_36_24

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How to cite this article: Okwara CC, Ekwuazi KE, Abonyi M, Ekochin F, Adiri W, Onwuchekwa I, *et al.* Awareness and frequency of encounter with subjects with antiphospholipid syndrome by medical practitioners in tertiary and some other health institutions in Southeast Nigeria. Int J Med Health Dev 2024;29:316-22.

and 1990 with no specific date in literature and also increasing understanding of the antiphospholipid antibodies till the late 1990s.[1]

Historically Sapporo criteria of 1999[2] used to be the universal criteria. However, APS classification criteria have been revised with the emergence of Sydney classification criteria[3] of 2006 and more recently that of the American College of Rheumatology/European Alliance of Associations for Rheumatology of 2023,[4] which recommended that a patient can be classified as having APS based on the presence of at least some clinical features such as thrombosis and fetal morbidity and mortality with a score of at least three points and laboratory features, such as antiphospholipid antibodies, with at least a score of 3.

APS is an established treatable cause of pregnancy losses[5] and a known cause of stroke in the young.[6] APS manifests with thrombosis in other organs and systems of the human body.

Over three decades ago, this APS was described yet the number of reported cases from Nigeria has remained within one digit figure[7-9] until recently Taiwo *et al*.[10] carried out a descriptive study at LAUTECH Teaching Hospital Ogbomoso Nigeria. They used triple autoantibody tests and found a 28.8% prevalence of APS among pregnant women with pregnancy complications attending antenatal care clinics.[10]

Other previous studies were only on frequencies of antiphospholipid antibodies among pregnant women rather than frequencies or prevalence of APS among Nigerians.[11] There is a paucity of knowledge of APS in Nigeria as alluded to by previous authors.[7-9] There has not been any previous prospective study that assessed the awareness of APS among medical practitioners and this applies also to Nigerian medical practitioners. Worrisome are the following questions: Are medical doctors in the tertiary institutions in South East Nigeria aware of antiphospholipid syndrome? Are there physician-related factors limiting case reports and diagnosis of the APS among Nigerians? We felt that the rarity of APS among Nigerians may have some yet unidentified physician-related factor. The awareness of medical practitioners and their consideration of this diagnostic possibility each time they come across patients may be one factor that is, not yet evaluated. The need to find out if the awareness (and consideration of APS in the differential diagnosis) is high among medical practitioners and exclude it as a cause of the apparent rarity of reported APS cases is the reason we embarked on this study.

This study aims to determine the awareness and frequency of encounters with APS cases by medical practitioners in three tertiary health institutions and some other hospitals in South East Nigeria.

Materials and Methods

It was a descriptive cross-sectional study. The convenience sampling method was employed for the recruitment of participants because it was the easiest. All medical practitioners met in the clinics of study centers and who were willing to participate in the study were recruited. Being a medical doctor and willingness to participate were the inclusion criteria. Those unwilling to participate were excluded. All cadres of the medical doctors that fulfilled the inclusion criteria were consecutively recruited at the clinics in five centers viz. the University of Nigeria Teaching Hospital Enugu, Enugu State University Teaching Hospital Enugu, Mount Camel Specialist Hospital Enugu, Raymond Anikwe Memorial Hospital Enugu, and Mother of Christ Specialist Hospital Enugu. Data collection was done using a pretest-modified self-administered questionnaire. Fifteen medical doctors were involved in the pretest self-administered questionnaire and their responses were used to prepare the modified self-administered questionnaire. The respondents were advised to give their honest responses so that the data collected would represent what the true situation was. The questionnaire had three subsections viz.: background information of respondent, awareness of APS, and frequency of encounter with APS and related condition(s). Ethical approval was sought and obtained from the University of Nigeria Teaching Hospital (UNTH) Health Research Ethics Committee in 2018. The Ethical approval number was NHREC/05/01/2008B-FWA00002458-IRB00002323. A written informed consent was obtained from each participant before recruitment into the study, and the study was performed in accordance with the ethical principles of Helsinki Declaration.

