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Global Research Trends on Schistosomiasis

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Abstract

Objective: This study aimed to determine the characteristics and trends of published articles on schistosomiasis through bibliometric analysis.

Method: The VOSviewer visualization methodology was used to conduct a bibliometric study. The data included articles from the Web of Science database, nations, institutions, journals, keywords, co-authorship, co-citations, international collaborations, and citation rates.

Results: A total of 23379 articles from 1970 to 2023 were included in the study. It has been determined that there has been a continuous increase in publications on schistosomiasis over a ten-year period. When analysing the top ten institutions supporting schistosomiasis research, the USA, the UK, England, China, Brazil and Portugal were the countries that supported schistosomiasis research the most. VOSViewer showed a strong collaboration between countries for schistosomiasis research. Most of the articles were in the field of parasitology, tropical medicine, immunology, Public environmental occupational health and infectious diseases. Network visualization using VOSViewer showed that the keywords used in schistosomiasis-related publications were divided into three clusters, with the keywords “prevalence”, “mouse” and “protein” standing out.

Conclusion: Over a period of ten years, a steady increase in publications on schistosomiasis has been found, demonstrating that schistosomiasis is still an important public health problem. Organisations and researchers in the USA, UK, Brazil and China lead the scientific production on schistosomiasis. Globally, developed countries were seen to be leading the way in controlling schistosomiasis.

Keyword: Schistosomiasis, publications, bibliometric analysis

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INTRODUCTION

Schistosomiasis is an acute and chronic parasitic disease caused by blood parasites of the Schistosoma genus (trematode worms) (1). Schistosomiasis, a serious infectious disease, is the second leading cause of morbidity in the world after malaria. *Schistosoma mansoni, S. japonicum,* and *S. haematobium* are the three primary schistosomes that infect humans (2).

Schistosoma species that settle in the human body may cause symptoms such as myalgia, urticaria, abdominal pain, diarrhea, fatigue, weakness, and fever, while *S. haematobium* may additionally cause symptoms such as hematuria. Inflammatory and obstructions that occur as a result of immunopathological reactions against *Schistosoma* spp. eggs located in the host tissues cause chronic symptoms. Chronic infections may result in anemia, growth retardation, hepatosplenomegaly, rectal prolapse, portal hypertension, bloody mucus diarrhea, cirrhosis, neurological complications and even death (3-6). S. mansoni and S. japonicum cause intestinal schistosomiasis by affecting the rectum, colon, and liver. *Schistosoma haematobium*, the most common of the Schistosoma species, causes urinary schistosomiasis. Hematuria, dysuria, hydronephrosis, and pain in the perianal and pubic region are symptoms of urinary schistosomiasis. In the later stages of the disease, bladder calcifications, urinary tract fibrosis, obstructive uropathy and bladder malignancies are seen (3, 7-9).

S. haematobium can cause different symptoms by affecting the urogenital organs in men and women. The most common clinical manifestations in women are dysmenorrhea, menstrual disorders, post-coital bleeding, pain during sexual intercourse, cervicitis, infertility, endometriosis, and nodules in the vulva. In men, epididymitis, infertility, and prostatitis are seen (1,10).

The World Health Organization (WHO) classifies schistosomiasis as a neglected tropical disease. According to WHO estimations, at least 236.6 million individuals in 2019 required preventative therapy. Morbidity will be reduced and avoided with preventive treatment, which must be repeated over several years (1). Globally, this disease is expected to affect approximately 250 million people in 78 countries, resulting in more than 280,000 deaths per year (2). However, only 51 endemic countries with moderate-to-high transmission rates require preventive chemotherapy for schistosomiasis, where large-scale treatment of individuals and communities is targeted (1). Although there are regional bibliometric

studies, no similar global studies were found (11-14). Existing studies are either localized in a sub-title (treatment/infection control) or in a country. This study was planned to evaluate global research on schistosomiasis.

METHODS

Study Design and Search Strategy

A bibliographic review (retrospective study) was conducted using the bibliometric analysis method. To build the literature dataset, the Web of Science Core Collection (WoSCC) electronic database was used, which offers a complete and standardized collection of data for export and is frequently used by academics.

