Epidemiological Burden of Lower Limb Spasticity in Adults: A Systematic Review

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Abstract

Background: The purpose of this study was to investigate the epidemiological burden of illness associated with adult lower limb spasticity (LLS) and its complications. **Methods:** A systematic search of MEDLINE and EMBASE identified nine studies published between November 2012 and July 2019 that assessed the epidemiological burden associated with LLS. **Results:** LLS was found to occur in one-third of adults after neuromyelitis optica spectrum disorder, one quarter to one-third with multiple sclerosis, one quarter to half with Parkinson's disease and roughly half with stroke. LLS limits mobility and reduces the quality of life. LLS complications, especially injuries following falls, are a common occurrence. **Conclusion:** The evidence on the burden of LLS is surprisingly limited given the condition's high prevalence among adults with common disorders, such as stroke. Further research is needed to explore the trends in the incidence and prevalence of LLS over time and across different geographical regions. The dearth of high-quality evidence for LLS suggests a lack of awareness of, and interest in, the problem, and therefore, the unmet need among patients and their carers.

Keywords: Epidemiological burden, Incidence, Lower limb spasticity, Muscle overactivity, Prevalence

Introduction

Lower limb spasticity (LLS), a movement disorder often described as muscle overactivity, is caused by the damage to the portion of the brain or spinal cord. This damage alters the balance of signals between the nervous system and the muscles; hence, the condition is associated with various neurological conditions.[1] Spasticity is one of the most frequent symptoms associated with multiple sclerosis (MS).[2] However, it may be caused by traumatic brain injury (TBI), spinal cord injury (SPI), stroke, and other related conditions.[1] In addition to this, spasticity is a main feature in several rare conditions such as tropical and hereditary spastic paraparesis.[3] Spasticity can affect the entire body,[4] but LLS is generally worse because it affects mobility, balance, and independence along with adding burden on the carers.[5] Spasticity can lead to muscle contracture, joint stiffness, reduced range of movement, broken skin, and pain[6] and can significantly restrict patients' mobility and functional ability, their activities of daily living and can diminish their quality of life.[7]

The incidence and prevalence of LLS vary geographically that its severity is associated with falls in persons with MS.[8] Distal paresis of the lower limb is considered an early predictor of spasticity in adults with ischemic stroke.[9] Although there are several common risk factors for spasticity, risk factors vary for various underlying conditions. For example, age is a risk factor for spasticity in stroke patients. Younger age at the time of stroke[10] is associated with the increased likelihood of spasticity. On the other hand, smoking is among common risk factors for spasticity. A history of smoking[11] is associated with an increased probability of spasticity. The most frequently reported symptom in spasticity is pain, and it increases with increasing age; however, there is no established correlation between spasticity and pain.[12]

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Management of spasticity depends on underlying pathologies. It is significantly different in patients with TBI due to behavioral and cognitive issues that affect their ability to participate in, or tolerate, treatment (e.g., their ability to follow instructions, monitor use of a spastic limb, or tolerate a cast).[6] The treatment of spasticity requires a multi-disciplinary approach and usually starts with physiotherapeutic approaches. However, a direct effect on abnormal muscle activity can only be achieved by pharmacological interventions. Systemically acting pharmacological interventions are used before employing locally acting drugs. In some cases, surgery is the final treatment option; however, it is hardly an option in the stroke population.[13]

The published research on the epidemiology of LLS is relatively rare. A systematic review published on this topic was back in 2013, which included literature between October 2002 and October 2012.[14] We have not found any other systematic review to summarize the research conducted, on the epidemiology of LLS, after October 2012. Hence, our systematic review has considered the literature published between November 2012 and July 2019 to identify studies specifically on the epidemiological burden associated with adult LLS. LLS affects both children and adults; however, this systematic review focuses only on adults.

Aim and objective

The aim of this systematic review is to describe and quantify the size of the problem (LLS) and to highlight the evidence gap.

Methods

This systematic review was conducted to identify evidence assessing the epidemiological burden of LLS. Preferred reporting items for systematic reviews and meta-analyses, reported at http://www.prisma-statement.org/statement.htm guidelines were followed throughout. We aimed to use a rigorous and transparent methodology to reduce bias in the selection of relevant studies.

