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Systematic review of Lyme disease in Turkey

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Abstract

A systematic review was conducted with the aim of describing the demographical data, features and outcomes of patients with Lyme disease (LD), reported from Turkey. Three international database (electronic PubMed, Web of Science and Scopus) and two national database (Ulakbim and Turkmedline) searches were performed using the following keywords (['Lyme' or 'Borrelia burgdorferi' or 'Borrelia' or 'Borreliosis'] and 'Turkey [and/country]'). National Notifiable Diseases Surveillance System (NNNDS) of Centers for Disease Control and Prevention (CDC) criteria were used for classification. A PRISMA-based algorithm was used for systematic review. There were a total of 75 LD cases in 36 different reports. Studies related to LD are confined to case reports. We believe that LD is an important healthcare problem in Turkey and to our knowledge this is the first systematic review from this country.

Keywords

Lyme disease, borreliosis, *Borrelia burgdorferi*, Borrelia, Turkey

Introduction

Lyme disease (LD) or borreliosis is a tick-borne bacterial infection caused by this species of the spirochete family, *Borraliaceae*. This zoonotic disease is mainly transmitted to humans by hard-backed *Ixodes* ticks.[1] It is predominantly seen in the northern hemisphere including Europe and Asia, while it is the most common reportable vector-borne disease in the United States.[2,3] LD may involve multiple systems including the cutaneous with characteristic skin lesions, of which *Erythema migrans*[1–4] is the most commonly seen. Extracutaneous manifestations may include neuroborreliosis, arthritis and myocarditis.[1–4]

Methodology

We conducted a systematic literature review to investigate the LD literature reported from Turkey with the following methodology, using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement,[5,6] whose SMA flow diagram is presented in Figure 1. Inclusion criteria were directly derived from the definitions of Population-Intervention-Comparison-Outcome (PICO) components (Table 1). Articles not related or which did not meet the reference standards and target conditions were excluded. Articles and seroprevalence studies without any clinical information were also excluded.

As published data on this subject are scarce, we included all studies which prospectively or retrospectively recorded patients with LD for any definition or clinical presentation. We excluded any studies with overlapped patient data.

Although LD diagnosis is often based on symptoms, tick exposure history, and physical and laboratory findings, in order to be more comprehensive and objective, we included clinical criteria and confirmed diagnosis for LD using the National Notifiable Diseases Surveillance System (NNNDS) of Centers for Disease Control and Prevention (CDC) criteria.[7]

No exclusion criteria regarding age, sex, intensive care unit admission, follow-up duration or co-morbidities were made.

A two-step laboratory testing process, recommended by CDC,[7] was accepted as the standard approach for the diagnosis of LD. The first step consists of enzyme immunoassay (EIA) or, rarely, an indirect immunofluorescence assay (IFA) test; the second step consists of an immunoblot test, commonly the Western blot. We

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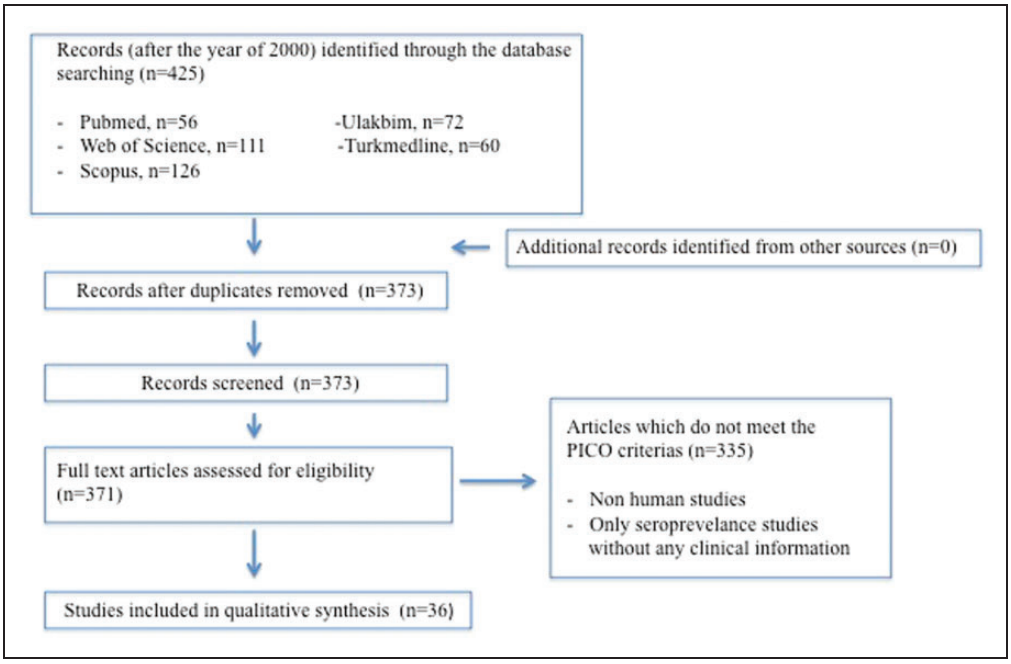

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram of the study selection.