Data Collection

The keywords 'schistosomiasis, Schistosoma, bilharziasis, bilharziases, and katayama' were used in this search. The literature search was conducted in a single day to avoid bias and take into account that the WoSCC database is frequently updated (April 5th, 2024). The year 2024 was omitted from the study because full data for 2024 were not available.

Criteria for Study Selection

A comprehensive search using the keywords schistosomiasis, Schistosoma, bilharziasis, bilharziases, and katayama in the WoSCC yielded a total of 31103 results. The search was then narrowed by eliminating Editorial Material, Notes, Meeting Abstracts, Proceeding Papers, Letters, Book Chapters, and Corrections from the Document Types tab, yielding 23900 results. The year 2024 was then excluded due to incomplete data, resulting in 23379 results. Two authors, one of whom was designated as the primary author, independently reviewed the publications and any discrepancies were resolved by the primary author.

Data Extraction and Visualization

Important data attributes that were extracted in Tab Delimited File format included the document titles, publication years, journal names, author(s) name(s), keywords, institutions, and countries. All extracted data, including the total number of publications and citations, came from the WoSCC database.

VOSviewer version 1.6.16 (Leiden University, Leiden, Netherlands) was used to visualize country collaboration networks and keywords relevant to schistosomiasis.

RESULTS

It has been determined that there has been a continuous increase in publications on schistosomiasis over a ten-year period. The number of publications has not shown a significant change annually in the last decade, and the highest number was reached in 2020 with 792 (3.4%) articles (Figure 1). It was determined that 22525 of the documents were articles and 96.3% of these articles were written in English. It was determined that 1.6% of the remaining articles were written in French, 0.8%

in Portuguese, 0.4% in German. USA, England, and Brazil are at the forefront of the countries that have published the most scientific studies on schistosomiasis (Table 1).

Network visualization using VOSViewer showed a strong collaboration between countries for schistosomiasis research (Figure 2). It is seen that cooperation is organised in three clusters, with the USA, the UK and Egypt in the first cluster, and Brazil and China in the second cluster

Table 1. Most productive countries on schistosomiasis research

Countries/Regions	Record Count	% of 23379
USA	6369	27.2
England	3038	13.0
Brazil	3022	12.9
China	2539	10.9
France	1604	6.9
Egypt	1554	6.6
Germany	1267	5.4
Switzerland	1052	4.5
Australia	948	4.0
Netherlands	893	3.8

Showing 10 out of 176 entries, 73 records (0.3%) did not contain data in the field being analyzed

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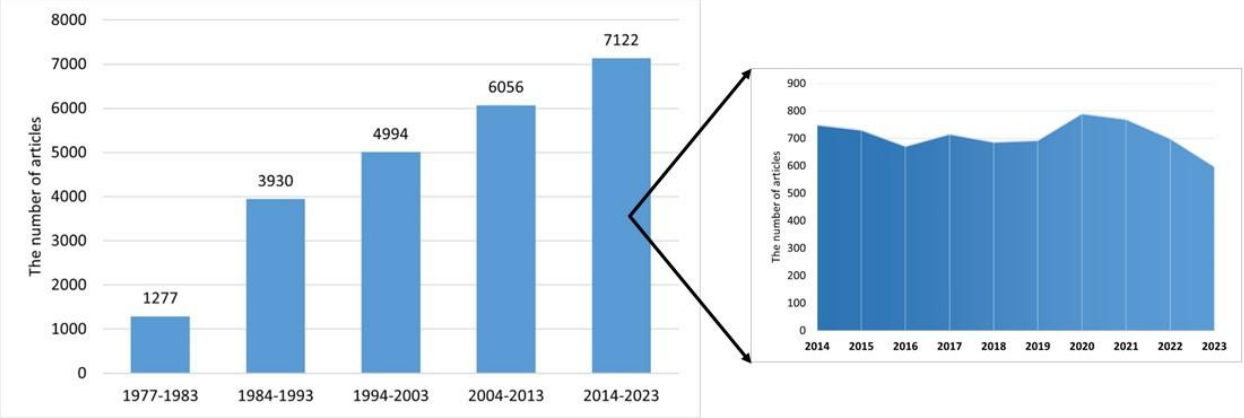

Figure 1. Distribution of publications by year.