Data sources and search strategy

We systematically reviewed the literature indexed in MEDLINE and EMBASE, published between November 2012 and July 2019, relating to the epidemiological burden associated with LLS in adults. The search strategy used is reported in the Supplementary Materials and was constructed from search terms relating to the epidemiological burden for spasticity, to the lower limb, and to the main underlying pathologies associated with LLS. The search was narrowed by applying filters to limit the studies only to adults, English language and human. The bibliography of each relevant article was cross-referenced with the search results to identify additional studies.

Study selection

The first 100 abstracts were screened independently by two researchers and any disagreements resolved by discussion. Each abstract was then screened by one researcher and included studies checked by another researcher. Inclusion criteria for study selection were primary research and systematic reviews relevant to adults with LLS from any cause, reporting epidemiological outcomes, published in English between 2012 and 2019. The inclusion and exclusion criteria are reported in full in Table 1 in Supplementary Materials.

The full texts were retrieved for all studies that definitely or possibly met the inclusion criteria for abstract screening. Full-text screening used the same inclusion criteria as abstract screening but focused on identifying studies with clinically relevant outcomes. The full-text screening was conducted independently by two researchers and disagreements were resolved by discussion. The methodological quality of included studies was assessed and documented based on the concise critical appraisal checklist reported in Table 2 in Supplementary Materials.

Data extraction

Data from the included studies were extracted into a pre-agreed template in MS Word by one researcher and all data extraction tables were checked by a second researcher. No statistical analysis was planned but the results were synthesized narratively to identify common themes and gaps in the evidence.

Results

The database search of MEDLINE and EMBASE identified 2357 citations, of which 447 were duplicates, leaving 1910 unique citations for screening. We identified many studies that reported on the management of spasticity in general, but the evidence base on LLS epidemiological burden was much smaller. A total of 25 articles were identified

Table 1: Inclusion and exclusion criteria

Category	Inclusion criteria	Exclusion criteria
Population	Patients older than 18 years of age with LLS that could have resulted from any of the following underlying diseases Stroke MS TBI Cerebral palsy Others, for example, PD	Studies investigating patients without LLS Studies on adolescents and children younger than 18 years of age with LLS
Epidemiologic outcomes	Prevalence and incidence of LLS due to different underlying pathologies, as listed above Trends of LLS over time Outcomes and prognosis of LLS Health and social problems associated with LLS Comorbidities associated with LLS	Articles without relevant data on any of the outcomes of interest Studies on genetic profiling Prevalence studies with fewer than ten participants Articles investigating the efficacy and/or effectiveness of botulinum toxin or any other investigation in the treatment of LLS Studies investigating the biomechanical factors associated with spasticity (e.g., electromyogram findings, joint angle, foot position, and muscle blood flow) Studies assessing the validity of instruments used to measure spasticity
Study design	Primary research including cohort studies, case–control studies, cross-sectional studies, case series, and randomized controlled trials (if available), database studies, and systematic reviews	Letters to the editor Narrative reviews Editorials Expert opinions Case studies
Year of Publication	November 2012 to July 2019	Studies prior to November 1, 2012 and after July 31, 2019
Language	English language	Non-English language

Filters applied: Human, adults. LLS: Lower limb spasticity, MS: Multiple sclerosis, TBI: Traumatic brain injury, PD: Parkinson's disease

Table 2: Quality assessment criteria for included studies

Criterion	Yes	Partly, or unclear	No
1. Methodology Is the study methodology appropriate for the aims of the study?	2	1	0
2. Transparency of reporting Are all relevant outcomes reported clearly in the paper?	2	1	0
3. Sample size Were enough patients recruited into the study to make the conclusions credible?	2	1	0
4. Conclusions Are the conclusions of the paper supported by the results reported?	2	1	0

as potentially meeting the inclusion criteria and were retrieved as full texts, and nine of these were subsequently included in the review [Figure 1].

