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Epidemiology of Traumatic Spinal Cord Injury in Developing Countries from 2009 to 2020: A Systematic Review and Meta-Analysis

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Keywords

Traumatic spinal cord injuries · Developing countries · Incidence · Epidemiology · Etiology

Abstract

Introduction: Traumatic spinal cord injury (TSCI) is a catastrophic event with a considerable health and economic burden on individuals and countries. This study was performed to update an earlier systematic review and metaanalysis of epidemiological properties of TSCI in developing countries published in 2013. **Methods:** Various search methods including online searching in database of EMBASE and PubMed, and hand searching were performed (2012 to May 2020). The keywords "Spinal cord injury," "epidemiology," "incidence," and "prevalence" were used. Based on the definition of developing countries by the International Monetary Fund, studies related to developing countries were included. Data selection was according to PRISMA guidelines. The quality of included studies was evaluated by Joanna

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Briggs Institute Critical Appraisal Tools. Results of meta-analysis were presented as pooled frequency, and forest, funnel, and drapery plots. Results: We identified 47 studies from 23 developing countries. The pooled incidence of TSCI in developing countries was 22.55/million/year (95% CI: 13.52; 37.62/ million/year). Males comprised 80.09% (95% CI: 78.29%; 81.83%) of TSCIs, and under 30 years patients were the most affected age group. Two leading etiologies of TSCIs were motor vehicle crashes (43.18% [95% CI: 37.80%; 48.63%]) and falls (34.24% [95% CI: 29.08%; 39.59%], respectively). The difference among the frequency of complete injury (49.47% [95% Cl: 43.11%; 55.84%]) and incomplete injury (50.53% [95% CI: 44.16%; 56.89%]) was insignificant. The difference among frequency of tetraplegia (46.25% [95% Cl: 37.78%; 54.83%]) and paraplegia (53.75% [95% Cl: 45.17%; 62.22%]) was not statistically significant. The most prevalent level of TSCI was cervical injury (43.42% [95% CI: 37.38%; 49.55%]).

Ali Golestani and Parnian Shobeiri are the first authors and contributed equally.

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Conclusion: In developing countries, TSCIs are more common in young adults and males. Motor vehicle crashes and falls are the main etiologies. Understanding epidemiological characteristics of TSCIs could lead to implant-appropriate cost-effective preventive strategies to decrease TSCI incidence and burden.

Introduction

Rationale

Traumatic spinal cord injury (TSCI) is a catastrophic event with a high mortality rate and physical and emotional difficulties for patients [1-3]. It is defined as injuries to the spinal cord, nerve roots, osseous structures, and disco-ligamentous components [4]. TSCI can be due to motorcar crashes, falling, violence, and sports [2]. Besides, it can cause a tremendous burden on societies [5, 6]. TSCI can cause pain, paralysis, spasticity, sensation loss, urinary, and fecal incontinence and makes patients susceptible to pneumonia, septicemia, urinary tract infections, pressure ulcers, and cardiac dysfunctions [7, 8]. Disabilities caused by TSCI can be permanent and not fully treated with medical care offered to patients today; therefore, preventive solutions might be valuable [9]. The global incidence of traumatic spinal injury (TSI) is about 10.5 cases per 100,000 persons [4]. The incidence of TSI showed more significant numbers in countries with low and middle income (13.69 per 100,000 persons) compared to countries with high income (8.72 per 100,000 persons) [4]. Despite higher incidence rates in developing countries, we see that information registration in these countries is less accurate and unreliable that it becomes hard to assess the global burden of TSCI [4, 10, 11]. The genuine registered information in developed countries cannot be implemented in developing countries because of different epidemiological patterns and causations.

Objectives

Because of inadequate information access, it is crucial to gather all epidemiological data in developing countries to plan more effective preventive strategies. The study aimed to, through a systematic synthesis and meta-analysis by updating our previous study published in 2013 [12], ease the access and interpretation of epidemiological properties and etiologic features of TSCI in developing countries.

Methods

All stages and structures of this systematic review and metaanalysis study are based on the PRISMA 2020 statement [13]. We also utilized methodological guidelines attributed to observational epidemiological systematic reviews reporting cumulative incidence and prevalence [14].

Eligibility Criteria

Instead of using the traditional PICO approach, including population, intervention, comparator, and outcome as inclusion structure, we applied the CoCoPop model (condition, context, and population) because it is more relevant to questions about prevalence and incidence, as is mentioned by Munn et al. [14].

Condition

In this review, we excluded studies of nontraumatic or mixed spinal cord injury (SCI) if it was not possible to distinguish different SCI major etiology groups clearly. Furthermore, we did not consider the TSI as same as TSCI, and we excluded all TSI injuries without mentioning the cord injury. To keep the generalizability of the result, we excluded studies focusing on a specific etiology (e.g., road traffic injuries), specific injury level (e.g., thoracic injury), or specific target population (e.g., workers).

Context

National and subnational studies of developing countries that reported the frequency of different traumatic etiologies, severity, or level of injury with adequate details were included. We defined the developing countries using the International Monetary Fund 2021 update. All included countries remained in developing countries group during the defined search period [15].

Population

Pediatric-onset (<16 years) TSCIs were excluded. All observational epidemiological studies related to our study were either survey- or registry-based.

Information Sources and Search Strategy

We updated our previous electronic search on EMBASE via Ovid SP and PubMed (including MEDLINE and PubMed Central, 2012 to 5th May 2020) [12]. We used the search strategy Jazayeri et al. [11] described in detail elsewhere. The keywords "Spinal cord injury," "epidemiology," "incidence," and "prevalence" were used. We checked the references of the retrieved eligible studies to find probable relevant missed articles from database searching. We also checked reference lists of systematic reviews since 2010 [4, 12, 16-20] to avoid losing any potentially missed papers before 2012. We also collected relevant abstracts from conference proceedings and checked for full-text availability. In addition, we searched grey literature [11] using 13 grey literature resources and 14 websites. We also contacted 306 investigators (corresponding authors of previous systematic reviews or persons whose e-mail was retrieved from registries) by e-mail and asked them for their unpublished articles about epidemiology of TSCIs. Most authors did not have any related new unpublished study and most registries referred to their previous published results. There were no language or country limitations in all resources' search processes.

The Selection Process, Data Collection Process, and Data Items Two independent reviewers (S.F.M. and M.A.D.O.) screened the titles and abstracts of each retrieved record from literature. Then based on eligibility criteria, the full texts of selected papers were evaluated. The disagreements were resolved by consensus, or the third reviewer (S.B.J.) decided. After the inclusion of relevant full-texts, two independent authors (S.F.M. and M.A.D.O.) extracted the following information (if they were available) from each record: coverage years, the number of patients, frequency of male and female, mean age of patients, incidence or prevalence, the severity of injuries, etiology, level of injuries, injuries frequency in different age groups, data collection type (prospective, retrospective, cross-sectional), study scale (population-based, hospitalbased, rehabilitation-based, etc.). The third author (S.B.J.) doublechecked the extracted data for accuracy and completeness, and data were rechecked by the fourth author (A.G.) before analysis.

Critical Appraisal

We used appropriate Joanna Briggs Institute critical appraisal tools for assessing the quality of included studies [21], which the checklist for case series was applied for this study [22]. This checklist contains ten questions related to the risk of bias assessment, including appropriate definition and selection, suitable reporting, and correct statistical analysis. One question regarding the outcome or follow-up result was not applicable. Therefore, the maximum score for each study would be nine. Answers to each question in the checklist could be "yes, no, unclear, or not applicable." For scoring each study, two independent researchers (S.F.M. and M.A.D.O.) assessed each study, and disagreements were resolved by the decision of a third researcher (A.G.). Our complete criteria for answering each question are explained in detail in online supplementary Appendix 1A (for all online suppl. material, see www. karger.com/doi/10.1159/000524867. We did not exclude any study based on critical appraisal, and the qualification of each study was evaluated to recognize the aspects of potential bias.

Data Synthesis

We used a tabular summary approach for the data synthesis of systematic review [14]. For meta-analysis by using the "metaprop" function, a random-effect model was applied to estimate Der Simonian and Laird's pooled effect of the percentages of injury severity (completeness vs. incompleteness and paraplegia vs. tetraplegia), injury etiologies (motor vehicle crashes (MVCs), falls, gunshots, violence/stab, sports, and others/unknown), and male gender. The meta-analysis and heterogeneity results summary were visualized by drawing a forest plot. The funnel plot was drawn to check publication bias. Egger's regression tests were used with a *p* value <0.05 to indicate potential publication bias more objectively [23]. The effect of publication bias was evaluated by the trim and fill analysis performed by adding studies and making symmetrical distribution consequently [24]. Cochrane's Q statistic was used for between-study heterogeneity evaluation. We used I^2 for quantification between-study heterogeneity, and a value of 0%, 25%, 50%, and 75% was considered as no, low, medium, and increased heterogeneity, respectively [25]. We performed a leaveon-out sensitivity analysis to assess a single study's effect on the overall meta-analysis estimate. A supporting figure to a forest plot is the drapery plot. It is applicable to indicate confidence intervals for different fixed significance threshold assumptions and prevents exclusive depending upon the p value <0.05 significance

threshold. All statistical analysis and visualizations were carried out using R version 4.0.4 (R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria) by using the following packages: "meta" (version 4.17-0), "metafor" (version 2.4-0), "dmetar" (version 0.0-9), and "tidyverse" (version 1.3.0). In all analyses, a *p* value of <0.05 was considered statistically significant.