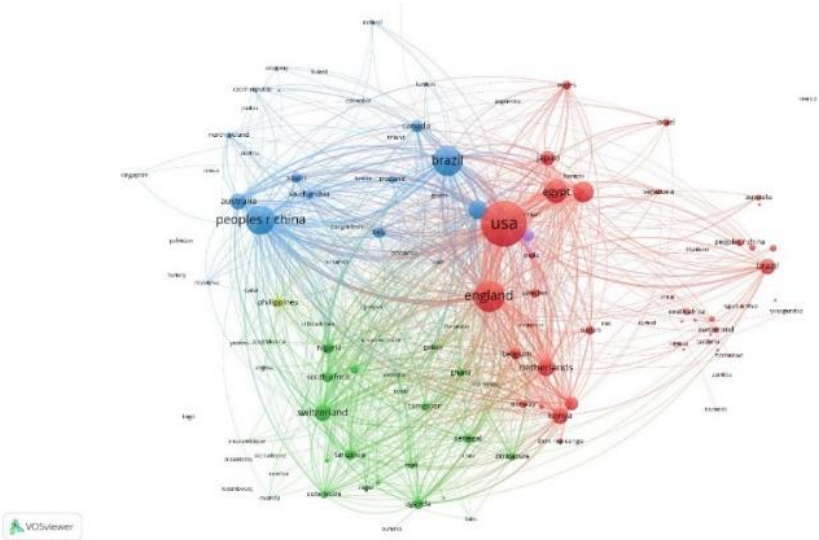

Figure 2. International collaboration network map.
*Collaboration is shown with lines linking nations. Stronger cooperation is indicated by thicker lines. Countries with larger circles or large fonts have a higher level of international cooperation.

A total of 54755authors published articles about schistosomiasis in world. The top 10 most productive authors are listed in Table 2. With 333 scientific articles, Utzinger J is the leading schistosomiasis researcher with the most publications. This is followed by McManus DP with 301 publications and Capron A with 252 publications. The most cited authors were Utzinger J (14123 citations), McManus DP (10175 citations), and Capron A (9445 citations). Network visualization using VOSViewer showed that there were many clusters in the author-citation network (Figure. 3).

Table 2. List of top-publishing authors on schistosomiasis

Authors	Record Count	% of 23379
Utzinger J	333	1.4
Mcmanus DP	301	1.3
Capron A	252	1.1
Rollinson D	240	1.0
Deelder AM	194	0.8
Stothard JR	172	0.7
Keiser J	169	0.7
Brindley PJ	166	0.7
Wilson RA	162	0.7
Colley DG	160	0.7

Showing 10 out of 54755 entries.