Nine studies included in this systematic review all described primary research on the epidemiological burden of LLS in adults with varying underlying pathologies. Five of these studies used observational cross-sectional methodologies; two studies used case–control methodology, one was a prospective cohort study and one was a systematic review. All studies reported epidemiologic outcomes, with two reporting multiple outcomes and one systematic

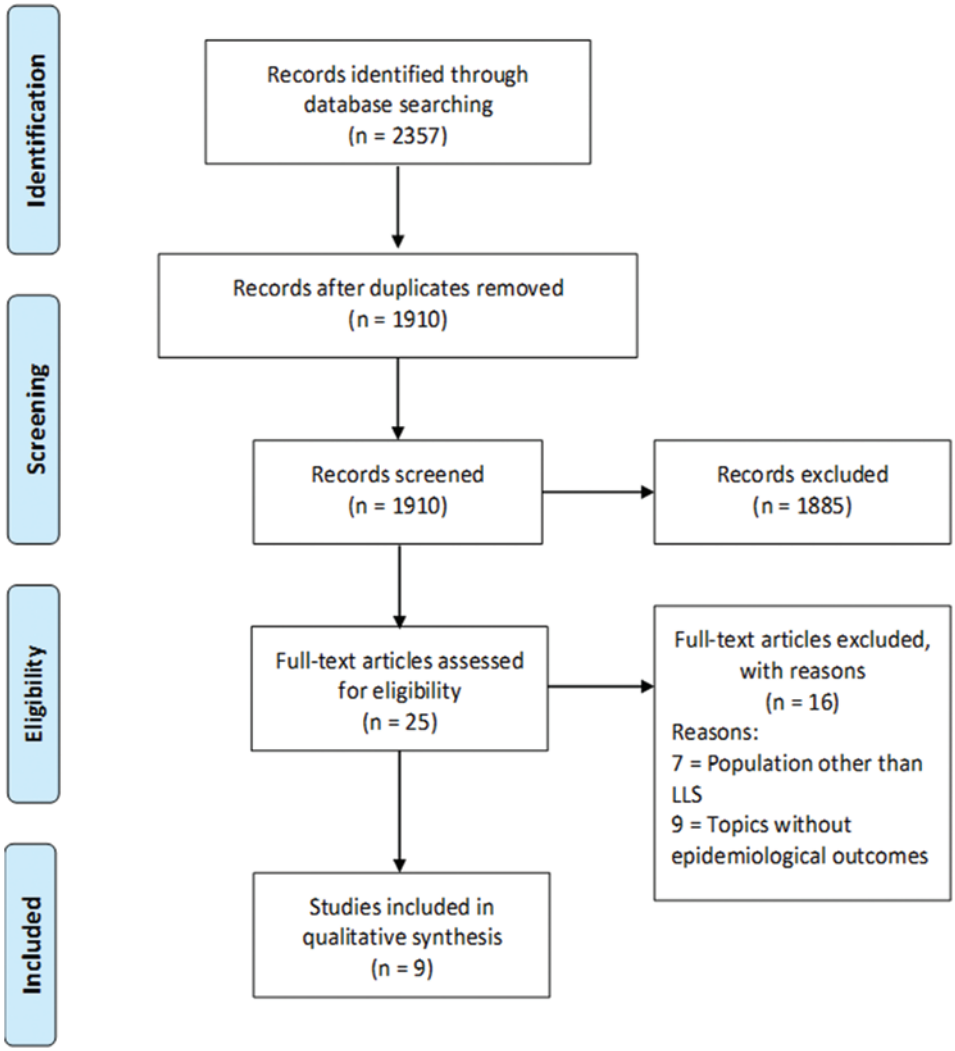

Figure 1: Preferred reporting items for systematic reviews and meta-analyses flow diagram. LLS: Lower limb spasticity

review of observational studies. The study characteristics of included studies are summarized in Table 3.

Eight studies reported on the prevalence of LLS in cohorts with a particular underlying disease. The pilot results of the national SONAR registry study reported the incidence of LLS in stroke patients. These are summarized in Table 4. Three studies focused on LLS in Parkinson's disease (PD) patients, three in MS patients, and one each in stroke, neuromyelitis optica spectrum disorder, and multiple etiologies patients. There was considerable variation between studies on the instruments used to measure LLS. The Modified Ashworth Scale was the only instrument reported as being used in more than one study.