Results

Study Inclusion

We recognized 1,115 records from EMBASE and 858 from Medline and pooled them in the EndNote X8 software database. Additionally, we recognized one book [26], 10 reports from national registries [27–29], 10 articles from reference checking, two studies from hand searching key journals, six from conference abstracts, and two studies from New Zealand and Russia after personal communication with 306 researchers. Then 783 duplicated records were excluded. Two team members (S.F.M. and M.A.D.O.) screened the titles and abstracts of the remaining 1,221 records. After excluding 1,093 irrelevant records which did not provide any epidemiological information (these studies were related to complications of traumas, surgeries results, etc.), full texts of 128 records were evaluated for eligibility; of which 81 were excluded: 16 reported nontraumatic or mixed injuries, 22 records were conference abstracts or review articles, five said only cervical SCI, and 38 were not related to developing countries. Overall, our search resulted in 47 studies [27-73] from 23 different developing countries. Figure 1 shows the flow diagram of different stages of study based on the PRISMA statement [13]. Table 1 and Table 2 show extracted available information from included studies. Among included studies, 37 were retrospective, 8 were prospective, and two studies were cross-sectional [54, 71]. Only four studies were population-based [28, 36, 46, 70], while 14 and 29 were hospital-based and rehabilitationbased, respectively. Although the Egypt study by Tallawy et al. [36] only included six TSCI patients, we had it in our study because it was a population-based door-to-door study among all city citizens. Its results were acquired by an extent valuable screening.

Methodological Quality

Results of the quality assessment are shown in Appendix 1B. The minor frequency of "yes" answers was related to questions about identification and inclusion criteria (questions 1–3), while questions about statistical analysis appropriateness (question 10) and reporting (questions 6

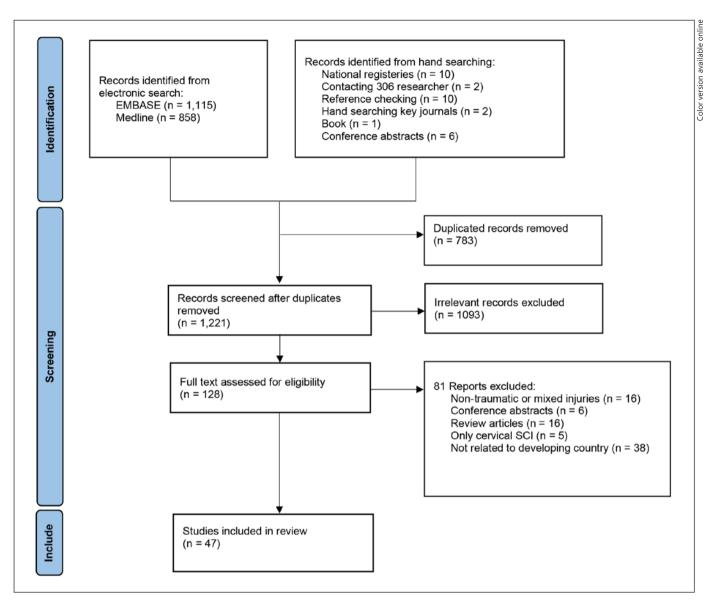


Fig. 1. Flow chart of studies based on the PRISMA statement.

and 7) could almost get "yes" among all studies. The total score of studies ranged from 4 to 9, and six studies got a maximum score [28, 38, 42, 44, 54, 70].

Review Findings

Gender, Age, and the Incidence

Considering gender proportion among included studies, only four studies did not provide exact information about the number of males and females in TSCI [31, 39, 61, 71]. A total of 43 studies were included in the metaanalysis. The estimation of male cases proportion among all included countries in the pooled sample of 25,780 individuals was 80.09% (95% CI: 78.29%; 81.83%, test of heterogeneity: $I^2 = 87.3\%$, *p* value <0.0001, Appendix Fig. 1A). While Turkey had the lowest male to female ratio (1.6:1) (male relative frequency: 61.9%) [37], Ethiopia showed the highest (7.6:1) (male relative frequency: 88.4%) [47]. Thirty-six studies provided information about mean age, and 27 studies reported the proportion of TSCIs in different age groups. The mean age of TSCI patients ranged from 28.9 in Saudi Arabia [51] to 50.1 years in China [58]. The most affected age group was under 30 years patients (Table 2). Only 10 included studies reported TSCI incidence, ranging from 10.23 cases per

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Study No.	Country	First author	Years of study	Patients, <i>n</i>	Male to female ratio	Mean age, years	Incidence case/ million people	Study design	AIS Impairment Scale	Complete Con paraplegia, tetr %	Complete tetraplegia, %	Incomplete paraplegia, %	Incomplete tetraplegia, %
-	Bangladesr	Bangladesh Rahman et al. [61]	2011-2016	2,068	I	I	I	Retrospective, rehabilitation center	I	Paraplegia: 55, tetraplegia: 45	etraplegia	1: 45	
2	Botswana	Löfvenmark et al. [48]	2011-2013	49	2.4:1	Peak 31–45: 39%	13	Prospective, hospital- based	AIS A + B: 61%, AIS C + D: 23%, AIS unknown: 16%	Paraplegia: 41, tetraplegia: 59	etraplegia	1: 59	
m	Brazil	Barbetta et al. [64]	2014	2,076	4.9:1	31.0±11.4	1	Retrospective, rehabilitation centers (Sarah Network of Rehabilitation Hospitals)	A: 60.9%, B: 13.4%, C: 12%, D: 7.3%, cauda equina: 5.6%	Complete: 744, incomplete: 25.6 ¹ , paraplegia: 67.7, tetraplegia: 32.3	incomple i: 32.3	te: 25.6 ¹ , par.	aplegia:
4	Brazil	Bellucci et al. [45]	2012	348	5.5:1	35.2±15	I	Retrospective, rehabilitation-based	A: 67%, B: 10.9%, C: 8.6%, D: 10.9%, E: 2.6%	Complete: 67%, incomplete: 33%	incomple	te: 33%	
ъ	Cambodia	Choi et al. [60]	2013-2014	80	5.2:1	37±13 Median: 32 Peak 16–30: 41%	1	Retrospective, hospital- based	A: 38%, B + C + D: 38%, E: 25%	Complete: 38, incomplete: 38%, non-SCI: 25	icomplete	:: 38%, non-5	Cl: 25
9	China	Chen et al. [59]	2009–2013	232	4.00:1	45.35±14.35	I	Retrospective, hospital- based	A: 14.22%, B: 15.09%, C: 32.76%, D: 37.93%	5.17 13		18.53	63.36
7	China	Hua et al. [38]	2001-2010	561	4.1:1	34.74±12.24	1	Retrospective, hospital- based	1	Complete: 49.9, incomplete: 51.1	incomplet	te: 51.1	
8	China	Li et al. [32]	2002	264	3.0:1	41.7 Range: 6–80	60.6	Retrospective, hospital- based	-	1		1	1
6	China	Ning et al. [33]	2004–2008	869	5.63:1	46±14.2 Range: 16−90 Peak 46−60: 39.4%	23.7	Retrospective, hospital- based	A: 25.2%, B: 18.2%, C: 14.7%, D: 41.9%	10.7 14.5		17.7	57.1
10	China	Ning et al. [55]	2009–2013	554	4.33:1	45.6±13.8	I	Retrospective, hospital- based	A: 39.4%, B: 8.7%, C: 21.1%, D: 30.8%	22.2 17.1		22.9	37.8
11	China	Yang et al. [63]	2003–2011	1,340	3.5:1	41.6±14.7 Median: 42 IQR: 20	I	Retrospective, hospital- based	I	Complete: 26.4%, incomplete: 73.6%	%, incomp	lete: 73.6%	
12	China	Wang et al. [42]	2007–2010	761	3.4:1	45±13 Range: 5−87	I	Retrospective, hospital- based	A: 25.6%, B: 11.8%, C: 27.3%, D: 35.2%	Complete: 25.6%, incomplete: 74.4%	%, incomp	lete: 74.4%	
13	China	Yang et al. [44]	2003–2011	3,519	3.0:1	I	I	Retrospective, hospital- based	1	I		1	I
14	China	Zhou et al. [58]	2009–2014	354	2.34:1	50.1±15.5 Range: 15−85	I	Retrospective, hospital- based	A: 20.4%, B: 7.6%, C: 23.2%, D: 48.8%	7.1 13.8		25.7	53.4
15	Egypt	Tallawy et al. [36]	2009–2012	9	5.0:1	40±16	Prevalence: 180	Prevalence: Prospective, population- 180 based door-to-door study	A: 16.7%, B: 0%, C: 16.7%, D: 66.7%	Complete: 16.7%, incomplete: 83.3%	%, incomp	lete: 83.3%	
16	Ethiopia	Lehre et al. [47]	2008–2012	146	7.6:1	31.7 Median: 28 Range: 15–81	1	Retrospective, hospital- based	A: 32.2%, B + C + D: 46.6%, E: 21.2%	Complete: 32.2%, incomplete: 46.6%, no injury: 21.2%	%, incomp	lete: 46.6%, r	injury:
17	Ghana	MK Ametefe et al. [52] 2012–2014] 2012–2014	185	3.2:1	36.25±13.62 Range: 4−86 Peak 31−45: 44%	I	Retrospective, hospital- based	A: 40%, B: 7%, C: 8.6%, D: 17.8%, E: 26.5%	Complete: 40%, incomplete: 33.5%, no injury: 26.5%	incomple	te: 33.5%, no	injury:

