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Full Length Research Paper

Risk factors for, and treatment of, Stevens-Johnson syndrome and toxic epidermal necrolysis: Evidence from the literature

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Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are adverse drug reactions. They occur in the form of mild and sometimes severe cutaneous eruptions, with high morbidity and mortality, requiring fast and appropriate diagnosis and treatment. The aim of this study was to describe and discuss the evidence regarding the risk factors, complications and treatment of SJS and TEN in inpatients. The present study is a literature review of case reports published between January 1981 and December 2016, in the following databases: The Virtual Health Library (*Biblioteca Virtual da Saúde* - BVS), MEDLINE (National Library of Medicine, USA), LILACS (Latin American and Caribbean Health Sciences Literature), and PUBMED – NCBI (National Center for Biotechnology Information). A total of thirteen case reports were selected. Most of the cases (54%) developed adverse reactions to anticonvulsant drugs. The most common were valproic acid, lamotrigine and carbamazepine. In 69% of all cases, the patients were female. The patients' age range varied from 18 to 82 years old. In two cases which correspond to 15%, the patients were either infected with HIV or were receiving chemotherapy treatment for cancer. These patients had a higher possibility for immunosuppression. In relation to the actions taken as treatment, the suspension of the drugs or the treatment of the skin lesions occurred in 85 and 54% of the cases, respectively. A total of 6 cases, corresponding to 46%, occurred in the Latin American and Caribbean region. In conclusion, the use of anticonvulsants, and female gender, are among the main risk factors identified by the study. The main therapeutic action for SJS and TEN is the suspension of the use of the drug that triggered the inflammatory process and the topical treatment of the lesions caused.

Key words: Stevens-Johnson syndrome, toxic epidermal necrolysis, adverse drug reaction.

INTRODUCTION

An adverse drug reaction (ADR) is a harmful response to drugs, occurring in doses usually employed in the prophylaxis, diagnosis, treatment or modification of physiological functions (Walley, 2000). An ADR may appear as a reaction of mild intensity, of little clinical relevance, medium intensity, or severe intensity, and can lead to hospitalization, with incapacitating or even lethal sequelae (Upadhyaya et al., 2012).

Studies have shown that approximately 4% of hospital admissions in the United States of America are due to

ADR and that 57% of these reactions are not recognized at the time of the patients' admission; such reactions affect more than 2.2 million people per year (Pereira, 2012).

In Europe, approximately 3.6% of all hospital admissions are due to ADR. Moreover, the percentage of hospitalized patients who die from ADR is below 0.5%, which corresponds to 419,000 deaths annually from this cause in this region (Bouvy et al., 2015).

Stevens Johnson syndrome and TEN are serious conditions that can lead to death and are characterized mainly by blisters in the region of the skin and mucosa. The lesions generally affect the trunk. Although these conditions are rare worldwide, with an incidence of 0.4 to 6 cases per million people per year, the mortality rate are high: 5 to 12% for SJS, 30% for TEN, and 33.3% for the two conditions combined (Tangamornsuksan et al., 2013).

Approximately 2 to 3 people per million/year have SJS or TEN in Europe and the United States of America. In Brazil, Stevens-Johnson syndrome varies from 1.2 to 6 cases per million people/year, and TEN varies from 0.4 to 1.2 million per year (Bulisani, 2006). For 2005 to 2007, the incidence rate of TEN in Japan was 0.28 to 0.52 per million per year (Kinoshita, 2017).

The difference between SJS and TEN is related to the extent of the body surface where epidermis is peeling away. In SJS, TEN and the combination of both conditions, respectively, at least 10%, over 30%, and between 10 and 30% of the body's surface area is affected (Sun et al., 2014).

In approximately 80% of these cases, drugs are the primary cause. The classes of drugs associated most with these conditions are the antiepileptics, antibiotics, and the xanthine oxidase inhibitors. The use of carbamazepine is considered to be the most common cause. Other factors related to the emergence of these reactions are immunization, viral infections, chemical products and mycoplasma pneumoniae (Tangamornsuksan et al., 2013).

One overlapping feature in SJS and TEN is the presence of fever and malaise (Kumar et al., 2005; Yamane et al., 2016). Although, SJS and TEN affect patients of all ages, races and genders, it is mainly related to the use of drugs (Bulisani, 2006). ADR's cost to the health services is normally underestimated, as the majority of the reactions occur in patients who are not hospitalized, these reactions, therefore, is being under reported (Nagao-Dias et al., 2004).

