BRIEF REPORT

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Level of Awareness of Acquired Hemophilia A Among Physicians in Türkiye: A Survey Study

Türkiye'deki Hekimlerde Edinsel Hemofili A Hakkında Farkındalık Düzeyi: Anket Çalışması

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Abstract

This survey study aimed to evaluate the level of awareness and knowledge of acquired hemophilia A (AHA) among physicians from various specialties. Data were collected by administering a questionnaire containing questions about two patient profiles to evaluate the approaches of physicians from different specialties. The study included a total of 945 physicians. The most common suspected diagnosis for the clinical patient profile was immune thrombocytopenia, followed by hemophilia. For the laboratory patient profile, the most common suspected diagnosis was hemophilia. While only 9.4% of the physicians stated that they had good knowledge of this disease, only 21.6% wanted to learn more about AHA. Most of the participating physicians do not rank AHA first in the differential diagnosis of a patient with clinical and laboratory findings of AHA. Appropriate educational activities to raise awareness of AHA will help reduce disease-related morbidity and mortality.

Keywords: Acquired hemophilia A, Surveys, Physicians' practice patterns, Awareness

Öz

Bu anket çalışması, çeşitli uzmanlık alanlarından hekimler arasında edinsel hemofili (AHA) hakkındaki farkındalık ve bilgi düzeyini değerlendirmeyi amaçlamıştır. Veriler, farklı uzmanlık alanlarından hekimlerin yaklaşımlarını değerlendirmek için iki hasta profili hakkında sorular içeren bir anket uygulanarak toplandı. Çalışmaya toplam 945 hekim katılmıştır. Klinik hasta profili için en çok şüphelenilen tanı immün trombositopeniydi ve bunu hemofili izliyordu. İkinci laboratuvar hasta profili için en sık şüphelenilen tanı hemofili olmuştur. Hekimlerin sadece %9,4'ü bu hastalık hakkında iyi bilgiye sahip olduğunu belirtirken, sadece %21,6'sı AHA hakkında daha fazla bilgi edinmek istediğini ifade etmiştir. Hekimlerin çoğu, AHA'nın klinik ve laboratuvar bulgularına sahip bir hastada ayırıcı tanıda AHA'yı ilk sıraya koymamaktadır. AHA hakkında farkındalığı artırmaya yönelik uygun eğitim faaliyetleri, hastalıkla ilişkili morbidite ve mortalitenin azaltılmasına yardımcı olacaktır.

Anahtar Sözcükler: Edinsel hemofili A, Anket, Hekimlerin uygulama yaklaşımları, Farkındalık

Introduction

Acquired hemophilia A (AHA) is a rare, potentially fatal coagulation disorder, which is usually seen in elderly individuals without a history of bleeding disorders and is associated with autoantibodies against factor VIII (FVIII) [1,2]. In half of these patients, autoimmune disorders, hematologic malignancies, solid tumors, respiratory system disorders, skin conditions, pregnancy, drug reactions, infections, and vaccinations have been reported to coincide with AHA [1,2,3,4,5,6].

AHA should be included in the differential diagnosis of any patient with a history of unexpected, new-onset bleeding and consistent physical findings. In cases where the platelet count, prothrombin time (PT), and thrombin time (TT) are normal but the activated partial thromboplastin time (aPTT) alone is

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prolonged, a mixing test (inhibitory screening test) is required to confirm the diagnosis.

Morbidity and mortality rates are high among symptomatic, untreated patients. The rareness of the disease, low levels of awareness among physicians, and the complexity of the laboratory assessments usually lead to delayed diagnosis [7,8]. Thus, raising awareness of AHA among physicians of patients with a high potential of having this disease is of utmost importance to ensure their immediate referral to an expert for appropriate management [7,9].

This survey study evaluated the levels of awareness and knowledge of AHA among physicians from various specialties.