Traumatic Spinal Cord Injury in Developing Countries

Table 1. Comparative analysis of TSCIs in developing countries

Study No.	Country	First author	Years of study	Patients, <i>n</i>	Male to female ratio	Mean age, years	Incidence case/ million people	Study design	AIS Impairment Scale	Complete Complete paraplegia, tetraplegia, %	e Incomplete ia, paraplegia, %	Incomplete tetraplegia, %
18	India	Chhabra et al. [35]	2002–2010	1,138	5.9:1	34.4 Median: 32 Peak 20–29: 34.18%	I	Retrospective, hospital- based	A: 71.12%, B: 14.68% C: 8.18%, D: 6.02%	51.94 19.24	14.72	14.09
19	India	Mathur et al. [49]	2000-2008	2,716	4.2:1	Peak 20–49: 71%		Prospective, observational study hospital-based	A: 43.9%, B: 6.4%, C: 8%, D: 16.4%, E: 13%, AIS unknown: 12.3%	Complete: 43.9%, incomplete: 30.8%, no injury: 13%, not tested: 12.3%	omplete: 30.8%, r 6	injury:
20	India	Singh et al. [71]	2013–2014	148	I			Cross-sectional, rehabilitation center	1	1	I	I
21	Iran	Derakhshanrad et al. [54]	2011-2015	1,137	3.8:1	29.1±11.2	Prevalence: 236	Prevalence: Cross-sectional, 236 rehabilitation center capture-recapture method	A: 53.5%, B: 18.7%, C: 17.6%, D: 9.6%, E: 0.6% 1	43.6 10.1	27.1	19.2
22	Iran	Sharif-Alhoseini et al. [43]	2010–2011	138	5.5:1	33.2±14.3	10.5	Retrospective, hospital- based	A: 86.2%, B: 3.6%, C: 2.2%, D: 8%	Complete: 86.2%, incomplete: 13.8% Paraplegia: 81.9%, tetraplegia: 18.1%	omplete: 13.8% raplegia: 18.1%	
23	Iran	Yadollahi et al. [68]	2009–2015	171	4.88:1	38.2±17.8		Retrospective, hospital- based	I	I	1	1
24	Kuwait	Prasad et al. [66]	2010–2015	155	4.3:1	. 36.4±14		Retrospective, rehabilitation center	A: 46.8%, B: 9%, C: 18%, D: 26.1%	Complete: 46.8%, incomplete: 53.2% Paraplegia: 41.3%, tetraplegia: 30.3% Cauda equina: 28.4%	omplete: 53.2% raplegia: 30.3%	
25	Macedonia	Jakimovska et al. [73]	2015-2016	38	5.3:1	43 Median: 41 Range: 17–83	13	Prospective cohort, hospital-based	A: 44.7%, B + C + D: 39.5%, AlS missing: 15.8%	Complete: 53.1%, incomplete: 46.9% ²	omplete: 46.9% ²	
26	Malawi	Jessica Eaton et al. [69]	2016–2017	46	4.7:1	36.5±13.8	1	Prospective, hospital- based	A: 23.9%, B: 4.3%, C: 10.9%, D: 10.9%, without injury: 50%	Complete: 47.8%, incomplete: 52.2% ³	omplete: 52.2% ³	
27	Malaysia	lbrahim et al. [39]	2006–2009	167	I			Retrospective, rehabilitation center	1	1	1	1
28	Malaysia	Joseph et al. [31]	2003–2006	57	I			Retrospective, hospital- based	I	1	1	I
29	Mexico	Rodríguez-Meza et al. [56]	2006–2013	464	3.5:1	37.9±15.9	1	Retrospective, rehabilitation center	A: 56.2%, B: 13.1%, C: 22.4%, D: 8.2%	43.3 12.9	21.6	22.2
30	Mexico	Zárate-Kalfópulos et al. [57]	2005-2012	346	4.8:1	33.9 Range: 12–65 Peak 20–29: 35.8%		Retrospective, hospital- based	A: 62.7%, B: 13.8%, C: 13.8%, D: 9.5%	Complete: 62.7%, incomplete: 37.3% Paraplegia: 63%, tetraplegia: 37%	omplete: 37.3% plegia: 37%	
31	Nepal	Shrestha et al. [41]	January 2008 381 and January 2011	381	2.7:1	Peak 21–30: 30.45%	1	Retrospective, rehabilitation center	A: 55.9%, B: 9.7%, C: 10.8%, D: 9.2%, E: 4.5%, AIS missing: 9.9%	Complete: 65%, incomplete: 35%	nplete: 35% ⁴	
32	Nigeria	Emejulu et al. [30]	2006–2008	62	3.1:1	Peak 15-40: 45.2%	1	Prospective, hospital- based	1	Complete: 52.1%, incomplete: 47.9%	omplete: 47.9% ⁵	
33	Nigeria	Nwankwo et al. [40]	2009–2012	85	4.3:1	34.8±3.3	1	Retrospective, hospital- based	A: 47.1%, B: 11.8%, C: 22.4%, D: 17.7%, E: 1.18%	Complete: 47%, incomplete: 52%	ıplete: 52%	
34	Nigeria	Yusuf et al. [72]	2014–2016	133	4.5:1	36.0±12.9		Retrospective, rehabilitation center	A: 52.6%, B: 9.8%, C: 11.3%, Complete: 52.6%, incomplete: 27.9% D: 6.8%, E: 19.5%	Complete: 52.6%, inco	omplete: 27.9%	

Table 1 (continued)

Study No.	Country	First author	Years of study	Patients, <i>n</i>	Male to female ratio	Mean age, years	Incidence case/ million people	Study design	AlS Impairment Scale	Complete Complete paraplegia, tetraplegia, %	Incomplete paraplegia, %	Incomplete tetraplegia, %
35	Pakistan	Farooq Khan et al. [65] 2008–2017	2008–2017	2,098	3.9:1	33.31 Range: 2–98	Prevalence 5.74	Prevalence: Retrospective, 5.74 rehabilitation centers	E: 0.4%	Complete: 77.8%, incomplete: 21.8%	mplete: 21.8%	
36	Pakistan	Hazrat Bilal et al. [53]	2008–2012	1,136	4.25:1	Peak 20–29: 31.4%	10.23	Retrospective, rehabilitation-based	1	Complete: 79.5%, incomplete: 20.5%	mplete: 20.5%	
			2008	242			11					
			2009	208			9.45					
			2010	234			10.63					
			2011	228			10.36					
			2012	224			10.18					
37	Russia	Mirzaeva et al. [70]	2012-2016	361	2.4:1	42.1±16.9	16.6	Retrospective, population-based cohort	A: 15%, B: 14.1%, C: 16.9%, D: 42.4%, AlS missing: 11.7%	Complete: 16.9%, incomplete: 83.1%	mplete: 83.1% ⁶	
			2012	53			12.4 Male: 20.02 Female: 6.3					
			2013	10			21.2 Male: 34.1 Female: 10.8					
			2014	79			18 Male: 31.3 Female: 7.4					
			2015	78			17.7 Male: 26.6 Female: 10.6					
			2016	60			13.6 Male: 20.6 Female: 8.1					
38	Saudi Arabi	Saudi Arabia Alshahri et al. [34]	2003-2008	307	7.3:1	29.5 Median: 27 Range: 14–70	1	Retrospective, hospital- based	1	29.3 21.5	18.2	31
39	Saudi Arabi	Saudi Arabia Alshahri et al. [51]	2012-2015	216	6.4:1	28.9 Median: 24 Peak 14–25: 54.6	1	Retrospective, rehabilitation center	1	37 16.7	24.5	21.8
40	South Africa	South Africa Joseph et al. [46]	2013–2014	145	5.9:1	33.5±13.8	75.6	Prospective, population- based	A: 39.3%, B + C: 24.2%, D: 36.5%	Complete: 39.3%, incomplete: 60.7%	mplete: 60.7%	
41	South Africa	South Africa Pefile et al. [29]	2009–2015	84	4.25:1	33.11±11.85	I	Retrospective, hospital- based	A: 44%, B: 5.9%, C: 27.3%, D: 19%, AIS missing: 3.5%	Complete: 44%, incomplete: 52.5%	plete: 52.5%	
42	South Africa	South Africa Phillips et al. [28]	2013–2014	13	3.33:1	48±20.1	20	Prospective, population- based	A: 23.1%, B + C + D: 76.9%	Complete: 23.1%, incomplete: 76.9% Paraplegia: 46.2%, tetraplegia: 53.8%	mplete: 76.9% aplegia: 53.8%	