Statistical analysis

The Statistical Package for Social Sciences (IBM Corp., Released 2021. IBM SPSS Statistics for Windows, Version 28.0, Armonk, NY, USA) was used for data entry, validation, and analysis. The proportion of variables was expressed as percentages. Data and results were presented in prose, figures, and tables. Scores in domains tested were used to compute the composite score for the overall knowledge of APS and a score above half was interpreted as a pass mark.

Result

A total of 581 study questionnaires were distributed by the researchers to medical doctors met at the clinics and clinical meetings of three tertiary health institutions and other big private hospitals in South East Nigeria. All respondents were medical doctors actively practicing their various specialties and training programs. Only 551 responses were received giving an responder rate of 94.84%. Age group distribution was young 462 (83.8%), middle-aged 78 (14.2%), and elderly 11 (2.0%). The gender distribution of males was 383 (69.5%) and females was 168 (30.5%).

Specialty distribution of respondents

Figure 1 shows the distribution of the respondents according to specialty. Preregistration doctors (i.e., house officers rotating through the four specialties of medicine, surgery, pediatrics, and obstetrics and gynecology) were the most frequently 177 (32.1%) encountered during the questionnaire delivery at the clinics and meetings and followed by other cadres of doctors in the medicine department 151 (27.4%).

Status in the training of respondents

Of the 551 respondents 213 (38.7%) were house officers, 126 (22.9%) were registrars, 116 (21.1%) were fellows, 75 (13.6%) were senior residents, and 21 (3.8%) were medical officers.

Awareness of APS as a multisystem autoimmune disorder

Four hundred and forty-five respondents (80.8%) were unaware of the autoimmune multisystemic nature of APS, 102 (18.5%) were not sure of their awareness status, and only 4 respondents (0.7%) were certainly aware that APS is a multisystem autoimmune disorder.

Awareness of who should primarily manage APS

Of the 551 respondents 348 (63.2%) were aware of the rheumatologist as the primary care physician for APS, 102 (18.5%) were unaware, and 97 respondents (17.6%) were uncertain about their awareness that APS is primarily managed by a consultant rheumatologist. Four (0.7%) of these respondents gave no response to the question on their awareness of who primarily manages APS.

Awareness of the multidisciplinary nature of the management of APS

About 456 (82.8%) responded that APS requires multidisciplinary management, 70 (12.%) were unsure,