Materials and Methods

Physicians from different specialties with a high potential of encountering patients with AHA were invited to take part in this cross-sectional survey study. The study was approved by the local ethics committee. All of the participating physicians provided their written informed consent. A sample size with a 95% confidence interval and 3% margin of error was estimated to include at least 940 participants. The study group consisted of specialists recruited from 6 different fields of medicine (obstetrics and gynecology, rheumatology, emergency medicine, internal medicine, medical oncology, and adult hematology) according to the distribution rate of specialties in Türkiye.

The questionnaire used in this survey study consisted of the 13 questions provided in Table 1. Physicians were given two patient profiles, one with clinical findings (Table 2) and the other with laboratory findings (Table 3) of AHA, and were asked to comment on the probable diagnoses of the patients and how they would approach and manage each case. Statistical analyses were performed using IBM SPSS Statistics 21.0 with a statistical significance level of 0.05. Numerical variables were expressed as means and standard deviations, while categorical variables were expressed as frequencies and percentages. Comparisons among subgroups were performed using the chi-square test.

Table 1. Questionnaire.

Section A: Demographic information
DI1. The city in which you live
DI2. Main specialty
- Gynecology
- Rheumatology
- Emergency service medicine
- Internal medicine
- Medical oncology
- Adult hematology

DI3. Main site of practice
- Public hospital
- Research and training hospital
- University hospital
- Private hospital

DI4. Name of institution for which you work

Section B: Query form
Q1. How many patients have you seen within the past 12 months? (Please count those whom you saw more than once in a month for control visits as 1 patient)
Q2. Have you encountered a patient similar to the sample profiles within the past 12 months?
Q2a. How many patients have you encountered matching the profile(s)?
Q3. Which disorder would you suspect in a patient presenting with such profile(s)?
Q4. Would you treat such a patient or rather prefer referring him/her to an expert?
Q5. Which medical specialty would you refer this patient to?
Hematology
- Pediatric hematology
- Internal medicine
- Other (Please specify) .....

Q6. Which of the following diseases is most likely to underlie the condition in the profile(s)?
- What could be the second most likely diagnosis?
- What could be the third most likely diagnosis?

(If you have no idea of the clinical condition given in the profile(s), please select "I don't know.")

- Hemophilia.
- Immune thrombocytopenia
- Sepsis
- Von Willebrand disease
- Other (Please specify)
- I don't know
- If your most likely diagnosis is "Hemophilia" in Q6:

Q6a. Which of the following diagnoses best matches the condition in the profile(s)?
- Congenital hemophilia
- Acquired hemophilia
- I am not sure/I don't know

Q7. Please rate your level of knowledge of acquired hemophilia on a 7-point scale.
Q8. What is the number of patients with acquired hemophilia you have encountered during your entire professional life?
Q9. Would you like to receive information about the management of acquired hemophilia
from the pharmaceutical companies working in this therapeutic field?

Results

A total of 945 physicians (mean age: 36.7±9.6 years; range: 24-70 years) working in different departments of hospitals were included. Over 66% of the physicians reported having seen cases with clinical profiles indicating AHA among a total of 7819±5497 (median: 7000) patients within the past 12 months (Table 4).

When physicians were asked about the diagnosis of the patient given in Table 2 using an open-ended question, the most common response was immune thrombocytopenia (ITP) (23.4%), followed by hemophilia (18.3%). The percentages of physicians suspecting hemophilia were significantly higher among hematologists (27.5%) and rheumatologists (29.5%) (Table 5). The rate of physicians who included AHA in the differential diagnosis was 31.1%. Almost all hematologists

Table 2. Profile 1.

Presence of the following clinical symptoms in patients with no previous personal or family history of bleeding:
1. Purpura (widespread ecchymoses), hematoma, and soft tissue bleeding
2. Prolonged postoperative bleeding
3. Persistent postpartum bleeding
4. Retroperitoneal bleeding
5. Gastrointestinal and urological bleeding
6. Compartment syndrome with neurovascular complications

Source: Türk Hematoloji Derneği, *Edinsel Hemofili Tanı ve Tedavi Kılavuzu* (Diagnosis and Treatment Guidelines for Acquired Hemophilia by Turkish Society of Hematology) [2].