Traumatic Spinal Cord Injury in Developing Countries

Table 1 (continued)

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Study No.	Study Country No.	First author	Years of study	Patients, <i>n</i>	Male to female ratio	Male to Mean age, years female ratio	Incidence case/ million people	Incidence Study design case/ million people	AIS Impairment Scale	Complete Complete Incomplete Incomplete paraplegia, tetraplegia, paraplegia, % % %	complete Incomplete araplegia, %
43	South Afric	South Africa Sothmann et al. [50]	2003–2014	2,042	5.25:1	34 Peak 20–30: 33.4%	1	Retrospective, hospital- based	1	Complete: 31.7%, incomplete: 68.3%	te: 68.3%
44	Tanzania	Haleluya Moshi et al. 2010–2014 [27]		288	4.19:1	39.1±16.3	26 Male: 43 Female: 11	Retrospective, hospital- based	1	1	1
45	Tanzania	Mehboob Rashid et al. 2011–2015 [62]		125	5.9:1	39.9±16 Range: 5−77	1	Retrospective, hospital- based	A: 45.6%, B + C + D: 54.4%	Retrospective, hospital- A: 45.6%, B + C + D: 54.4% Complete: 45.6%, incomplete: 54.4% based	te: 54.4%
46	Turkey	Erdogan et al. [37]	2007–2011	409	1.6:1	46.82±19.05	I	Retrospective, hospital- A + B + C + D: 15.9%, E: based 84.1%	A + B + C + D: 15.9%, E: 84.1%	1	1
47	Turkey	Tasoglu et al. [67]	2013–2014	206	2.9:1	1	1	Retrospective, rehabilitation center	1	1	1
11 23 case	n this article, <i>f</i> es. ⁴ Due to 38	ASI A and B considered as ASI A and B considered as 17	complete injui 7 AIS E cases, co	ries. ² Due to	6 AIS miss s/incomple	sing cases, completen steness was calculated	ess/incomple 1 in 326 knov	eteness was calculated in 32 wn neurological deficits. ⁵ Cc	known neurological deficits.	¹ In this article, ASI A and B considered as complete injuries. ² Due to 6 AIS missing cases, completeness/incompleteness was calculated in 32 known neurological deficits. ³ Clinical evidence of spinal cord injury was present in 23 cases. ⁴ Due to 38 AIS missing cases, completeness was calculated in 32 known neurological deficits. ³ Clinical evidence of spinal cord injury was present in 23 cases. ⁴ Due to 38 AIS missing cases and 17 AIS E cases, completeness was calculated in 32 known neurological deficits. ⁵ Completeness/incompleteness/incompleteness/incompleteness/incompleteness/incompleteness/incompleteness was calculated in 46 neurological deficits. ⁶ Due to 42	ord injury was present in jical deficits. ⁶ Due to 42

million (cpm) in Pakistan [53] to 75.6 cpm in South Africa [46] annually. For the meta-analysis, we included eight studies with sufficient details which were not age-standardized. The estimation of incidence among all included countries was 22.55/million/year (95% CI: 13.52; 37.62/million/year, test of heterogeneity: $I^2 = 100\%$, *p* value = 0; Appendix Figure 1B). In all studies which reported sex-disaggregated incidence rate, TSCI incidence was higher in males than females [27, 70].

Severity of TSCI

Thirty-nine studies reported severity of TSCIs, of which 37 used the American Spinal Injury Association (ASIA) Impairment Scale for classification [74]. Studies showed an extensive variation in the proportion of complete versus incomplete injuries. The frequency of complete injuries caused by TSCIs ranged from 16.7% in door-to-door Egypt [36] study to 86.2% in Iran [43]. The observed discrepancies in a study in China [59] between the percentage of AISA classification and complete/incomplete injuries (Table 1) which is not discussed in details are probably due to different definitions for classifications. For the meta-analysis, a total of 36 studies were included. The frequency of complete injury in the pooled sample of 19,857 individuals was 49.47% (95% CI: 43.11%; 55.84%, test of heterogeneity: $I^2 = 98.9\%$, p value = 0, Fig. 2a), while the frequency of incomplete injury was 50.53% (95% CI: 44.16%; 56.89%, test of heterogeneity: *I*² = 98.9%, *p* value = 0, Fig. 2b). Appendix Figure 2A and B show drapery plots of complete and incomplete injuries, respectively, which visualizes the meta-analysis results based on the *p* value functions of each study (*p* value on the *y*-axis and the effect size on the *x*-axis). After removing the outliers which resulted in 19 included studies, the frequency of complete and incomplete injury changed to 48.27% (95% CI: 45.17%; 51.37%, test of heterogeneity: *I*² = 70.2%, *p* value < 0.0001, Appendix Fig. 3A) and 51.73% $(95\% \text{ CI: } 48.63\%; 54.83\%, \text{ test of heterogeneity: } I^2 = 70.2\%,$ p value <0.0001, Appendix Fig. 3B), respectively. The funnel plots did not show a publication bias for complete and incomplete injury frequency; the Egger's regression test did not indicate publication bias (p = 0.234) (Appendix Fig. 4A).

Considering tetraplegia versus paraplegia caused by TSCI, relevant data were retrieved from 16 studies. Similar to the completeness or incompleteness of injury, tetraplegia or paraplegia among injured patients included a wide range; the lowest proportion of paraplegia was 18.53% in China [59], while the greatest frequency was related to Iran by 81.9% [43]. The proportion of tetraple-

AIS missing cases, completeness/incompleteness was calculated in 319 known neurological deficits