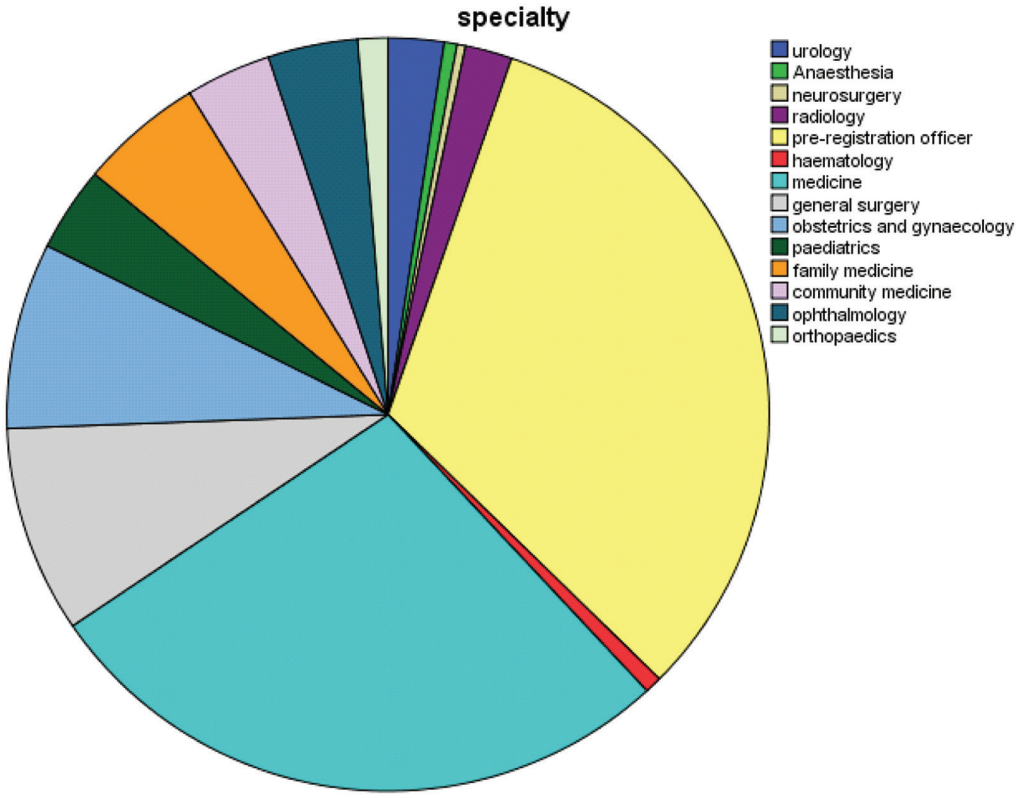

Figure 1: Distribution of respondents by specialty of practice

and 25 (4.5%) responded that APS does not require multidisciplinary management.

Awareness of presenting clinical features of APS

The frequency of awareness of presenting features for APS was assessed and it was found that of the 551 respondents 392 (71.1%) knew about fetal losses and intrauterine growth retardation as presenting clinical features. The frequencies of awareness of other clinical features of APS are shown in Table 1. The frequency of uncertainty about the presenting features of APS as reported by respondents was 238 (43.2%) for pre-eclampsia. Other frequencies are shown in Table 1.

Awareness of the rarity of APS

The respondents that were aware that APS is rare were 290 (52.6%), unaware 65 (11.8%), and 184 (33.4%) were uncertain. However, 12 (2.2%) respondents did not answer this question.

Overall knowledge of APS

This was derived by giving a score of 1 for each correct answer in the questions (a) awareness of multisystemic nature of APS, (b) awareness of rheumatologist as primary care physician for APS, (c) awareness of clinical features of APS: (i) fetal losses and intrauterine growth retardation, (ii) thrombosis, and (iii) pre-eclampsia, (d) awareness of rarity of APS, and (e) awareness that APS requires multidisciplinary management giving a maximum score of 7 and minimum of 0. Scores were whole numbers and a score of 4/7 represented at least 50% of the maximum score. Five hundred and forty-seven respondents filled these sections of the questionnaire and of these 366 (66.4%) had scores of 4 and above, whereas 181 (32.9%) had scores of 3 and below. Four (0.7%) respondents had incomplete filling of the section of the questionnaire.

Frequency of encounter by respondents with clinical features that suggested APS and suspected APS

Of the 551 medical practitioners, 326 (59.1%) had had encounters with unexplained miscarriages, 255 (46.2%) with intrauterine growth retardation, and 429 (77.8%) with hypertension in pregnancy. The other encounters frequencies are shown in Table 2. Of the 126 medical practitioners (22.8%) that came across suspected cases of APS, only 4 followed up the cases for confirmation as APS. Of these four confirmed APS cases, presenting complaints that suggested APS were pregnancy losses and thrombotic events in 75% and 25%, respectively.

Awareness of international classification criteria (ICC) for APS

Of the 551 respondents, only 62 (11.3%) were aware of an ICC for APS, 454 (82.4%) respondents were unaware, and 35 (6.4%) respondents did not answer this question.

Autoantibodies awareness

Out of all the 551 respondents, 274 (49.8%) were unaware of the autoantibody antiβ2glycoprotein 1. The frequencies of awareness for lupus anticoagulants and false-positive venereal disease research laboratory (VDRL) are shown in Table 3. The frequencies for unawareness for the autoantibodies and serologic tests for APS are also shown in Table 3.