Table 3. Profile 2.

Presence of the following findings in a patient with no personal or family history of bleeding tendency:

1. Isolated prolonged aPTT (activated partial thromboplastin time >40 seconds, normal thrombin time, normal prothrombin time, no anticoagulation therapy) in a patient with or without signs of bleeding
2. Age >65 years or history of pregnancy in the past 1 year
3. Failed correction of prolonged aPTT in mixing study suspicious for presence of an inhibitor

aPTT: Activated partial thromboplastin time.

Source: Türk Hematoloji Derneği, *Edinsel Hemofili Tanı ve Tedavi Kılavuzu* (Diagnosis and Treatment Guidelines for Acquired Hemophilia by Turkish Society of Hematology) [2].

Table 4. Number of physicians who encountered patients matching the provided profiles in the last 12 months.

Specialty	n	Matching the clinical profile (Profile 1)	Matching the laboratory profile (Profile 2)
Emergency medicine	152	119 (78.3%)	55 (36.2%)
Adult hematology	80	72 (90%)	54 (67.5%)
Internal medicine	302	227 (75.2%)	111 (36.8%)
Gynecology	249	195 (78.3%)	73 (29.3%)
Medical oncology	101	69 (68.3%)	35 (34.7%)
Rheumatology	61	39 (63.9%)	19 (31.1%)
Total	945	721 (76.3%)	347 (36.7%)

Table 5. Number of physicians stating or choosing "Hemophilia" as the most likely diagnosis for the patients described in the profiles.

		Clinical profile (Profile 1)		Laboratory profile (Profile 2)	
	n	Hemophilia as the most likely diagnosis in the open-ended question	Hemophilia as the most likely diagnosis in the multiple-choice question	Hemophilia as the most likely diagnosis in the open-ended question	Hemophilia as the most likely diagnosis in the multiple-choice question
Emergency medicine	152	25 (16.4%)	49 (32.2%)	37 (24.3%)	68 (44.7%)
Adult hematology	80	22 (27.5%)	39 (48.8%)	26 (32.5%)	60 (75%)
Internal medicine	302	48 (15.9%)	80 (26.5%)	79 (26.2%)	170 (56.3%)
Gynecology	249	40 (16.1%)	68 (27.3%)	71 (28.5%)	114 (45.8%)
Medical oncology	101	20 (19.8%)	41 (40.6%)	31 (30.7%)	59 (58.4%)
Rheumatology	61	18 (29.5%)	25 (41%)	19 (31.1%)	35 (57.4%)
Total	945	173 (18.3%)	302 (32%)	263 (27.8%)	506 (53.5%)

Table 6. Physicians' self-evaluation of their level of knowledge of acquired hemophilia.

	n	Low knowledge	Limited knowledge	Good knowledge
Emergency medicine	152	24 (15.8%)	121 (79.6%)	7 (4.6%)
Adult hematology	80	1 (1.3%)	44 (55%)	35 (43.8%)
Internal medicine	302	52 (17.2%)	230 (76.2%)	20 (6.6%)
Gynecology	249	60 (24.1%)	179 (71.9%)	10 (4%)
Medical oncology	101	17 (16.8%)	72 (71.3%)	12 (11.9%)
Rheumatology	61	10 (16.4%)	46 (75.4%)	5 (8.2%)
Total	945	164 (17.4%)	692 (73.2%)	89 (9.4%)

(93.8%) indicated that they would treat the patient with the given profile, while the majority of non-hematologists (81.2%) stated that they would rather refer the patient to a different specialty, mainly to hematology (87.0%).