Stud	Study Country	First author	SCI level, %			Etiology, %)						Age groups, %	w 'sdn			
			cervical	thoracic	lumbar/sacral	MVCs	falls	gunshot injuries	violence/ stab injuries	sports injuries	others/ unknown	0-15	16–30 3	31-45 4	46-60 61-75	5 >75
	Bangladesh	Rahman et al. [61]	1	I	1	27.4	47.9	I	I	I	Fall of object: 18.9, bull attack: 1.9, others: 4	I		I	I	I
5	Botswana	Löfvenmark et al. [48]	59	37	4	68	10	I	16	2	Struck by objects: 4	4	37 3	39 1	14 2	5
m	Brazil	Barbetta et al. [64]	32.2	60.5	7.2	43.7	13.7 Falls from standing height: 1.1	28.4 g	0.3	0.4 Diving: 5.5	5.7	1	1	1	1	I
4	Brazil	Bellucci et al. [45]	42.5	46.3	11.2	38.5 Car: 16.3, motor: 15.8, pedestrian/ bicycle: 6.3	28.7	21.5	I	Diving: 7.7	3.7	1			1	T
2	Cambodia	Choi et al. [60]	27.5	28.75	43.75	29	53	I	I	ı	18	-	41 3	34 1	16 8	I
Q	China	Chen et al. [59]	76.29 Cervicothoracic: 3.88	10.34	Thoracolumbar: 4.7, lumbosacral: 4.7	42.67	36.21 Fall <1 m: 22.41, Fall >1 m: 13.79	all -	1	5.17	12.5 Falling object: 3.45	0	17.67 3	31.90	36.64 >60: 13.79	
~	China	Hua et al. [38]	47.23 cervicothoracic: 3.38	40.28	Thoracolumbar: 7.13, lumbosacral: 5.52	51.2	31.9 Fall from height: 23.9, fall ground level: 8	11	m	Diving: 1.1	3.1 Falling object: 8.6	1		1		1
8	China	Li et al. [32]	4.9	28	66 (lumbar, thoracolumbar, lumbosacral)	22.3	41.3	I	0.4	1.1	16.3 Falling object: 18.6	I			1	I
6	China	Ning et al. [33]	71.5	13.3	15.2	34.1	Fall <1 m: 37.6, fall >1 m: 19.3	1	1.4	0.2	1 Falling object: 6.3	I	15.30 3	31.60	39.40 12	1.70
10	China	Ning et al. [55]	54 C4–C6: 36.8	T11-L2: 30.3	1	21.8	61.7 Fall <1 m: 10.8, fall >1 m: 50.9	ı 	I	0.5	2.6 Falling object: 13.2	1.30	12.80 3	36.20	33.70 15.10	0.70
1	China	Yang et al. [63]	61	20.5	22.8	37.8	42.5 Fall <1 m: 1.5	I	8.7	1.3	1 Falling object: 8.8	<20: 7.4	21–40: 39.6	~ ~	41–60: >61: 9.7 43	9.7 Unknown: 0.4
12	China	Wang et al. [42]	46.3	20.4	33.3	21.2	65.3 Fall <1 m: 12.7, fall >1 m: 52.6	۱ 	8.1		Struck by object: 5.4	1.20	12.10 4	42.60	31.10 61–99: 13	ö
13	China	Yang et al. [44]	I	I	ı	23.6	14.8	I	3.5	0.7	57.2 Falling object: 21.2, not reported: 19.6	<21: 10	21–40: 4 37.6 3	41–60: 37 <i>.7</i>	>60: 13.4	13.4
14	China	Zhou et al. [58]	67.2	17.5	15.2	35.9	55.1 Fall <1 m: 33.6, fall >1 m: 21.5	ı 	1.4	2.8	1.9 Falling object: 2.8	0.28	12.71 2	23.18 4	40.39 19.20	4.80%
15	Egypt	Tallawy et al. [36]	50	16.7	33.3	I	I	ł	I	I	I	I	1	I	I	
16	Ethiopia	Lehre et al. [47]	34.2	21.9 Thora- columbar: 2.7	41.1	54.1	26.7	0.7	2.1	I	1.4 Falling object: 14.4, unknown: 0.7	T	1	I	I	I
1																

Table 2. Etiology, level, and age distribution of TSCIs in developing countries

Traumatic Spinal Cord Injury in Developing Countries

3																
Stud	Study Country	First author	SCI level, %			Etiology, %)						Age groups, %	%			
.02			cervical	thoracic	lumbar/sacral	MVCs	falls	gunshot injuries	violence/ stab injuries	sports injuries	others/ unknown	0-15 16-30	30 31-45	45 46-60	60 61-75	>75
17	Ghana	MK Ametefe et al. [52]	67.5	18	14.5	69.7 Car: 53, motor : 10.2, pedestrian/ bicycle: 6.5	24.3	ı	2.7	T	3.2	3.20 30.8	43	.8 17.3	ю. 0.	1.1
18	India	Chhabra et al. [35]	37.32	57.83	4.86	45	39.6	1	5.2	2.28	1.2 Falling object: 2.4	1	1	T	ı	ı
19	India	Mathur et al. [49]	51.5	Thora- columbar: 48.5	28	53.4	1	I	1	Falling object: 10.8, mis- cellaneous: 7.8	<19:12.6	20-49: 50-69: 71.1 14.4		>70: 2.5		
50	India	Singh et al. [71]	. 1	1	1	43	29	I	-	15	12	1	I	I	I	I
51	Iran	Derakhshanrad et al. 31.5 [54]	l. 31.5	57.9	10.6	61.8	24.5	1	3.8	2.8	1.9 Falling object: 5.2	6.70 56.80	30 27.80	80 7.60	1.10	1
22	Iran	Sharif-Alhoseini et al. [43]	I	I	1	40.6	45.7	1	1	I	13.8	I	1	1	1	1
23	lran	Yadollahi et al. [68]	I	I	1	66.8 Car: 46.2, motor: 18.1, pedestrian/ bicycle: 2.5	14.6	I	6.6	1	Suicide: 7.6, struck by object :0.6	15-44: 45-64: 75.4 17		>65:7.6		
24	Kuwait	Prasad et al. [66]	30.3	39.4	30.3	52.9	32.9 Fall ground level: 3.9	1	0.6	1.9	1.9 Falling object: 5.2	<31: 36.80 38.7	30 18.10		>60: 6.5	
25	Macedonia	Jakimovska et al. [73]	65.7	15.7	18.4	42.1 Car: 28.9, motor: 5.2, pedestrian/ bicycle: 2.6, others: 5.2	39.4 Fall from height: 26.3, fall ground level: 13.1	1	2.6	7.8	5.2 Unknown: 2.6	Missing 31.60 age: 7.9	50 21.05	21.05	10.52	7.90
26	Malawi	Jessica Eaton et al. [69]	41.3	21.7	23.9	45.7	39.1	I	8.7	I	6.5	1	I	I	I	I
27	Malaysia	lbrahim et al. [39]	1	1	1	66	28	I	4	2	I	1	T	I	I	I
28	Malaysia	Joseph et al. [31]	1	1	I	52.6	43.8	I	3.5	1	1	1	1	1	ı	ı
29	Mexico	Rodríguez-Meza et al. [56]	35.6	56.7	7.8	36.2	41.6	1	13.1	2.8	6.2	1	1	I.	ı	1
30	Mexico	Zárate-Kalfópulos et al. [57]	30.9	51.4	8.6	43.4 Cars: 82.7, motor: 10.6	30.9	16.8	0.86	8.09	1	I	I	I	1	I
31	Nepal	Shrestha et al. [41]	17.84	49.34	32.81	18.63	68.24	1	1	1	13.12	<21: 21–30: 13.12 30.45		31–40: 41–50: 23.1 19.16	50: 51–60: 6 7.87	: >60: 5.77
32	Nigeria	Emejulu et al. [30]	51.6	14.5	8.06 Without deficit: 21	59.7 Car: 32.3, motor: 27.4	30.6	1	1.61	1.61	6.45	9.68 15–40: 45.2		40–60: >60: 8.1 37.1	: 8.1	
33	Nigeria	Nwankwo et al. [40]	52.9	22.4	24.7	55.3	23.5	8.2	7.1	I	5.9	8.30 32.90	90 37.70	70 14.10	0 7.10	I
34	Nigeria	Yusuf et al. [72]	62.4	24.1	6 Thoracolumbar: 7.5	72.2	14.3	2.3	0.8	I	Falling object: 10.5	<20: 20–29: 6.8 26.3		30–39: 40–49: 36.8 12.8	49: 50–59: 1 12	>60: 5.3

Neuroepidemiology 2022;56:219–239 DOI: 10.1159/000524867 Golestani et al.

Table 2 (continued)

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Table 2 (continued)	Study Country No.	35 Pakistan