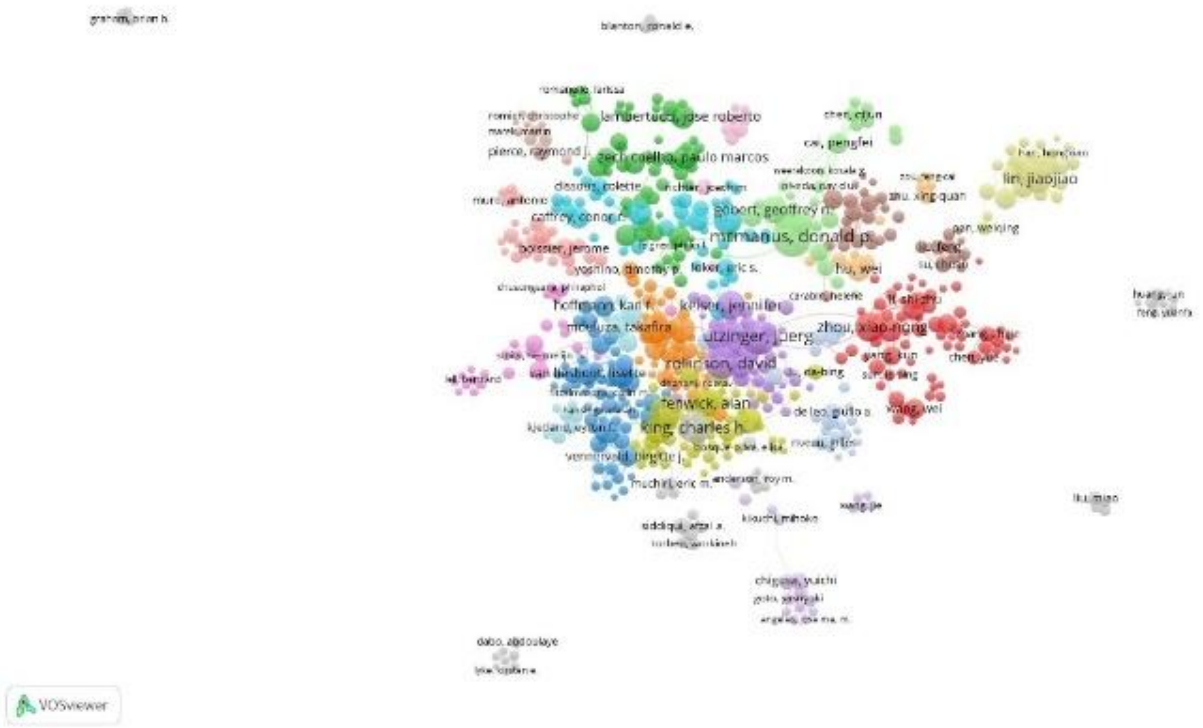

Figure 3. Authors with at least 5 publications and 100 citations are shown on the map.

Most of the articles were in the field of parasitology (37.1%), tropical medicine (23.4%), immunology (13.1%), Public environmental occupational health (12.6), and infectious diseases (11.7%). The distribution of publications according to the research area is shown in Table 3.

The three institutions providing the most support for schistosomiasis research are the United States Department of Health and Human

Services, the National Institutes of Health USA and the National Institute of Allergy and Infectious Diseases (Table 4). When analysing the top ten institutions supporting schistosomiasis research, the USA, the UK, England, China, Brazil and Portugal were the countries that supported schistosomiasis research the most.

Network visualisation using VOSViewer showed that the keywords used in publications on shistosomiasis fell into three clusters. In the first cluster, the keyword "prevalence", "control", and "intervention" stands out. In the second cluster the keywords "mouse", "cytokine", "granuloma", and "t cell" are prominent, and in the third cluster the keywords "protein" and "gene" are prominent (Figure 4).

Table 3. Most WOS researched areas of schistosomiasis

Research Areas	Record Count	% of 23379
Parasitology	8669	37.1
Tropical Medicine	5475	23.4
Immunology	3069	13.1
Public Environmental Occupational Health	2946	12.6
Infectious Diseases	2727	11.7
Biochemistry Molecular Biology	2091	8.9
Pharmacology Pharmacy	925	4.0
Zoology	894	3.8
Microbiology	880	3.8
General Internal Medicine	874	3.7

Showing 10 out of 135 entries, 1 record did not contain data in the field being analyzed.

Table 4. Funding Agencies most supportive about Schistosomiasis

Funding Agencies	Record Count	% of 23379
United States Department of Health and Human Services	2516	10.8
National Institutes of Health USA	2427	10.4
National Institute of Allergy and Infectious Diseases	1408	6.0
National Natural Science Foundation of China	1016	4.3
Wellcome Trust (England)	810	3.5
National Council for Scientific and Technological Development (Brazil)	769	3.3
UK Research and Innovation	467	2.0
Coordenaçao de Aperfeiçoamento de Pessoal de Nivel Superior	449	1.9
European Union	326	1.4
Medical Research Council	319	1.4

Showing 10 out of 7402 entries, 13723 records (58.7%) did not contain data in the field being analyzed.

DISCUSSION

UTI treatment should be initiated by evaluating guideline recommendations and local epidemiologic data (6). The gold standard diagnostic test in the diagnosis of UTI is urine culture. However, the process of determination of the causative pathogen in urine culture and antibiogram takes two days and therefore empirical treatment is initiated in most clinics. In this context, the antibiotic to be selected in empirical treatment should be chosen correctly. For this, the most common causative agents of the region or health center and the antibiotic resistance of the causative agents should be

monitored and analyzed well (7,8). In order to start empirical antibiotic treatment in patients diagnosed with urinary tract infection, the resistance rate against the drug to be given should be below 20% (9).