Table 1. Population-Intervention-Comparison-Outcome (PICO) framework.

Population	Intervention	Comparison	Outcome
In adults (age > 18 years) Patients with LD diagnosis	Treatment of LD via indicated antibiotic regimens	Treatment regimens and/or clinical presentations of LD in terms of clinical response	Clinical response and/or relapse
In children Patients with LD diagnosis	Treatment of LD via indicated antibiotic regimens	Treatment regimens and/or clinical presentations of LD in terms of clinical response	Clinical response and/or relapse

also included the polymerase chain reaction (PCR) test, in addition to the mentioned serological tests, for confirmation.

In October 2018, three international databases (PubMed, https://www.ncbi.nlm.nih.gov/pubmed/; Web of Knowledge, http://appswebofknowledge.com; and Scopus, https://www.scopus.com) and two national databases (Ulakbim, http://uvt.ulakbim.gov.tr/uvt/ and Turkmedline, http://wwwturkmedline.net) searches were performed using the following keywords (['Lyme' or '*Borrelia burgdorferi*' or '*Borrelia*' or 'Borreliosis'] and 'Turkey [ad/country]') for the international databases and (['Lyme' veya '*Borrelia burgdorferi*' veya 'Borelyoz']) for the national databases. We applied no language restrictions to the electronic searches, but we included only the studies that were published after 2000.

We checked the reference lists of all relevant studies for additional studies.

We selected studies initially from title and abstract screening by the review authors (UO and HAE). We then obtained the full text for each potentially eligible study. The principal author (UO) and HAE assessed these papers against the inclusion criteria. Discordances were resolved by involving the other authors (AUO and ORS) and/or by consensus.

We extracted data to a study-specific form, which included the following list of clinical questions under the PICO framework (Table 1).

Analysis of all results was performed according to the authors, study publication year, design of the study, total number and classification of patients, signs and symptoms, diagnostic methods, treatments, clinical responses and follow-up periods.

Statistical analysis was performed via χ^2 test and a P value < 0.05 was considered significant with the help of IBM SPSS Statistics version 20.0.

No ethical committee permission was required as this was a systematic review of the literature.

Results

Initial search results revealed a total number of 425 articles. After the detailed search with the removal of duplicates and articles, which were non-full text or did not meet the PICO criteria (Table 1), a total number of 36 studies were included in our review.[8–43] None of the papers were meta-analyses or systematic reviews or randomised controlled trials.

A total of 75 cases of LD (57.3% women; mean age = 31.1 ± 2.3 years) were found. Adult case ratio (> 18 years) was 75% and 60% had a history of tick bite. Cases were classified as suspected (n = 7, 9.3%), probable (n = 9, 12%) and confirmed (n = 59, 78.7%) according to CDC-NNNDS criteria.[8]

Erythema migrans was present in 33 cases (44%) as an early sign of the disease while the most common involved site was the legs (n = 10, 13%) followed by the upper extremities (n = 7, 8%) and chest (n = 6, 7%).

Neuroborreliosis was present in 20 cases (26.7%) with Bell's palsy in six (8%), arthritis in three (4%), endocarditis in two (2.7%) and acrodermatitis chronica atrophicans in one case (1.3%) as late manifestations.

Laboratory diagnosis was confirmed via bacteriologic culture only in one case and western blot test was performed in only 38 cases (50.7%). In addition to this, PCR tests for *Borrelia burgdorferi* were found positive in 15 cases (20%) with two seronegative cases among them (who seroconverted on follow-up). Investigation of cerebrospinal fluid (CSF) could be performed in 13/20 in patients with neuroborreliosis. CSF protein levels were in the range of 45–211 mg/dL, CSF glucose levels were in the range of 2.9–3.9 mmol/L and CSF white blood cell count was in the range of 0–300 cells/mm^3. Serological examination of CSF was available in seven cases and western blot test was performed and found to be positive in only four cases.

The most commonly used antibiotic was doxycycline in 38 (50.7%) followed by third-generation cefalosporin in 31 cases (41.3%) and co-amoxyclav in eight cases (10.7%). Clinical response observed with these was 93.5% (29/31), 100% (38/38) and 87.5% (7/8), respectively. There was no significant difference in terms of efficacy between each treatment arm versus others: 29/31 vs. 44/44 ($P = 0.566$); 38/38 vs. 34/37 ($P = 0.115$); and 7/8 vs. 65/67 ($P = 0.291$).

Three patients with no clinical response were analysed further. Two were diagnosed as neuroborreliosis and were treated with third-generation cefalosporin; one was associated with Parry–Romberg syndrome and was treated with co-amoxyclav. Intravenous immunoglobulin treatment was given to 10 patients and plasmapheresis was performed in three cases with neuroborreliosis as an adjunctive treatment. One patient with neuroborreliosis, who had no clinical response, had received both plasmapheresis and immunoglobulin while another patient with neuroborreliosis, who also had no clinical response, received only immunoglobulin as adjunctive treatment.