Traumatic Spinal Cord Injury in	
Developing Countries	

Stud	Study Country No	First author	SCI level, %			Etiology, %)						Age groups, %	ips, %			
			cervical	thoracic	lumbar/sacral	MVCs	falls	gunshot injuries	violence/ stab injuries	sports injuries	others/ unknown	0-15 1	16–30 31	31-45 46	46-60 61-75	5 >75
35	Pakistan	Farooq Khan et al. [65]	22.9	56.2	20.8	31.1	22.3 Fall from height: 21.3, fall ground level: 1	I	21.9	4.3 Diving: 1.5	3.2 Natural disaster: 8.2, falling object: 7.6	<21: 16.7 21-40: 55.1 41-60: 21.8 >60: 6.4				
36	Pakistan	Hazrat Bilal et al. [53] 22.4	s) 22.4	58.2	19.4	21.5	35.3	I	21.1 Stab wound: 0.4	Diving: 2.2	4.5 Natural disaster: 2.5, falling object: 12	1	1	I	I	I
37	Russia	Mirzaeva et al. [70]	49.3	24.7	23.5 Level missing: 2.5	18.9	49.8 Fall <1 m: 15.9, fall >1 m: 33.9	ı 	6.2	3.7 Diving: 5.9	6.5 Unknown: 9	1	1	I	I	I
38	Saudi Arabia	Saudi Arabia Alshahri et al. [34]	I	I	I	85	9.1	4.5	I	Diving: 1	I	e e	64 23	7	m	I
39	Saudi Arabia	Saudi Arabia Alshahri et al. [51]	1	1	1	90.8	3.2	1	1	9	1	14–25: 2 55 2	26–35: 36 24.5 7.4	36–45: 46 [.] 7.4 7.4	46–55: 56–65: 7.4 3.7	66:2.3
40	South Africa	South Africa Joseph et al. [46]	53.1	38.6	8.3	26.3	11.7 Fall <1 m: 3.4, fall 1–3 m: 2.7, fall >1 m: 4.8, others or unknown: 0.8	30.8 m:	28.5	0.7	2	18–30: 2 54	28 12		>60: 6	
41	South Africa	Pefile et al. [29]	29.7	40.4	17.8 Level missing: 11.9	60.7	19	I	8.3	1.2	5.9 Not reported: 4.7	1	50 33	14	>60: 2	
42	South Africa	Phillips et al. [28]	1	1	I	38.5	30.8	I	15.4	I	15.4	1	1	I	I	I
43	South Africa	South Africa Sothmann et al. [50] 59.3] 59.3	27.2	11.2 Unknown: 2.3	44.6 Motorcycle: 1.8, bicycle: 1.1	15.5	14.4	12.8	6.1 Diving: 3.8 Rugby: 2.3	3.6					1
4	Tanzania	Haleluya Moshi et al. 38 [27]	. 38	21.6	33.3 SCIWORA: 7.1	34.3	48.3 Fall from height: 29.1, fall ground level: 19.2	1	7.5	I	6.6	2.80	30.9 37	37.20 18.	18.10 8.30	2.80
45	Tanzania	Mehboob Rashid et al. [62]	47.2	30.4	22.4	39.2	52	I	2.4	I	6.4	4	28 32	32.80 22	22.40 11.20	1.60
46	Turkey	Erdogan et al. [37]	19.3	29.3	48	25.2 Pedestrian: 20.8, automobile: 13.9, motorcycle: 2.7	71.4 Fall >1 m: 50.6, fall <1 m: 20.8	·	I	3.4	1	1	1	I	I	I
47	Turkey	Tasoglu et al. [67]	25.3	48	26.7	43.7	38.4	8.3	1.5	Diving: 2.4	Falling object: 5.9	6.80 4	28.2	.2 16.6	6 7.30	1.50

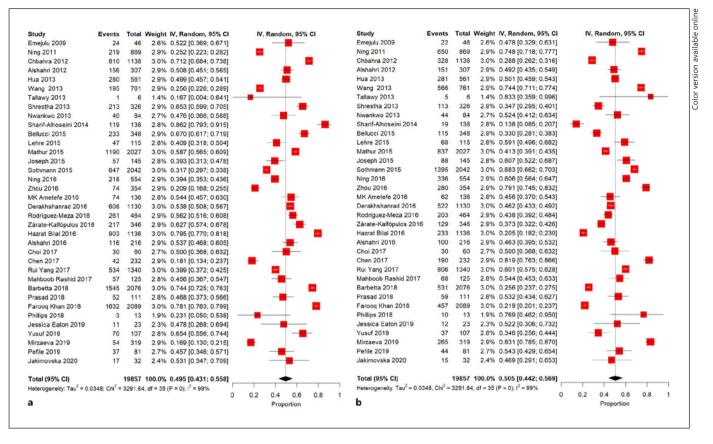


Fig. 2. Severity (completeness vs. incompleteness) of TSCIs meta-analysis in developing countries. **a** Complete injuries. **b** Incomplete injuries.

gia and paraplegia in the pooled sample of 10,072 individuals in 16 included studies was 46.25% (95% CI: 37.78%; 54.83%, test of heterogeneity: $I^2 = 98.2\%$, *p* value <0.0001, Fig. 3a) and 53.75% (95% CI: 45.17%; 62.22%, test of heterogeneity: $I^2 = 98.2\%$, p value <0.0001, Fig. 3b), respectively. Drapery plots of tetraplegia and paraplegia were visualized in Appendix Figure 2C and D, respectively. After removing the outliers which resulted in nine included studies, the frequency of tetraplegia changed to 45.19% (95% CI: 39.48%; 50.96%, test of heterogeneity: I^2 = 87.6%, *p* value <0.0001, Appendix Fig. 3C), while for paraplegia it changed to 54.81% (95% CI: 49.04%; 60.52%, test of heterogeneity: $I^2 = 87.6\%$, p value <0.0001, Appendix Fig. 3D). The funnel plots were symmetrical for tetraplegia and paraplegia caused by TSCI; the Egger's regression test for publication bias was insignificant (p =0.361) (Appendix Fig. 4B). Nine studies reported a combination of completeness/incompleteness and tetraplegia/paraplegia caused by TSCIs. While in four studies, incomplete tetraplegia was the most common injury severity. Interestingly, all of them were attributed to China [33, 55, 58, 59]. The most frequent combination in the other five studies was complete paraplegia [34, 35, 51, 54, 56].

Etiologies of TSCIs

Two main etiologies were MVCs and falls; in 27 and 17 studies, MVCs and falls were the main cause of TSCI, respectively. MVCs' relative frequency ranged from 18.63% in Nepal [41] to 90.8% in Saudi Arabia [51]. Some studies indicated types of MVCs which in almost all of them, vehicle occupants were the most injured group. Based on meta-analysis of 46 included studies, MVCs had the highest relative frequency of TSCI etiologies; the relative frequency of MVCs in the pooled sample of 28,110 individuals was 43.18% (95% CI: 37.80%; 48.63%, test of heterogeneity: $I^2 = 98.2\%$, *p* value = 0, Fig. 4), while after removing the outliers which resulted in 24 included studies, it changed to 43.25% (95% CI: 40.53%; 45.99%, test of heterogeneity: $I^2 = 76.2\%$, *p* value <0.0001, Appendix Fig. 3E). The funnel plot showed a publication bias for MVCs'

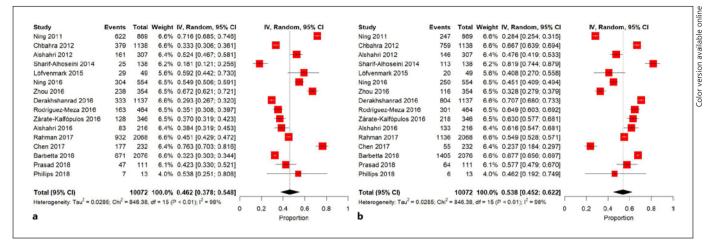


Fig. 3. Severity (tetraplegia vs. paraplegia) of TSCIs meta-analysis in developing countries. a Tetraplegia. b Paraplegia.

frequency; the Egger's regression test indicated publication bias by the presence of funnel plot asymmetry (p = 0.009) (Appendix Fig. 4C).

A wide range of TSCIs' relative frequency was related to falls, from 3.2% in Saudi Arabia [51] to 71.4% in Turkey [37]. Interestingly, in six out of nine China studies [32, 33, 42, 55, 58, 63], falls were the most common cause of TS-CIs. Some studies subcategorized falls into ground-level falls (or falls <1 m) and falls from height (or falls >1 m); only in 3 out of 15 studies were ground-level falls more common [33, 58, 59]. For meta-analysis of fall proportion, 46 studies were included. The frequency of falls in the pooled sample of 28,110 individuals was 34.24% (95% CI: 29.08%; 39.59%, test of heterogeneity: $I^2 = 98.9\%$, p value = 0, Fig. 5), while after removing the outliers which resulted in 22 included studies, it changed to 33.69% (95% CI: 30.83%; 36.61%, test of heterogeneity: $I^2 = 74.0\%$, p value <0.0001, Appendix Fig. 3F). Publication bias for fall frequency was not shown by funnel plot; the Egger's regression test was not significant (p = 0.379) (Appendix Fig. 4D).

Gunshot injury was reported in 11 studies, ranging from 0.7% in Ethiopia [47] to 30.8% in South Africa [46]. In a study in South Africa [46], it was the main etiology of TSCIs. The frequency of gunshots in the pooled sample of 6,403 individuals from included studies was 10.40% (95% CI: 4.92%; 17.55%, test of heterogeneity: $I^2 = 98.3\%$, *p* value <0.0001, Appendix Fig. 1C), while after removing the outliers which resulted in seven included studies, it changed to 10.18% (95% CI: 5.58%; 15.93%, test of heterogeneity: $I^2 = 92.7\%$, *p* value <0.0001, Appendix Fig. 3G). Publication bias for gunshots frequency was not demonstrated by the funnel plot; the Egger's regression test was insignificant (p = 0.137) (Appendix Fig. 4E).

Considering violence/stab as the etiology of TSCI, a total of 36 studies were included in the meta-analysis. The frequency of violence/stab in the pooled sample of 20,873 individuals was 5.68% (95% CI: 3.92%; 7.73%, test of heterogeneity: $I^2 = 97.1\%$, *p* value <0.0001, Appendix Fig. 1D), while after removing the outliers which resulted in 23 included studies, it changed to 5.35% (95% CI: 4.17%; 6.66%, test of heterogeneity: $I^2 = 74.6\%$, *p* value <0.0001, Appendix Fig. 3H). For violence/stab frequency, the Egger's regression test did not indicate publication bias (*p* = 0.447), and the funnel plot was symmetric (Appendix Fig. 4F). Only in 3 studies, the relative frequency of violence/stab was more than 20% [46, 53, 65].