Some factors may predispose patients to develop SJS and TEN. These include multiple morbidities and the use of drugs for treating the following: advanced age, genetic propensity, and diseases which affect the immune system (Bulisani, 2006). Mortality caused by SJS and TEN increases with age and according to the region of the body affected. SJS and TEN are conditions that can result in a severe cutaneous reaction, requiring rapid and appropriate diagnosis (Bulisani, 2006).

Renal function, electrolyte fluid balance, eye and affected regions care, pain control and infection prevention are priority measures (Schneider, 2017). In addition, referral of patients to the intensive care unit or burn unit is recommended (Alerhand et al., 2016).

This article's objective is to describe and discuss the evidence regarding the risk factors, prevalence, mortality, complications, treatment and prevention of SJS and TEN; when these occur in hospitalized patients. In spite of the seriousness and high mortality of these reactions and the fact that they are not yet totally understood, few studies have yet been undertaken (Arantes et al., 2017). Besides the known risk factors such as infections and the use of drugs, there are probably other related factors which have not yet been identified (Mockenhaupt, 2011). The investigation of risk factors, clinical cases and treatment options could be useful for health teams in managing patients with SJS and TEN (Chantaphakul et al., 2015).

This study mainly investigates the population which is affected by these conditions and the discussion of the associated risk factors, based on the comparison of our results with those already published in the literature. The study of risk factors is fundamental in promoting policies aimed at preventing ill health and promoting clinical management.

METHODOLOGY

The study consists of a review of the scientific literature on the topic. The following databases were consulted for articles: MEDLINE (National Library of Medicine, USA), LILACS (Latin American and Caribbean Health Sciences Literature) and PUBMED – NCBI (National Center for Biotechnology Information), published between January 1981 and January 2016, and which included the following MeSH (Medical Subject Headings) and DeCS (*Descritores em Ciências da Saúde*) descriptors: Stevens-Johnson syndrome, toxic epidermal necrolysis, and drug-related side effects and adverse reactions.

Selection criteria

Inclusion criteria: Only case reports were selected.
Exclusion criteria: clinical trial, systematic review, observational studies, reviews, letters to the editor and update articles. In the literature researched, the following were described and discussed: the evidence regarding risk factors, prevalence, mortality, complications, treatment and prevention of SJS and TEN in