Table 1: Awareness of presenting clinical features of APS

Test	Aware *N* (%)	Unaware *N* (%)	Uncertain about response *N* (%)	No response *N* (%)
Awareness that APS presents with fetal losses and intrauterine growth retardation	392 (71.1)	13 (2.4)	126 (22.9)	20 (3.9)
Awareness that APS presents with thrombosis	361 (65.5)	20 (3.6)	162 (29.4)	8 (1.5)
Awareness that APS presents with pre-eclampsia	278 (50.5)	31(5.6)	238 (43.2)	4 (0.7)

Table 2: Frequency of encounters by respondents with clinical features that suggested APS and suspected APS

Encounter with specified clinical feature	Never seen *N* (%)	Seen at least 1 per year *N* (%)	Seen 1 in 2–3 years *N* (%)	Rarely	No response *N* (%)
Unexplained thrombotic events	207 (37.6)	183 (33.2)	71 (12.8)	45 (8.2)	45 (8.2)
Unexplained stroke in the young	196 (35.6)	165 (29.9)	94 (17.1)	59 (10.7)	37 (6.7)
Unexplained miscarriage	71 (12.9)	326 (59.1)	77 (14.0)	42 (7.6)	35 (6.4)
Intra-uterine growth retardation	95 (17.2)	255 (46.2)	49 (8.9)	76 (13.8)	76 (13.8)
Hypertension in pregnancy	31 (5.6)	429 (77.8)	27 (4.9)	15 (2.7)	49 (8.9)
Pre-eclampsia	94 (17.1)	298 (54.1)	73 (13.2)	33 (6.0)	53 (9.6)
Suspected APS	375 (68.1)	55 (10.0)	25 (4.5)	46 (8.3)	50 (9.1)

Awareness of the availability of serological tests for diagnosis of APS in South East Nigeria

About 448 (81.3%) respondents were unaware of the availability of antiβ2glycoprotein 1 antibodies testing in Enugu. Awareness of the availability of antibody testing was recorded by 171 (31%) for lupus anticoagulants, and the rest was shown in Table 4.

Diagnosis of APS competence

On the questions that tested their choice of parameters for the diagnosis of APS (a) clinical features only, (b) serologic tests only, (c) combination of clinical and serologic tests, and (d) ICC for diagnosis of APS. About 404 (73.3%) did not respond, 51 (9.3%) responded they would use ICC, 62 (11.3%) reported they would use clinical features only, and 34 (6.1%) reported they would use serologic tests only.

Discussion

This study showed that most of the study participants (>80%) had poor awareness of the multisystemic nature of APS. If the multisystemic nature of a disease entity is not borne in mind, that disease entity will not likely be put up in the list of differential diagnoses during the evaluation of a patient with multisystemic presentation. This low knowledge can have a remarkable effect on their index of suspicion in the face of a probable case or potentially possible case of APS. However, the finding over 80% of the respondents knowing that there is a need for multidisciplinary management makes difficult the interpretation of the finding of poor awareness of multisystemic nature. Our search of the published data did not yield any previous studies in the medical literature that specifically looked at awareness by medical doctors of the multisystemic nature of APS. Therefore, this is the first of such a study and can form the basis on which further study can be done.

This study also found that a significant number of the respondents have never encountered any patient with features suggestive of APS. This could be due to some factors, such as a reasonable number of the respondents were pre-registration officers and as such they had fewer than a year of medical practice experience. Other plausible explanations may be the intrinsic low knowledge base of the respondents and or the not well-established fact that APS is not a common disease. The responses to the other domains of awareness revealed majority had good knowledge of these other aspects of APS. Moreover, for the score of overall knowledge of APS, the majority demonstrated at least 50% overall knowledge of APS. This is, however, a designed convenient and composite analysis. Again our search of the published data did not yield any previous studies in the medical literature that specifically looked at the frequency of encounters of patients with features suggestive of APS by medical doctors. Therefore, this is the first of such a study and can form based on which further study can be done.

The presence of autoantibodies is one of the parameters in the ICC for the diagnosis of APS. The diagnosis of APS is evidence-based, and the parameters are clinical and laboratory. Both must be fulfilled for the patient to be classified as having APS. From the results, the majority of the respondents were unaware of the diagnostic criteria for APS. This can affect their thought process during probable or true APS case presentation to them and eventual evaluation. Looking at the respondent's autoantibodies responses, apart from β2 glycoprotein 1 antibody, the majority of the respondents were aware of the autoantibodies to screen for. However, the majority of them reported that they were not aware of the availability of these serological tests in Enugu. Therefore, this suggested that the awareness of the availability of serological markers is still low among medical practitioners in the study