Thirty studies were included in the meta-analysis for sports as the TSCI etiology. The frequency of sports in the pooled sample of 23,289 individuals was 3.02% (95% CI: 2.00%; 4.22%, test of heterogeneity: $I^2 = 96.3\%$, *p* value <0.0001, Appendix Fig. 1E), while after removing the outliers which resulted in 18 included studies, it changed to 2.18% (95% CI: 1.75%; 2.65%, test of heterogeneity: $I^2 = 28.9\%$, *p* value = 0.1218, Appendix Fig. 3I). The symmetrical funnel plot was congruent with insignificant Egger's regression test for sports frequency (*p* = 0.489) (Appendix Fig. 4G).

Others/unknown etiologies of TSCIs, including falling objects, suicide, natural disasters, etc., are considered as a group. Falling objects were the most common cause of TSCIs among others/unknown etiologies, and in one study, it consisted of the highest relative frequency of etiologies with 57.2% [44]. The frequency of others/unrec-

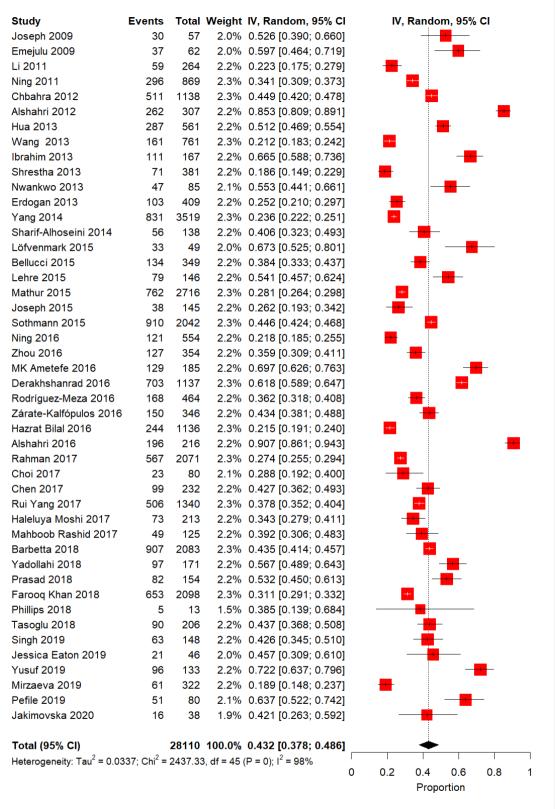


Fig. 4. MVCs meta-analysis as the etiology of TSCIs in developing countries.

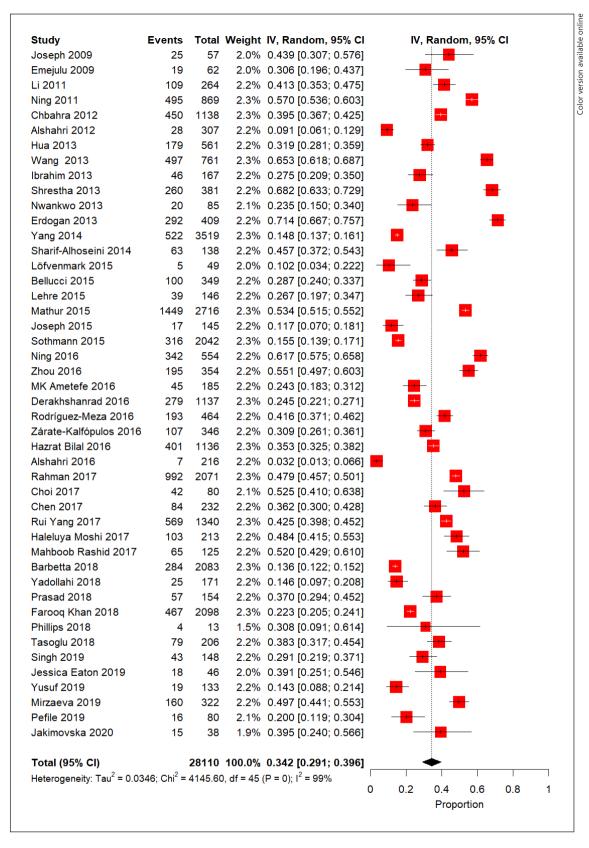


Fig. 5. Falls meta-analysis as the etiology of TSCIs in developing countries.

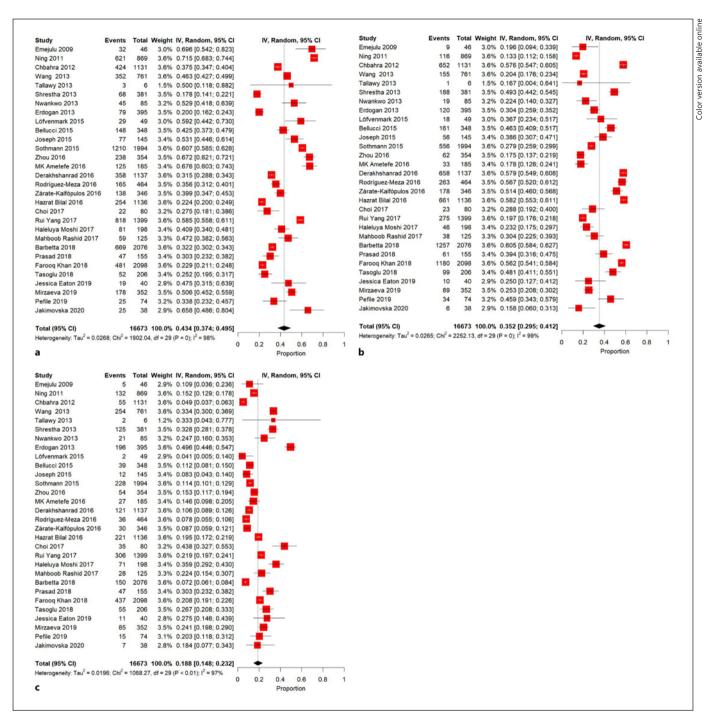


Fig. 6. Level of TSCIs meta-analysis in developing countries. a Cervical injuries. b Thoracic injuries. c Lumbar/sacral injuries.

ognized etiologies in the pooled sample of 26,608 individuals in 40 included studies was 10.37% (95% CI: 7.84%; 13.19%, test of heterogeneity: $I^2 = 99.2\%$, *p* value = 0, Appendix Fig. 1F). While after removing the outliers, which resulted in 27 included studies, the frequency of other eti-

ologies changed to 9.80% (95% CI: 8.37%; 11.32%, test of heterogeneity: $I^2 = 75.7\%$, *p* value <0.0001, Appendix Fig. 3J). Appendix Figure 2E–I show drapery plots related to different etiologies.

Level of TSCIs

Thirty-seven studies reported the level of injuries. In 22 studies, most injuries occurred at the cervical level. In comparison, in 12 studies, the thoracic level was the most prevalent level of injury, and only in 3 studies, the lumbosacral level had the highest injury relative frequency. The highest relative frequency of cervical, thoracic, and lumbosacral injuries was 76.3% in China [59], 60.5% in Brazil [64], and 66% in China [32], respectively. For the meta-analysis, we only considered studies that categorized the level of injuries into three groups; cervical, thoracic, or lumbosacral, which resulted in a total of 30 studies. We excluded all studies that reported combinational injuries (e.g., cervicothoracic, thoracolumbar, etc.). The frequency of cervical, thoracic and lumbosacral in the pooled sample of 16,673 individuals were 43.42% (95% CI: 37.38%; 49.55%, test of heterogeneity: $I^2 = 98.5\%$, p value = 0, Fig. 6a), 35.22% (95% CI: 29.49%; 41.16%, test of heterogeneity: $I^2 = 98.7\%$, p value = 0, Fig. 6b), and 18.84% (95% CI: 14.82%; 23.20%, test of heterogeneity: *I*² = 97.3%, *p* value = 0, Fig. 6c), respectively. After removing the outliers which resulted in 16 included studies for cervical and lumbosacral level, the frequency of cervical and lumbosacral changed to 42.49% (95% CI: 38.37%; 46.66%, test of heterogeneity: $I^2 = 79.00\%$, p value <0.0001, Appendix Figure 3K) and 20.41% (95% CI: 17.94%; 22.99%, test of heterogeneity: $I^2 = 70.6\%$, p value <0.0001, Appendix Fig. 3M), while removing outliers for thoracic level resulted in 15 included studies and its frequency changed to 31.09% (95% CI: 26.57%; 35.79%, test of heterogeneity: $I^2 = 81.8\%$, p value <0.0001, Appendix Fig. 3L). The funnel plots did not show a publication bias for all levels of injury relative frequency; the Egger's regression test did not indicate publication bias (p = 0.578 for cervical, p =0.187 for thoracic, p = 0.134 for lumbosacral) (Appendix Fig. 4H). Appendix Figure 2J-L show drapery plots related to different levels of injuries.