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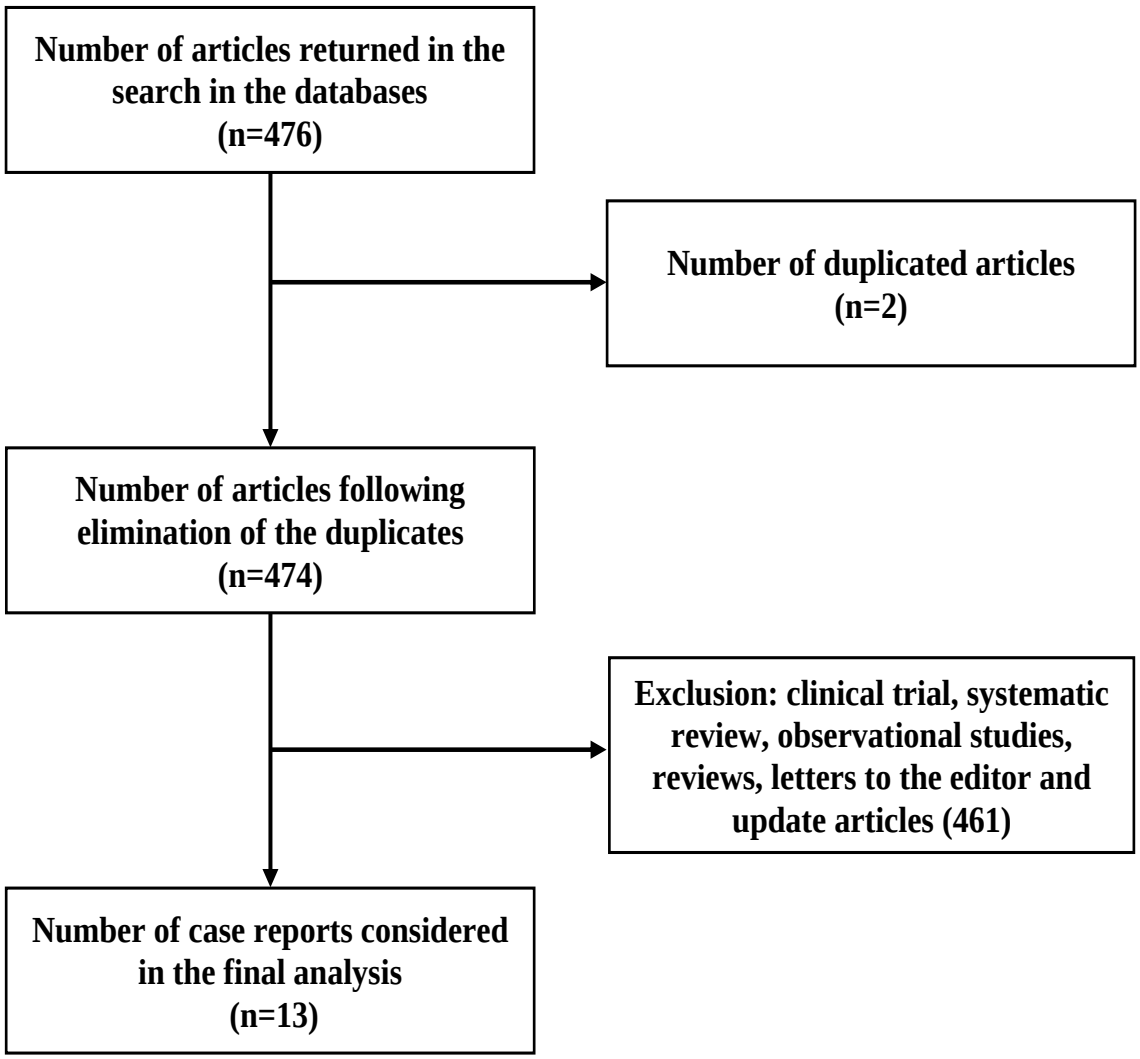

Figure 1. Process of study selection.
Source: Adapted figure: Galvão et al. (2015) and Williams et al. (2015).

hospitalized patients.

Study populations' ages were classified in accordance with the suggestions of the National Institute of Health. Age filters include: "80 and over: 80+ years; Aged: 65+ years; Middle Aged: 45-64 years; Adult: 19-44 years; Adolescent: 13-18 years; Child: 6-12 years; Preschool Child: 2-5 years; Infant: 1-23 months; Newborn: birth-1 month" (NIH, 2014).

Countries were classified according to economic development category as either 'High-income' (HI), 'Upper-middle income' (UMI), 'Lower-middle income' (LMI), or 'Low-income' (LI), depending on how they were categorized by the World Bank (2017).

The World Bank classifies countries into four income groups. Economies were divided according to 2016 Gross National Income (GNI) per capita with income being categorized as: "(i) Low income: per capita GNI of US$1,025 or less, (ii) Low-middle income: per capita GNI between US$1,026 and US$4,035, (iii) Upper-middle income: per capita GNI between US$4,036 and US$12,475, and (iv) High-income: per capita GNI of US$12,476 and over".

Countries were classified according to geographical regions (continental), based on their categorization by the United Nations (2016).

RESULTS

A total of 13 case reports were selected for the research (Figure 1). Five case reports were found in the LILACS database, four in MEDLINE, and four in PUBMED (Table 1). Reports on pediatric patients who suffered SJS and TEN were not found in the literature.

The data obtained from the case reports selected were grouped in Table 1, using the following information from each study: study's countries of origin, patient age, sex, etiology, diagnosis, drug which caused ADR and treatment. The countries with the highest number of studies published were India (2), Brazil (2), Colombia (2) and United States (2). In all of the cases reviewed, the lesion was treated topically and with corticosteroids in order to delay the unregulated immune response caused by SJS and TEN, in addition to removal of the drug that caused the ADR (Table 1). All the patients presented

Table 1. Description of the cases diagnosed as SJS, TEN and SJS/TEN in the MEDLINE, LILACS and PubMed databases (January 1981 - January 2016).