The incidence of LLS in patients with ischemic stroke in the internal carotid artery territory was 44.9% due to the first-ever stroke in the first 10 days after stroke onset.[15] The LLS severity level was varied among patients, 32.5% presented with mild neurological deficit while 27% were bedridden.[15]

Matsubara *et al.* had studied spasticity with various underlying pathologies. The prevalence of LLS in patients with PD and multiple system atrophy (MSA) was 12.7% and 5.8%, respectively. About 50% of PD patients had bilateral spasticity and 50% PD patients had unilateral spasticity.[16]

Atlas of Social Protection Indicators of Resilience and Equity (ASPIRE) is the largest existing international database on spasticity, which

Table 3: Characteristics of studies included in this review

References	Underlying pathology	Country	Participants (*n*)	Male	Focus of study
Francisco *et al*.[17]	Multiple etiologies	International	727	348	Prevalence
Dornak *et al*.[15]	Stroke	Czech Republic	256	157	Incidence
Matsubara *et al*.[16]	PD	Japan	63	NR	Prevalence
Matsubara *et al*.[16]	MSA	Japan	17	NR	Prevalence
Matsubara *et al*.[16]	PSP	Japan	11	NR	Prevalence
Yang *et al*.[19]	PD	China	-	-	Prevalence
Matsubara *et al*.[18]	PD	Japan	27	NR	Prevalence
Matsubara *et al*.[18]	MSA	Japan	5	NR	Prevalence
Matsubara *et al*.[18]	PSP	Japan	2	NR	Prevalence
Matsubara *et al*.[18]	CBD	Japan	2	NR	Prevalence
Al-hussainy and Hatem[20]	MS	Iraq	110	36	Prevalence
Barzegar *et al*.[23]	NOSD	Iran	122	NR	Prevalence
Carnero *et al*.[21]	MS	Argentina	427	NR	Prevalence
Lebrato Hernández *et al*.[22]	MS	Spain	120	NR	Prevalence

MS: Multiple sclerosis, NOSD: Neuromyelitis Optica Spectrum Disorder, MSA: Multiple system atrophy, PSP: Progressive supranuclear palsy, CBD: Corticobasal degeneration, PD: Parkinson's disease

Table 4: Prevalence of lower limb spasticity in different conditions

Study	Country	*n*	Muscle groups	Prevalence of LLS (%)
Multiple etiologies				
Francisco *et al*.[17]	International	727	Any LL	84.2
Stroke				
Dornak *et al*.[15]	Czech Republic	256	Any LL	46.9
PD				
Matsubara *et al*.[16]	Japan	91	Any LL	49.2
Yang *et al*.[19]	China	-	Leg	14.0
Matsubara *et al*.[18]	Japan	36	Any LL	34.3
MS				
Al-hussainy and Hatem[20]	Iraq	110	Leg	17.3
Carnero *et al*.[21]	Argentina	189	Leg	29.1
Lebrato Hernández *et al*.[22]	Spain	120	Leg	23.3
NOSD				
Barzegar *et al*.[23]	Iran	40	Leg	26.8

NOSD: Neuromyelitis Optica Spectrum Disorder, LLS: Lower limb spasticity, MS: Multiple sclerosis, PD: Parkinson's disease

prospectively evaluates demographics and clinical characteristics of spasticity across multiple etiologies including stroke, MS, other etiologies, cerebral palsy, TBI, and SPI. The database includes patients who have a disability and a caregiver. The prevalence of LLS in ASPIRE database patients was reported 84.2%.[17] These data on the prevalence of LLS in different underlying pathologies are summarized in Table 3.

Matsubara *et al*. had studied spasticity with various underlying pathologies. The prevalence of LLS in patients with PD and corticobasal degeneration was 22.2% and 50%, respectively. However, the prevalence of LLS in MSA and progressive

supranuclear palsy patients was 0%.[18] The authors did not find any evidence on the comparative rate of prevalence of bilateral spasticity and unilateral LLS. No studies reported on the severity of spasticity in patients with PD.