Overall treatment success rate was 96% while the mean duration of the treatment was 30.1 ± 2.9 days. Relapse was observed only in two of 52 cases who had data follow-up (mean duration = 14.9 ± 2.3 months). In two adult cases with relapse, treatment regimens were ampicillin-sulbactam and third-generation cefalosporin. None of these two cases had late manifestations of LD.

Discussion

In the USA, 985 inpatient admissions for LD and 44,445 outpatient LD diagnoses between the years of 2005 and 2010 were reported with an estimated annual incidence as 106.6 cases per 100,000 persons.[44] Seroprevelance studies on LD show that *Borrelia burgdorferi* seropositivity is in the range of 0.9–14.5% in different cities of Turkey,[45–50] whereas these rates are in the range of 2.6–5.4% in different subgroups and different countries of Europe.[51,52] Weather conditions or regional distribution of specific tick vectors may explain these differences.

A position paper from the ESCMID study group for Lyme borreliosis (ESGBOR) recommends that in cases of typical erythema migrans, LD should be diagnosed clinically and no laboratory testing is required, but the diagnosis of neuroborreliosis requires laboratory investigation of CSF including intrathecal antibody testing.[53] Although the former seems to be subjective, we agree with this recommendation and believe that it is important in counties where access to serological tests is not easy.

A systematic review and meta-analysis revealed that direct detection methods, culture and PCR of tissue or blood samples were not as sensitive or timely compared to serological testing.[54] On the other hand, it seems that owing to heterogeneity with risk of bias, the usefulness of serological tests depends on the pre-test probability and subsequent predictive values in the setting. Two-tiered algorithms or antibody indices did not outperform single test approaches.[55] We suggest that molecular tests such as PCR or new alternative tests should be tested in prospective well-planned studies with a large number of patients in the future.

An alternative, azithromycin, as a first-line agent (2b grade evidence) has been proposed.[56] A meta-analysis of randomised studies about neuroborreliosis

provides positive efficacity in the use of doxycycline, penicillin G, ceftriaxone or cefotaxime for European neuroborreliosis.[57] We found that although patient numbers were limited, no statistical significant difference in terms of clinical response between antibiotic regimes. Similar efficacities have been likewise reported, but emphasised their side-effects.[58] Data concerning adjunctive treatment of neuroborreliosis are limited.[59,60] More randomised controlled studies with a higher number of patients (or higher power) should be performed to resolve this question.

Our study has some limitations. First, the details of western blot tests were not available in all reported cases. Second, lumbar puncture had not been performed in all neuroborreliosis cases. Third, follow-up data of some patients were not available. Furthermore, our study represents the data mainly from case reports and there are no published randomised controlled trials nor systematic pooled studies on LD in Turkey. Nonetheless, we believe our study adds important insight into the current situation in the country.

Declaration of conflicting interests

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Article

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The burden and risk factors for postnatal depression and depressive symptomatology among women in Kampala

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Abstract

Major depressive disorder (MDD) is a major global health challenge and postnatal women may be at an increased risk for this disorder. Very few studies have tested this hypothesis in sub-Saharan Africa (SSA), so it is uncertain whether risk factors implicated elsewhere in the world are relevant in SSA. We explored prevalence and risk factors for MDD and depressive symptomatology among postnatal mothers in Kampala. Three hundred postnatal mothers at Nsambya Hospital were assessed for MDD using the DSM IV-based MINI; prevalence and risk factors were determined using frequencies and regressions, respectively. Four women (1.33%) had MDD; however, 94 (31%) had 'sub-threshold' or depressive symptomatology, with which partner violence is particularly associated. MDD is rare among postnatal women in a paying hospital in Kampala; however, the high prevalence of depressive symptomatology suggests susceptibility to MDD. Longitudinal studies should investigate this hypothesis and the susceptibility due to partner violence should guide appropriate interventions.

Keywords

Maternal, depression, postnatal, urban

Introduction

Maternal mental-health disorders are a big problem to women, their infants, families and society, constituting a major public health challenge.[1] A meta-analysis of mostly Western studies reported 18% women having a depressed mood during pregnancy with nearly 13% suffering from major depressive disorder (MDD).[2] Studies from South Asia have documented postnatal depression rates in the range of 19.8–28%.[3–5] Other mental disorders in pregnancy mainly reported in the West include: generalised anxiety disorder (8.5%);[6,7] panic disorder (1–2%);[6] post-traumatic stress disorder (PTSD) (3.5%);[7,8] obsessive-compulsive disorder (OCD) (0.2–1.2%);[6,7] anorexia (1.4%);[9] bulimia (1.6);[9] alcohol abuse (7%);[10] and postpartum psychosis (0.1–0.2%).[11]

Poor psychological transitioning into parenthood is thought to underlie perinatal mental disorder and all women can develop mental disorder during or after pregnancy, but poverty, migration, extreme stress, unemployment, exposure to violence, emergency and conflict situations, natural disasters, food insecurity, low social support and HIV/AIDS common in sub-Saharan Africa (SSA) are believed to increase the risk

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