When the same question was asked in a multiple-choice format (Table 1, Q6), ITP (39.6%) and hemophilia (32.0%) were the most frequently selected choices. Nearly 50% of the hematologists associated the given patient profile with hemophilia. Hemophilia was significantly less considered among physicians aged ≥41 years compared to younger age groups (65.7% vs. 83.5% and 84.4%, p=0.001). Only 40.2% of the physicians and 59.7% of the hematologists who suspected hemophilia further associated the clinical profile with AHA (Table 1, Q6a).

More than one-third of the physicians reported having seen cases consistent with the second profile (cases with laboratory findings indicative of AHA) within the past 12 months (Table 3). Hemophilia ranked first among the probable diagnoses for this profile, being suspected by 27.8% of the physicians (Table 5). AHA was considered (Table 1, Q6a) by 21.3% of hematologists and only 3.5% of all physicians. Hemophilia and AHA were indicated by 53.5% and 67.7% of the physicians, respectively, when given as multiple-choice options.

Only 9.4% of the physicians stated that they had a high level of knowledge regarding AHA and an additional 21.6% expressed their interest in learning more about AHA (Table 6). This interest was significantly higher in the age group of ≤30 years (p=0.003).

Discussion

Increased awareness of AHA is essential to prevent delays in the diagnosis and treatment of this highly fatal disease [10]. In our study, 18.3% of the physicians listed AHA among the probable diagnoses for the given clinical patient profile. In a recent study with similar results, Taher et al. [5] suggested that the awareness of healthcare professionals should be raised and their level of knowledge regarding AHA should be improved. One-third of the physicians in our study indicated ITP as the most probable diagnosis even when hemophilia was also given as an option. Misdiagnosis is a global issue that is primarily associated with the rareness of the disease and probably also related to the underrepresentation of AHA in the medical education curricula, both of which contribute to low levels of awareness regarding the disease. A survey study conducted among non-hematologists working at tertiary medical centers in the Arabian Gulf showed that 42% of the responders were not aware of AHA [11].

Our study showed that physicians in the higher age groups had significantly lower levels of knowledge of AHA. This might be explained by the recent activities aiming to raise awareness of acquired hemophilia, which mainly target younger physicians in the field.

A great majority of the participants (90.6%) reported having limited or low levels of knowledge regarding the disease. Despite this, overall interest in learning more about AHA remained low with the exception of physicians aged ≤30 years, which might suggest that younger physicians have a higher motivation for learning.

Studies indicate that hematologists should play a major role in creating policies to increase physicians' awareness of AHA and provide guidance on its appropriate diagnosis and treatment [5]. In an expert opinion paper recently published by Dolan et al. [12], 10 key principles are listed for the management of AHA. Considering the importance of the issue, it seems to be crucial that these principles be globally implemented by integrating AHA into the training programs of medical schools and the curricula of both specialty training and continuing medical education activities to ensure an accurate and timely diagnosis and appropriate management.

Conclusion

The results of our study demonstrate that the level of awareness of AHA among physicians from various specialties in Türkiye is not adequate for the appropriate and timely diagnosis and treatment of the disease. Raising awareness of AHA, particularly among non-hematologists, would contribute significantly to

early diagnosis and help reduce the morbidity and mortality rates associated with AHA. We hope that our study will inspire the development of strategies and national education projects to improve countrywide awareness of AHA.

Ethics

Ethics Committee Approval: This study was approved by the local ethics committee (Trakya University Medical School Scientific Ethics Committee: TUTF-BEK 2021/399).

Informed Consent: All of the participating physicians provided their written informed consent.

Authorship Contributions

Concept- A.M.D., M.C.A., F.Ş., M.A.; Design- A.M.D., M.C.A., F.Ş., M.A.; Data Collection or Processing- A.M.D., M.C.A., F.Ş., M.A.; Analysis or Interpretation- A.M.D., M.C.A., F.Ş., M.A.; Literature Search- A.M.D., M.C.A., F.Ş., M.A.; Writing- A.M.D., M.C.A., F.Ş., M.A.

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