Discussion

In this study, we presented an update of our previous study on the epidemiology of TSCIs in developing countries [12]. While most available data of TSCI epidemiological information are related to developed countries, it seems there is inadequate evidence about TSCI in developing countries [11, 75]. More details on TSCIs' epidemiological characteristics are necessary for implanting cost-effective preventive strategies in developing countries. In our earlier study, search of which was performed

Traumatic Spinal Cord Injury in Developing Countries

in 2012, 64 studies published from 1978 to 2011 were identified from 28 developing countries [12], while in this study, search of which was performed on 5th May 2020, we could recognize 47 studies published from 2009 to 2020 from 23 countries. In other words, during the last decade, considering two common papers with our previous study [33, 34], publications related to TSCI in developing countries are 43% (47/109) of the all-time publications. This accelerated trend of TSCIs' publications in developing countries could lead to a comprehensive understanding of TSCIs and implanting appropriate strategies for controlling TSCIs' effects.

The pooled incidence of TSCI in developing countries was estimated at 22.55 cpm annually, which is congruent with other studies. Our previous study estimation of incidence was 25.5/million/year [12]. In a survey of the Middle East and North Africa region, including Turkey, Iran, Saudi Arabia, Egypt, Jordan, Kuwait, and Qatar, the annual incidence of TSCI was 23.24 cpm [75]. In another study, the TSCI incidence rate ranged from 12.7 to 29.7/million/year in developing countries [16]. Considering different timelines of these studies, it seems TSCI incidence rate has not changed during these years, which shows the importance of implanting more efficient strategies for reducing and controlling them. Considering developed and developing countries' comparison of TSCI incidence, there are disparities among different studies. Totally, there is a wide range of TSCI incidence among different countries; while some developing countries show a low TSCIs incidence; some developed countries show a high TSCIs incidence [4, 11, 16]. This difference could be related to some reasons; first, the definition and sampling method vary among papers, especially in developed countries where prehospital death is included, and registry systems are more efficient. However, some developing countries like Russia and South Africa promoted more developed registry system; in Russia study [70], hospitals of Saint Petersburg which reported TSCIs based on ICD-10 were included, and in South Africa studies [28, 46], admissions of private or government-funded healthcare systems of Cape Town were identified. Second, TSCIs' medical diagnosis techniques in developing countries are less mature than in developed countries, causing overlooking of TSCIs with mild symptoms [16]. Furthermore, there is a considerable lack of information on many developing countries; for example, in other studies, there were data of only seven out of 21 Middle East and North Africa countries [75] and three out of 46 African countries [11], which both consisted of developing countries.

Similar to our previous study, young adults and physically active age group consisted majority of patients. However, in some studies, it was stated that the mean age of TSCI patients is higher in developed countries [12]; despite other studies showing a slightly higher mean age of patients in developed countries, this difference is insignificant, and totally, TSCIs is a problem toward under 40 age groups [4, 16]. This situation is not just a health problem, and TSCIs cause a substantial economic burden on families and countries and productivity loss. Like all previous reports, TSCI is more prevalent in males. This could be due to unique occupational hazards or riskier behaviors in males [76]. As a result, changing TSCI gender distribution toward more females than before could indicate cultural and social changes.

Classification of etiologies was different among included studies, while some subcategorized MVCs and falls, others categorized suicide or struck by an object as different groups from others/unknown. It seems there is a need for more standardized classification such as the one reported by DeVivo et al. [77], which could lead to more realistic results for comparison. For consistency with our previous study, we used the same classification. Furthermore, any etiology which was not in our main classification, classified as others/unknown. We also regarded diving as a sport etiology. The findings of this study showed MVCs and falls were two main etiologies of TSCIs, which is congruent with our previous study. The relative frequency of MVCs and falls was 43.18% and 34.24%, respectively, while in our previous study, they were 41.4% and 34.9%. Furthermore, due to significance of Egger's regression test, publication bias has occurred for MVCs, and pooled result is possibly overestimated. While in some previous studies, falls were considered the main etiology of TSCIs in developing countries, and MVCs were typical main etiology in developed countries [4, 16, 17], our findings showed that etiology trends have changed. As a possible explanation for this change, it has been demonstrated urbanization could increase the likelihood of MVCs in developing countries [78]. In studies in which falls are still the main etiology of TSCIs, different explanations were provided; some considered reduction of MVCs due to appropriate legislations [37, 70], living in rural regions or high height geographies [41, 53, 61], and occupations like being farmer or worker [32, 43]. Interestingly, ground-level falls occur mainly in the elderly, while falls from height are related to the physically active age group [55]. Based on the World Health Organization, only 7% of road traffic death happened in developed countries in 2016, while these countries consist 15% of

population and 40% of vehicles [79]. Regarding the importance of MVCs as one of the leading causes of TSCIs in developing countries, serious actions for prevention and control should be done by policymakers. Among all interventions in developed countries, vehicle design improvement has enormously reduced MVCs, and timely emergency care has prevented MVCs' consequences [80, 81]. However, developed countries' policies are not necessarily efficient in developing countries due to population and sociopolitical variations [82], and before implanting any strategy, all aspects of it should be evaluated because any trauma-precipitating plan should be based on economic and cultural facts [83]. Like our previous study, violence-related injuries are still prominent in South Africa, indicating a need for more serious policies for controlling them [46].

Regarding the severity of TSCIs, the proportion of tetraplegia and paraplegia in our study was 46.25% and 53.75%, which was statistically insignificant. In comparison, the relative frequency of tetraplegia and paraplegia in our previous study was 40.7% and 58.6% and statistically insignificant [12]. Another study [16] mentioned that tetraplegia is more prevalent in developed countries, while most injuries cause paraplegia in developing countries. As discussed before, the pattern of etiologies is considered different between developed and developing countries and this pattern changing might be related to urbanization and lifestyle changes in developing countries. The proportion of complete and incomplete injuries in our study was 49.47% and 50.53%, and similar to our previous study, statistically insignificant, which relative frequency of complete and incomplete injuries was 56.5% and 43%, respectively. Almost all reviewed papers used ASIA Impairment Scale for classification, which is a considerable improvement for developing countries, compared to our previous study, which ASIA Impairment Scale was not a usual reporting system in developing countries [12]. Only two studies did not mention ASIA Impairment Scale for classification of TSCIs severity [38, 53], and 31 studies reported the number of patients in each group of the ASIA Impairment Scale. Considering the level of injury, cervical, thoracic, and lumbosacral were the most prevalent level of TSCI among developing countries, respectively.

Our study has some limitations: First, there are variations in the definition and diagnosis criteria among different studies. However, it seems some improvements have been made during the last decade. But still, for more representative results of TSCIs' epidemiological patterns among different countries, studies should follow international guidelines for data sharing. Second, there is no information about TSCI situation from most developing countries and all available data are related to a limited number of developing countries. Thus, it is necessary to keep in mind that the results of this study and all similar papers could be over or underestimated compared to reality. Furthermore, selection bias could affect the accuracy of results based on study design (hospital-based, rehabilitation-based, etc.) and inclusion criteria.

Conclusion

TSCI is a catastrophic event with a high mortality rate and physical and emotional difficulties for patients. Fortunately, the number of publications regarding TSCIs in developing countries has increased substantially, leading to a comprehensive understanding. However, there is still a need for more studies based on international classifications and registries for achieving more comparable results. TSCIs are more common in young adults, males, and MVCs and falls are the main etiologies in developing countries. By understanding different epidemiological characteristics of TSCIs, appropriate country-based preventive strategies and resource allocation could be implanted to decrease TSCI incidence and burden.

Statement of Ethics

The Ethics Committee of Tehran University of Medical Sciences approved the study, and the reference number is IR.TUMS. SINAHOSPITAL.REC.1400.036.

Conflict of Interest Statement

The authors announce that there is no conflict of interests about our research.

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Author Contributions

V.R.-M. and S.M.G. conceived the presented idea and supervised the project. Z.G. provided critical feedback and edited the draft. S.F.M., M.A.D.O., and E.M. contributed to data collection. A.G. and P.S. analyzed the data and A.G. wrote the draft. M.S.-N. contributed to data interpretation. S.B.J. did the search strategy. All authors discussed the results and contributed to finalizing the manuscript.

Data Availability Statement

All datasets of this study are available from the corresponding author on reasonable request.

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