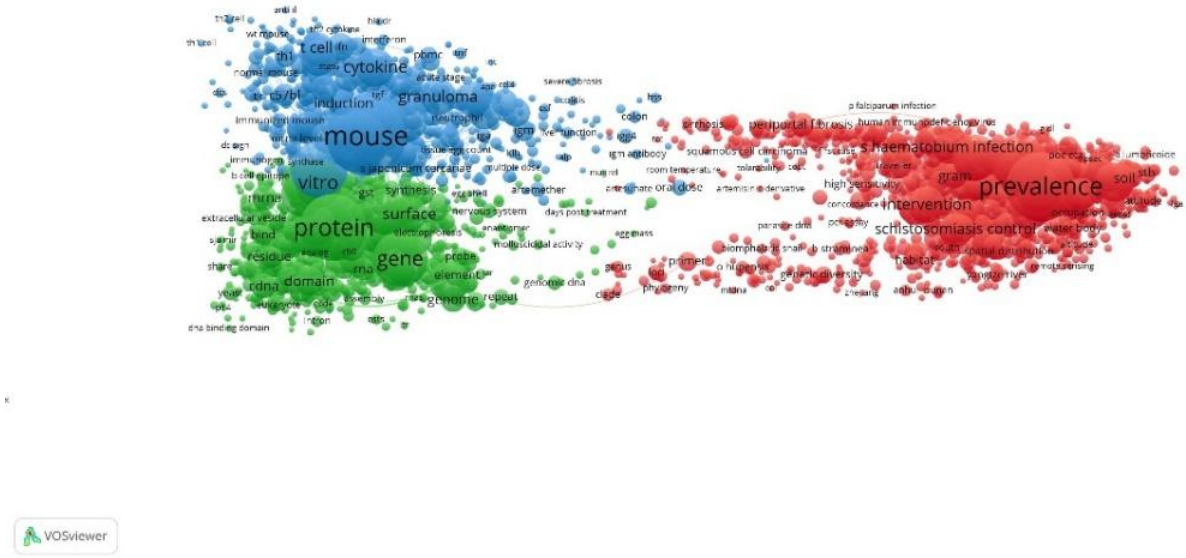

Figure 4. Article keyword visualization map with at least 5 repetitions.

**Converging lines are indicative of relationships in articles. Keywords represented with larger circle size or font size had a relatively higher occurrence in the articles

The most common causative agent of urinary tract infections in our country and in the world is *E. coli.* Due to increasing resistance rates, the current antibiotic susceptibility profile should be taken into consideration for empirical treatment to be effective (10). Keskin et al. found the frequency of *E. coli* in urinary tract infections to be 73% (11). Similar to our study, Çakır and Acar found a prevalence of *E. coli* in urinary tract infections of 39.1% (12). In our study, *E. coli* was the most common causative agent (31.7%). According to our data, nitrofurantoin, fosfomycin, imipenem, amikacin, meropenem, piperacillin-tazobactam and gentamicin have low resistance rates.

Oral antibiotics are frequently preferred as the first choice in empirical treatment. In studies, the rate of resistance to ampicillin in *E. coli* strains was found to be more than 60% (13–16). In our country, AMC resistance is observed between 38.5-46% in *E. coli* strains (14,17,18). Due to high resistance rates, ampicillin and AMC are not recommended in the treatment of urinary infections in our country. In our study, a resistance rate of 60.4% to ampicillin and 31.5% to AMC was found. When we analyzed our data according to years, we observed an increase in resistance rates for both ampicillin and AMC. This is thought to be due to the fact

that these antibiotics are still frequently preferred in our hospital.

The resistance rate of piperacillin/tazobactam, the other beta lactam/beta lactamase combination in our study, was found to be low (10.3%) as in other studies conducted in Türkiye (3,14,19). Especially in urinary tract infections caused by ESBL positive E. coli, piperacillin/tazobactam can be used effectively in treatment to prevent carbapenem resistance (20). In our study, an increase in the resistance rate of piperacillin/tazobactam was found over the years.