Reference	Occurrence	Years	Sex	History	Diagnosis	Drug	Treatment
Andreoli et al. (2008)	Argentina	20	F	Epilepsy.	SJS, TEN	Lamotrigine	-Suspension of lamotrigine; treatment of the lesions; venous hydration.
Falcão et al. (2008)	Brazil	26	M	Antibiotic use (72 h)	SJS	Trimethoprim-sulfamethoxazole	-Suspension of the drug; treatment with corticosteroids and surgery; treatment of the cutaneous lesions.
Jao et al. (2010)	USA	57	F	Patient with HIV	SJS and liver failure	Nevirapine	-Topical treatment of the cutaneous lesions; suspension of the drug; liver transplant.
Hsieh et al. (2009)	China	82	F	Patient receiving treatment for leukemia	SJS	Imatinib combined with allopurinol	-Intensive care; oral steroids with anti-histamines were used in the treatment of the severe cutaneous reaction.
Castana et al. (2009)	Greece	38	M	Epilepsy	SJS	Valproic acid	-Specific treatment for burns; interruption of the drug; steroids and topical antibiotics.
Salama (2009)	USA	29	M	Crohn's Disease and treatment with adalimumab (subcutaneous route). Progressed to cellulitis in a lower limb.	Non-specific ADR and SJS	Adalimumab	-Suspension of the drug; - Antibiotic therapy.
Mantilla et al. (2009)	Colombia	21	F	Epilepsy treated with valproic acid and phenytoin	TEN	Valproic acid	Suspension of the drug; -Venous hydration; -Administration of corticosteroids.
Garcia et al. (2010)	Brazil	61	F	Postherpetic neuralgia	SJS, TEN	Carbamazepine	-Suspension of the drug; -Venous hydration.
Quinones et al. (2011)	Cuba	69	F	Amygdalitis treated with antibiotics over two week.	SSJ, TEN.	Antibiotic - ciprofloxacin	-Clinical, dermatological and otorhinolaryngological monitoring; -Venous hydration.
Das et al. (2011)	India	18	F	Malaria	SJS	Chloroquine	-Surgery and superficial lamellar dissection of the cornea to separate conjunctival-corneal adhesions; -Suspension of the drug; -Topical treatment of the lesions.
Martínez-Pérez et al. (2012)	Spain	36	M	Epilepsy and alcoholism	SJS	Calcium carbimide - Tryptizol	Suspension of the drugs; -Use of intravenous corticoids; - Topical antibiotics; - Treatment of skin lesions.

Table 1. Contd.

Dominguez et al. (2012)	Colombia	67	F	Treatment of epilepsy with phenytoin: 100 mg intravenous bolus and 300 mg/day (oral)	SJS	Phenytoin	-Suspension of the drug; -Correction of electrolyte disturbance; -Treatment of the skin lesions with dipyrone.
Kaur (2013)	India	47	F	Epilepsy	TEN	Valproic acid/lamotrigine	-Intensive care; -Suspension of the drug; -Clobazam 20 mg/day was initiated for prophylaxis of the epileptic crises.
Kaur (2013)	India	26	F	Bipolar and obsessive-compulsive disorder Treatment with lamotrigine	TEN	Valproic acid/propanalol/ risperidone/lamotrigine	Treated with prednisolone 40 mg/day; -Venous hydration.

sequelae and scars from the epidermal lesions. Those who were affected in the oral and ocular mucosa recovered more slowly than those who had been affected in other parts of the body.

Most of the cases (54%) developed adverse reactions to anticonvulsant drugs. The most common were valproic acid, lamotrigine and carbamazepine. The incidence of reactions with these drugs was higher in female patients (86%). Several cases (15%) were related to the use of antibiotics.

In 46% of the cases, the patients had a history of epilepsy. It can be confirmed that in only two cases (HIV, and a patient receiving chemotherapy treatment for cancer), corresponding to 15% of cases, was there a higher possibility of the patients' immunosuppression. Corticosteroid use was present in 46% of the cases. In 69% of all cases, the patients were female. The patients' age range varied from 18 to 82 years old. In relation to age groups, 54% of the cases were adult, 23% were middle-aged, 15% were aged, 8% were adolescents and 8% were aged, over 80 years old. Regarding the actions taken as treatment, the suspension of drugs and the treatment of skin lesions were undertaken in 85 and 54% of the cases, respectively. None of the evaluated studies were used as treatment for immunomodulating therapies.