Pooled prevalence of LLS in PD patients was 14%. The prevalence was lower in Asia (12%) than outside of Asia (16%). The authors found a relatively higher prevalence in females (13%) than in males (11%).[19] The prevalence of LLS in MS patients ranged from 17.3% to 29.1% in our systematic review.[20-22]

Discussion

The epidemiologic burden of LLS is significantly high but may change over time as the epidemiology of the underlying conditions changes. For example, there is evidence that the prevalence of stroke has fallen in developed countries[24] but may increase again in the future with aging of the population.[25] The prevalence of stroke and cardiovascular disease is increasing, especially in developing countries. Increasing the use of motor vehicles and lifestyle changes may lead to an increase in people with LLS. Although advanced medical technologies have improved the survival after predisposing events, this improved survival may increase LLS prevalence, we did not find any study providing the evidence of an association between long-term survival and LLS. The prevalence of spasticity vary widely based on underlying conditions. The prevalence of spasticity following stroke is between 17% and 46%,[26] however, post-stroke LLS indicated in our research is 46.9%, which is marginally higher from the previous research and maybe contributed by chance only. The prevalence of spasticity in PD patients ranges from 0% to 38%.[19]

There is an association between LLS and falls. A study conducted on MS patients found that the severity of knee flexors and ankle plantar flexors spasticity was significantly higher in the fallers compared to non-fallers.[8] Injuries after fall due to LLS are increasing in elderly people with an increase in aging populations, especially in Western countries.[27] The evidence of LLS complications including falls and injuries after fall is scarce. We have found only one study concluding the association between LLS and falls in MS patients. A most common complaint by the patients is pain; however, we did not find any clear association between LLS and occurrence of pain.

International studies on the prevalence of LLS are scarce. We found only one international study on the prevalence of LLS and associated burden of illness. We did not find any specific LLS patterns or trends based on geographical location or underlying conditions. All the included studies meet our quality assessment criteria.

Evidence gaps

We found limited evidence on the burden of illness associated with LLS. This is partly because we focused on studies published between November 2012 and July 2019 to ensure that the review reflects the most recent disease epidemiology. However, we believe that there is relatively little published research on the epidemiology and impact of LLS, during this approximately 7 years period, compared to other medical conditions. Moreover, we found only one study on the incidence of LLS, which is astounding especially for the countries who have national health-care databases. This indicates that LLS either does go unrecognized by health-care professionals or is not considered as an individual illness.

Substantial gaps in this systematic review need to be addressed through conducting:

- More research to determine the prevalence and incidence of LLS, and the trends in the incidence and prevalence of LLS over time and across different geographical regions
- More research to understand the association of LLS and its complications, regardless of the underlying causative mechanisms.

Conclusion

Our research has indicated that a substantial proportion of adults with stroke, MS, PD, cerebral palsy, and other motor neuron disorders may have LLS. However, we cannot be sure of the overall burden of LLS due to the lack of global epidemiological data. Further research on the evidence gap areas is necessary for a greater understanding of the problem.

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Supplementary Material

Search strategy

ab = abstract; ti = title; sh = MeSH: Medical subject heading (MEDLINE medical index term)
Filters: Humans, English, Publication dates: November 1, 2012 to July 31, 2019.

1. Epidemiologic string
    1. Incidence.ti,ab
    2. prevalence.ti,ab
    3. incidence.sh
    4. prevalence.sh
    5. epidemiology.sh
    6. "epidemiological data".ti,ab
    7. epidemiology.ti,ab
    8. epidemiologic.ti,ab
    9. epidemiological.ti,ab
    10. "unmet need".ti,ab
    11. access.ti,ab
    12. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11
2. Disease string
    1. Spasticity.ti,ab
    2. palsy.ti,ab
    3. rigidity.ti,ab
    4. hemiparesis.ti,ab
    5. hemiplegia.ti,ab
    6. "brain injury".ti,ab
    7. stroke.ti,ab
    8. "multiple sclerosis".ti,ab
    9. hypertonic*.ti,ab
    10. "cerebral palsy".ti,ab
    11. botulinum.ti,ab
    12. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11
    13. leg.ti,ab
    14. "lower limb".ti,ab
    15. calf.ti,ab
    16. thigh.ti,ab
    17. knee.ti,ab
    18. foot.ti,ab
    19. ankle.ti,ab
    20. hip.ti,ab
    21. 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20
    22. 12 AND 21
3. 1 AND 2
4. 3 NOT (child)