Fluoroquinolones and TMP-SXT are among the most commonly used antimicrobial agents in empirical treatment due to their ease of oral administration. In the IDSA guidelines, TMP-SXT is recommended as the first choice, and quinolones are recommended as an alternative in regions with over 20% resistance to this antimicrobial agent. However, resistance to these antibiotics has increased in recent years (1,6,21). Avcıoğlu and Behçet found ciprofloxacin resistance in 41% and TMP-SXT resistance in 40% of *E. coli* strains isolated from urine (17). Duran et al. determined ciprofloxacin resistance as 42.9% and TMP-SXT resistance as 42.6% (14). Yüksek et al. found ciprofloxacin resistance to be 31.8% and resistance to TMP-SXT to be 38.9% (22). Çakır and Acar found 20.3% resistance to ciprofloxacin and 31.3% resistance to TMP-SXT (12). In our study, ciprofloxacin resistance rate was 32.1% and TMP-SXT resistance rate was 35.1%, which is lower than the resistance rates in Türkiye. However, due to the resistance rates detected, both fluoroquinolones and TMP-SXT are not an appropriate approach in the empirical treatment of urinary tract infections in our region. In our study, an increase in resistance to both ciprofloxacin and TMP-SXT was observed over the years.

In the Infectious Diseases Society of America (IDSA) guidelines, nitrofurantoin and fosfomycin with low resistance rates are recommended in the treatment of uncomplicated urinary tract infections due to their ease of oral use (23,24). In our country, resistance rates to these two agents are generally below 10% (3,14,17,18). In our study, resistance rates to fosfomycin and nitrofurantoin were 4.3% and 2.8%, respectively, and when we analyzed our data according to years, we observed a decrease in resistance rates. Our findings support that these two antibiotics may be appropriate empirical treatment options in our region.

Due to the widespread use of cephalosporins, especially third generation cephalosporins in urinary tract infections, resistance rates have increased in our country (25). In the study of Tuna et al., resistance to ceftriaxone was found to be 14.3% (8). In our study, ceftriaxone resistance rate was 31.4%. When we analyzed

the resistance of *E. coli* to ceftriaxone over the years, no change was observed.

ESBL positivity in *E. coli* is increasing day by day and makes treatment difficult. In studies conducted in our country, ESBL positivity rate in *E. coli* strains isolated from urine samples varies between 8-42% (6,19,26). In our study, the rate of ESBL positive *E. coli* strains was 27.3%.

Aminoglycosides are successfully used in urinary infections because they can eradicate bacteria in the urinary system at a high rate and reach high concentrations in urine. Although their use is limited especially in patients with renal failure due to their nephrotoxicity, they are preferred in the treatment of resistant infections due to their low resistance profiles (3,18,19,27). In our study, the low resistance rate to amikacin (4.5%) indicates that this agent is an important alternative for our region. However, when we look at the resistance profile of amikacin over the years, a significant increase is observed. Amikacin should be used more carefully due to this increase. Gentamicin, on the other hand, has shown a decrease in resistance over the years.

Carbapenems are frequently preferred in parenteral treatment of UTIs caused by resistant microorganisms. In many studies, the lowest resistance rates were reported against carbapenems in urinary tract infections caused by *E. coli* (19,27). Çaycı et al. found imipenem resistance to be 0.12% for *E. coli* and 0.15% for meropenem (13). Kömürlüoğlu et al. found imipenem resistance in *E. coli* isolates as 1.5% and meropenem resistance as 1.3% (27). In our study, imipenem resistance was 4.4% and meropenem resistance was 4.9%. When we analyzed the resistance rates of *E. coli* according to the years, imipenem resistance did not change, while meropenem resistance decreased. We think that this is due to the addition of amikacin to the treatment protocol instead of meropenem in inpatients.

In other studies, *E. coli* was isolated in 60.4%-72.8% of outpatients and 39-46% of ward patients (28–30). In our study, *E. coli* was isolated in 88.8% of the samples obtained from outpatients, while it was isolated in 11.2% of the ward patients.

CONCLUSION

In conclusion, our study shows that nitrofurantoin may be a good treatment alternative with a low resistance rate in the treatment of urinary tract infections caused by *E. coli*. Our data will guide clinicians in choosing the appropriate antibiotic and preventing unnecessary antibiotic use. Therefore, it is also important for each center to create its own data and follow it regularly.

Ethics Committee Approval: This study did not require ethics committee approval because no animal or human studies were conducted.

Peer-review: Externally peer-reviewed

Author Contributions: Concept: SA, ŞY, ÖA, EG, AGH, Design: SA, ŞY, ÖA, EG, AGH, Data Collection and Processing: SA, ŞY, ÖA, EG, AGH, Analysis and Interpretation: SA, ŞY, ÖA, EG, AGH, Writing: SA, ŞY, ÖA, EG, AGH.

Conflict of Interest: The authors declared no conflict of interest.

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