A large proportion of the countries where the cases of SJS, TEN and the combination of both took place were high or upper middle income (Table 2). A total of six cases, corresponding to 46% of total cases, occurred in the Latin American and Caribbean region. SJS in association with TEN is concentrated in Latin America and the Caribbean, and in upper middle-income countries (Table 2). SJS affected patients in the following countries: Brazil (1), China (1), Greece (1), United States (2), India (1), Spain (1), and Colombia (1). TEN, on the other hand, was found in Colombia (1) and India (2). The combination of these two conditions was found in Argentina (1), Brazil (1) and Cuba (1).

DISCUSSION

The present study showed that the anticonvulsants were drugs suspected to be related to SJS and TEN conditions. Moreover, the antibiotics were involved in more than one case. The main drugs mentioned in the literature as triggers of the SJS and TEN reactions were the sulfonamides, anti-inflammatories, penicillin, barbiturates, allopurinol, antiepileptics and vaccines (French, 2006; Mendonça, 2009). Another study by Arantes et al. (2017), conducted in the city of Brasilia, Brazil, found that anticonvulsants, antibiotics and analgesics were the main drugs suspected to be related to these conditions. The study's results, therefore, appear to be consistent with the data in the already-published literature.

One possible explanation for the development of SJS and TEN reactions in patients seems to be related to thehuman leukocyte antigen (HLA) system, as a study by Adkinson Jr. et al. (2002) suggested that there is a correlation between the use of an anticonvulsant in the case of their study, carbamazepine and the activation of the unregulated cytotoxic response, via the HLA system, with consequent appearance of the characteristic SJS and TEN reactions.

Chloroquine and nevirapine were also drugs used by the patients who had these reactions, according to the present study's results. This finding too is consistent with already-published

Table 2. Countries where the cases of SJS, TEN and the combination of both took place were high or upper middle income .

Country	Geographic Region	Income Level	Number of cases
Argentina	Latin America	Upper middle income	1 case: SJS associated with TEN
Brazil	Latin America	Upper middle income	1 case: SJS; 1 case: SJS associated with TEN
China	Asia	Upper middle income	1 case: SJS
Colombia	Latin America	Upper middle income	1 case: SJS; 1 case: TEN
Cuba	Caribbean	Upper middle income	1 case: SJS associated with TEN
Greece	Europe	High Income	1 case: SJS
India	Asia	Lower middle income	1 case: SJS; 1 case:TEN
Spain	Europe	High income	1 case: SJS
The United States	Northern America	High income	2 cases: SJS

Source: United Nations (2016); World Bank (2017).

studies, as one systematic review by Patel et al. (2013) showed that chloroquine and nevirapine were associated with the conditions of SJS and TEN in 7 and 4% of cases, respectively.

Biological therapies such as Adalimumab have also been related to severe reactions. This study showed that one patient developed SJS after treatment with this drug. Another study, published by Owczarczyk-Saczonek et al. (2016) showed that etarnecept, which is of the same class as Adalimumab, that is to say, a tumor necrosis factor-α inhibitor, has been associated as a cause of severe reactions such as SJS and TEN. In the case of these reactions, both etarnecept and Adalimumab have been used for treating inflammatory diseases mediated by the immune system, such as rheumatoid arthritis and Crohn's disease (Kuek et al., 2007).

The use of calcium carbimide has been associated with unpleasant reactions, including dermatological reactions. There are also safety concerns related to effects on the liver (Verge et al., 2006). One of the studies selected (Martínez-Pérez et al., 2012), mention the case of a patient with SJS whose history included the use of calcium carbimide for treatment of alcoholism. In this case, the patient was prescribed paracetamol and amoxicillin for treating the effects of general malaise, fever, rash and itchiness in the eyes, which had first led the patient to seek medical attention. After some hours, following the use of these drugs, the patient presented the characteristic reactions of SJS. In this case, as the use of amoxicillin has been associated with SJS (Zaidi et al., 2017), the use of this product may be a confounding factor in the analysis of the causal relationship between calcium carbimide and SJS. In relation to paracetamol, on the other hand, one recently-published study by Lebrun-Vignes (2017) suggested that there is no evidence for a causal relationship between the use of paracetamol and the occurrence of SJS and TEN.

According to the present results, most patients had a history of epilepsy. This condition seems to be directly related not to the effects of SJS and TEN, but rather to the use of drugs for controlling epileptic crises, such as carbamazepine and phenytoin, which have an already well-established causal relationship with SJS and TEN (Trivedi et al., 2017). Approximately, 75% of cases of SJS and TEN are caused by drugs (Mockenhaupt, 2017).