Table 3: Awareness of autoantibodies for APS

Autoantibody	Awareness of autoantibodies *N* (%)	Unaware of autoantibodies *N* (%)	Nonresponse *N* (%)
Anticardiolipin antibodies	372 (67.6)	154 (27.9)	25 (4.5)
Antiβ2glycoprotein 1 antibodies	198 (35.9)	274 (49.8)	79 (14.3)
Lupus anticoagulant	355 (64.4)	139 (25.2)	57 (10.3)
False positive VDRL	389 (70.6)	114 (20.7)	48 (8.7)

Table 4: Awareness of the availability of serological tests for diagnosis of APS in South East Nigeria

Autoantibody	Aware of autoantibodies availability in Enugu South East Nigeria *N* (%)	Unaware of autoantibodies availability in Enugu South East Nigeria *N* (%)	Non response *N* (%)
Anticardiolipin antibodies	122 (22.2)	408 (74.0)	21 (3.8)
Antiβ2glycoprotein 1 antibodies	59 (10.7)	448 (81.3)	44 (8.0)
Lupus anticoagulant	171 (31.0)	348 (63.2)	32 (5.8)
False positive VDRL	117 (21.2)	401 (72.8)	33 (6.0)

area. Again no such previous studies in the literature for comparison. The lack of knowledge of classification criteria and the availability of these tests locally could have contributed to their inability to recognize cases and thus to the low diagnosis rate in the areas of practice of these medical practitioners. Lack of awareness of diagnostic criteria and lack of diagnostic acumen may explain the failure of these respondents who had encountered these suspected cases of APS but did not pursue the evaluation to a logical diagnosis. It may also be inferred that these two areas of deficiencies viz. low knowledge of the multisystemic nature of APS and low diagnostic acumen could have contributed to the low report of APS cases in the region. This low awareness could explain partly the reported incidence and prevalence of APS in Nigeria. The above findings are worrisome because the disease entity in question APS is a major cause of morbidity and a significant but easily treatable disease. The medical literature is awash with the etiopathogenesis and pathology of APS. There is a dearth of publications of study on knowledge and awareness of APS in the medical literature. Our search did not reveal such a publication in the past, hence comparison with previous publications in this was not done. There is a great need to fill in the knowledge gap hence we embarked on this study. APS is increasingly being recognized as an important predisposing medical condition to the development of thrombosis, especially ischemic stroke in the young and recurrent pregnant losses and intrauterine fetal morbidities.

The cost of tests to establish this diagnosis is exorbitant. Health in Nigeria is paid for largely out of pocket. Thus, even when the need for this important screen is entertained, the financial power becomes a major hindrance. However, missing this all-important diagnosis in a patient is also very costly eventually considering the morbidity and mortality that could result.

Study limitations

Limitations of this study include the possibility that many doctors would have been missed since the study was done only during clinic hours and meetings and the dependence on the respondents' recall nature for the answers to the questions.

Conclusion

APS awareness among medical practitioners in South East Nigeria is suboptimal. The reported encounter and eventual diagnosis of APS are low.

Recommendations

The low awareness of APS in this study among practitioners can cause potentially significant adverse emotional and physical distress among affected patients. Hence, concerted efforts including the creation of awareness should be undertaken to address this knowledge gap as well as upgrade the diagnostic capacity of this condition in hospitals.

Declaration of Helsinki

The study was conducted according to the principles of the Helsinki Declaration.

Acknowledgment

The author would like to acknowledge Nkechi Aleke (permission obtained) who helped with the data entry.

Author contributions

CCO: conceptualization, design, data collection, statistical analysis, writing of draft and revision of manuscript, and final approval for publication. KEE: data collection, draft writing and revision, and final approval for publication. MO, FE, WA, CN, IO, NO, IO, HN, NE, TN, and GO: draft writing, draft revision, and final approval for publication.

Data availability

The authors are available and ready to supply the data upon any request through the corresponding author.

Ethical approval

Ethical approval was sought and obtained from the UNTH Health Research Ethics Committee in 2018. The Ethical approval number was NHREC/05/01/2008B-FWA00002458-IRB00002323.

Informed consent

A written informed consent was obtained from each participant before enrollment into the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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