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The Frequency of Neuropsychiatric Sequelae After Traumatic Brain Injury in the Global South

A systematic review and meta-analysis

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Abstract:

Countries in the 'global south' are characterized by factors that contribute to the increased incidence of traumatic brain injury (TBI). This systematic review and meta-analysis aimed to assess the prevalence of neuropsychiatric sequelae following a TBI, specifically among the Western Asian, South Asian, and African regions of the global south. A literature review was conducted until August 20, 2021, for publications that measured psychiatric or cognitive impairment after TBI from the 83 countries that constitute the aforementioned regions. The main databases, such as PsycINFO, Scopus, PubMed/MEDLINE, ProQuest (English), Al-Manhal (Arabic) and Google Scholar, were selected for grey literature. Following the evaluation of the articles using the Joanna Briggs Institute guidelines, the random effects model was used to estimate the prevalence of depression, anxiety, posttraumatic stress disorders (PTSD), sleep disturbance related to TBI (TBI-SD), obsessive–compulsive disorder (OCD), and cognitive impairment. Of 56 non-duplicated studies identified by the initial

search, 27 studies were eligible for systematic review and 23 for meta-analysis. The pooled prevalence of depression in a total sample of 1882 was 35·35% (95% CI=24·64–46·87%), of anxiety in a total sample of 1211 was 28·64% (95% CI=17·99–40·65%), of PTSD in a total sample of 426 was 19·94% (95% CI=2·35–46·37%), of OCD in a total sample of 313 was 19·48% (95% CI=0·23–58·06%), of TBI–SD in a total sample of 562 was 26·67% (95% CI=15·63–39·44%), and cognitive impairment in a total sample of 941 was 49·10% (95% CI=31·26–67·07%). To date, this is the first critical review that has examined the spectrum of post–TBI neuropsychiatric sequelae in the specified regions. While existing studies lack homogeneous data due to variability in the diagnostic tools and outcome measures utilised, the reported prevalence rates are significant and comparable to statistics from the global north.

Keywords: traumatic brain injury; neuropsychiatric sequelae; global south; systematic review; meta-analysis; cognitive impairment; anxiety; depression

Introduction

A widely accepted definition of what constitutes traumatic brain injury (TBI) has yet to be established.[1] Concisely, TBI is a condition that can classically be attributed to external mechanical forces that injure brain tissues, which, in turn, compromise the integrity of brain functioning. The outcome is a cascade of biopsychosocial disturbances that lead to transient or chronic functional outcomes.[1,2,3,4] Among the various secondary conditions that commonly follow TBI, neuropsychiatric sequelae include cognitive, emotional, behavioural, and sensorimotor disturbances. The frequencies of behavioural and emotional disturbances have been extensively studied, with Ponsford et al[5] reporting that 18·3% to 83·3% of those who sustain TBI have these outcomes. This wide variation in the rate of post–traumatic secondary conditions is likely to be due to many factors, including the time since the injury, the diagnostic tool used, and the quantification of the severity of TBI and case ascertainment.[6,7]

According to the *Diagnostic and Statistical Manual of Mental Disorders* (DSM), mild or major neurocognitive disorders due to TBI have the potential to contribute to dependency and disability.[8-10] TBI coupled with secondary neuropsychiatric symptoms tend to account for the greater part of the cost of healthcare utilisation compared to populations without these symptoms.[11-13] Studies have also reported that a critical predictor of poor psychosocial outcomes following TBI is the initial level of impairment of cognition or functioning.[14,15]

Around the world, approximately 69 million people sustain a TBI each year.[16] Lower-middle-income countries in the global south have shown a prevalence of TBI of 811/100,000.[16] However, this indicated rate could be considered to be just the tip of the iceberg due to the lack of high–quality data from these regions.[16,17] The mortality and disability rate after TBI in these countries is high, representing one third to one–half of trauma–related causes of death and injury in the world.[18] The vast majority of those injured are in their prime productive years between the ages of 11 and 40.[18,19]

Although it is inappropriate to paint all developing countries with the same broad strokes, the common healthcare issues common to several of these countries include infectious and environmental diseases, high infant mortality rates, and lack of food security. However, non-infectious diseases and associated long–term health concerns are gaining importance, with recent estimates suggesting that 2·4 billion people have a disability, including an estimated 49 million whose disability can be attributed to TBI.[20],[21] Despite the increasing tide of non-communicable diseases such as TBI, efforts in Western Asian, South Asian and African countries have generally been geared toward cure-orientated biomedical care commonly associated with communicable diseases. TBI is often relegated to the sphere of minor health concerns by government healthcare planners, giving it the characteristic trait of a ‘silent epidemic’.[16]