The medical histories of the patients in the present study were consistent with the groups at risk of developing SJS and TEN. According to the present study's results, the medical history of some patients is related to infections, such as HIV, amygdalitis and antibiotic use. The patients with HIV and cancer identified in the present study, furthermore, had a higher possibility of presenting immunosuppression. According to the scientific literature, the condition of compromise of the immune system is considered to be a risk factor for SJS and TEN (Wong et al., 2016).

One study by Mockenhaupt (2017) suggested that other possible causes for the development of SJS and TEN are bacterial infections, nonspecific viral infections affecting the airways, human immunodeficiency virus, vaccination and graft-versus-host disease. There are also idiopathic cases, in which no adjacent cause is identified.

Regarding the complications reported, two of the patients studied died, as a result of sepsis and multiple organ failure (Garcia et al., 2010; Quinones et al., 2011), while one of the patients presented clinically relevant ocular complications (Das et al., 2011). The literature corroborates these results, as the most frequent complications resulting from SJS and TEN are sepsis, which can lead to death, and keratoconjunctivitis, which can lead to conjunctival retraction, scarring, and corneal lesions. In these cases, the sequelae are more common in the later phase of the development of TEN (Sotelo-Cruz et al., 2005).

The medical treatment of SJS and TEN is the immediate suppression of the use of the drugs which could have been causing the reactions, clinical, dermatological and otorhinolaryngological monitoring, correction of electrolyte disturbance, intensive care, venous hydration, liver transplant, clobazam for prophylaxis of the epileptic crises, and administration of systemic corticoids and topical antibiotics. The treatment

of the cutaneous lesions was also undertaken in all cases (Andreoli et al., 2008; Dominguez et al., 2012). According to our study's results, corticosteroids were not administered to all patients. One study by Chantaphakul et al. (2015) suggested that corticosteroid use was greater in a group of patients with SJS and TEN who survived, in comparison with a group of patients who did not. This same study, moreover, suggested that the use of corticosteroids in these patients prevents ocular complications. On the other hand, a separate study by Lee et al. (2012) suggested that it is necessary to undertake controlled clinical trials in order to assess the real benefits of corticosteroid use in patients with SJS and TEN.

According to the results of this study, immunomodulating therapies were not used in the patients' treatment. In a systematic review study published in the literature, treatment of patients with SJS and TEN with immunomodulating therapies, including glucocorticosteroids, intravenous immunoglobulins, cyclosporine, plasmapheresis, thalidomide, cyclophosphamide, hemoperfusion, tumor necrosis factor inhibitors, and granulocyte colony-stimulating factors, only glucocorticosteroids and cyclosporine were the most promising (Zimmermann et al., 2017). Another study showed that the use of cyclosporin in patients with SJS and TEM was associated with decreased mortality (Kirchhof et al., 2014). One systematic review with meta-analysis suggested that intravenous immunoglobulin combined with corticosteroid may reduce the recovery time of patients with SJS and TEN, mainly among Asians (Ye et al., 2016).

According to the results, the incidence of SJS and TEN was high in the age range from 18 to 82 years old. Furthermore, this incidence was greater among the adults. According to the NIH (2014), the adult age range is from 19 to 44 years old. According to Çekiç et al. (2016), the conditions of SJS and TEN affect all age groups, but have been observed more among adults. One study by Bequignon et al. (2015) showed that the incidence varied in the age range from 17 to 91 years old. The results of another study, this one by Lim et al. (2016), showed that SJS and TEN were more likely to affect women (56.6%) and that the patients' mean age was 54.3 years old. That is to say, in relation to gender, our results are in accordance with the literature; however, this study indicated that the age group made up of the middle-aged was affected most, which diverges from our results.

Another study by Wang (2017) showed that female gender, age above 70 years old and infection status were not significantly different between the patients who survived and those who died. In that same study, furthermore, the number of cases with SJS and TEN in the group aged 10 years old or less, and in the group aged between 81 and 91 years old, was low, with 1 and 2 patients, respectively. The age ranges with the most cases were 31 to 40 years old (20 patients), 21 to 30 years old (17 patients), and 51 to 60 years old (16 patients).

A study by Yang et al. (2016) showed age to be a risk factor for mortality from SJS and TEN. Mortality among patients aged 40 years old or over was significantly higher in comparison with groups of patients aged below 40 years old.

Although the results showed that more cases originate from countries in Latin America, the data from the literature suggests that few countries from Latin America have published scientific work on SJS and TEN. Although, Brazil and Mexico are on the list of countries publishing most worldwide, when one compares their production with that of countries from other continents, such as North America, Europe and Asia, it may be seen that they are among the last on the list (Sweileh, 2017).

It is believed that the low number of cases selected in this study is a limiting factor in the discussion and conclusion regarding the relationship between the occurrence of SJS and TEN and aspects relating to countries' levels of economic development and ethnic characteristics of the populations of different continents. According to Hsu et al. (2016), future studies should investigate different populations' ethnic, genetic and economic aspects as well as their access to health care and their use of drugs.

Asian countries, such as India and China, were among the countries where there were cases of SJS and TEN, according to the present study's results. Asians are more likely to develop these conditions because of the use of specific drugs, such as carbamazepine, due to specific genetic characteristics related to the HLA system. Hispanics, on the other hand, seem to be less affected by SJS and TEN (Blumenthal et al., 2015).

Infection by HIV is also a risk factor for developing SJS and TEN (Thong, 2013). Some countries of Africa and Asia, such as India, have a high number of people living with the virus. In India, for instance, over 2,100,000 people live with the virus (WHO, 2017). The population of South Africa is only 0.7% of the world's total population, but has 17% of the burden caused by the HIV virus.

In poorer countries, there is a paucity of data on SJS and TEN (Kannenberg et al., 2012). Generally speaking, studies on the incidence and prevalence of SJS and TEN are undertaken in the developed countries (Knight et al., 2015). The difficulties related to the precise diagnosis of SJS and TEN may be related to underestimating the number of cases (Lim et al., 2016).

The results showed that most countries where the cases occur are upper middle and high-income. However, in the Latin American and Caribbean region, where there were the most cases of SJS and TEN, according to the present study's results, in spite of the advances which have taken place over the last 60 years, inequalities in accessing the health services remain high (Barreto et al., 2012). One problem to be faced in less-developed countries is the limited access to medical resources,

which could stabilize the health conditions of patients affected by SJS and TEN (Thong, 2013). Asians may be more prone to developing SJS and TEN, due to genetic characteristics (Blumenthal et al., 2015). Some countries in the South of Asia, such as India, are among those where one finds the world's largest social and economic inequalities, which also have an impact on healthcare (Zaidi et al., 2017). It follows that the patients who are most vulnerable to reactions linked to SJS and TEN may experience difficulty accessing the health services. According to Ellender et al. (2014), patients with extensive skin involvement should be admitted to an intensive care unit or a burn unit if possible. In countries with fewer resources, intensive care units may lack adequate infrastructure for protecting the patients' lives.

As a limitation of this study, emphasis is placed on the fact that the clinical trials and systematic reviews have not been included. This study only included case reports. Despite being considered a low level of scientific evidence (Oxford Centre for Evidence-based Medicine, 2009), case reports are important for hypothesis generation and can lead to more controlled studies (Burns et al., 2011). Although this impact on the quality of the results generated, the study contributes to the discussion of important questions, such as the severity of these conditions, which have as yet been little studied. In addition to this, the low number of studies selected could compromise the generalization of the results.

Conclusions

Among the main risk factors identified by the study, one finds the use of anticonvulsants and female gender. The immunosuppressed, such as patients infected by HIV or who are receiving chemotherapy and individuals of middle age were also identified as being at-risk groups. Most cases of SJS and TEN were caused by drug use. Previously healthy people who were making use of drugs such as antibiotics and nonsteroidal anti-inflammatories may also develop adverse reactions. These reactions are not yet totally understood and there are cases without a defined cause. There may be other, currently unknown, factors acting in the development of these conditions. The main therapeutic action for SJS and TEN is the suspension of the use of the drug that triggered the inflammatory process, and the topical treatment of the lesions caused. SJS and TEN have been found in regions where the patients experience difficulty accessing the health services. This may be a problem, as patients affected by SJS and TEN require rapid attendance and the presence of available medical resources. Considering the impact that these conditions have on patients' health, it is important that further studies should be undertaken in order to investigate the risk factors, ethnic and genetic aspects, the costs associated, effective preventive and therapeutic measures, and access to healthcare among the different populations affected by these conditions.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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