Data suggest that after TBI, mortality during hospitalisation is decreasing, particularly in the global north.[22] Improved outcome rates can be largely attributed to access to specialised intensive care units, often unavailable to those of lower socioeconomic status living in developing countries with scarce resources.[23] While TBI affects all age groups, detailed analyses have shown that the occurrence of TBI follows a trimodal distribution, often occurring in children, early adults and senior citizens.[24,25] Many countries in the global south are suggested to be in the midst of the second phase of demographic transition, where there is a high birth rate and an increasing life span.[26] These demographic changes have heightened the concentration of the 'youth bulge' in the population structure with people living longer, which also correlates with the increased use of automobiles.[27,28] Due to this increased exposure to risk factors coupled with sparse healthcare resources, the global south is likely to experience a higher burden of TBI compared to countries in the global north.[16]

This is especially necessary to consider due to some of the significant differences in the TBI condition between the global south and the global north. One key distinction is the epidemiology of TBI, with Africa and Southeast Asia reporting the highest incidence rates among younger demographics due to 'road traffic accidents', in contrast to TBI in North America, where a significant cause is falls in the elderly.[18] People from the global south also have twice the odds of death after severe TBI compared to their counterparts in the global north.[29] A majority (93%) of the TBI prognostication models are also based on samples from the global north.[30] These are significant factors that call for management protocols that are sensitive and specific to these demographically distinctive groups.

With these factors in mind, it is important to note the lack of systematic reviews and statistics on TBI and related adverse short– and long–term neuropsychiatric outcomes from western Asia, South Asia, and Africa, regions that are part of the 'global south'.[16] A study by Tropeano et al[31] reflects this trend, indicating that a higher proportion of publications evaluating the burden of TBI was from countries of the global north, as opposed to those of African and South East Asian regions, despite approximately 80% of the world population residing in the latter.[32]

This systematic review and meta-analysis aimed to assess the prevalence of psychiatric and cognitive impairment following TBI, specifically among the western Asian, South Asian and African regions of the global south. It is essential to consider psychiatric symptoms and cognitive impairment in tandem due to the bidirectional relationship between them with respect to aetiology, presentation, and treatment. Critical evaluation of existing literature on the magnitude of neuropsychiatric disturbances in the post–TBI population will help to lay the groundwork for evidence–based management and rehabilitation promotion programmes such as WHO's Rehabilitation 2030.[33] The global south is a geopolitical term used as a shorthand to denote economically, politically, or culturally marginalised regions outside of Europe and North America.[34] While the global south consists of a vast region that includes South and Latin America, Pacific Islands, Africa and Asia, for brevity, the present review of the prevalence of neuropsychiatric complications after TBI will focus specifically on the regions of western and southern Asia and Africa.

Materials and Methods

The present systematic review was conducted in accordance with an established protocol, using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta–Analyses) guidelines and included all articles published and in print up to August 20, 2021.[35] This systematic review has been registered under PROSPERO (registration ID. CRD42021270604). The article extraction process began with the use of search terms across different levels delimited using the Boolean operators "AND" and "OR". The first level (for TBI) included search terms such as "Traumatic brain injury" OR "head impact" OR "brain injury". Level 2 (for psychiatric and cognitive symptoms) included the following search terms: "mental disorder" OR "psychiatric disorder" OR "mental illness" OR "cognitive impairment" OR (other specific individual mental disorders such as "depression", "anxiety", "eating disorders", "PTSD", "dementia", cognitive decline, etc.). The final level included the individual country names [GCC: Oman, Kuwait, Bahrain, Saudi Arabia, Qatar, and the United Arab Emirates. Western Asia: Israel, Iraq, Jordan, Palestine, Lebanon, Iran, Syria, Afghanistan, Pakistan, Bahrain, Kuwait, Qatar, Oman, United Arab Emirates, Saudi Arabia, and Yemen. South Asia: Bhutan, Bangladesh, Pakistan, India, Sri Lanka, Nepal, Afghanistan, and the Maldives. Africa: Algeria, Angola, Botswana, Benin, Burundi, Burkina Faso, Cabo Verde, Central African Republic (CAR), Cameroon, Comoros, Chad, Republic of Congo, Democratic Republic of Congo, Djibouti, Cote d'Ivoire, Egypt, Equatorial Guinea, Eswatini (formerly Swaziland), Eritrea, Gabon, Ethiopia, Ghana, Gambia, Guinea–Bissau, Guinea, Lesotho, Kenya, Libya, Liberia, Malawi, Madagascar, Mali, Mauritius, Mauritania, Mozambique, Morocco, Niger, Namibia, Nigeria, Rwanda, Sao Tome and Principe, Seychelles, Senegal, Somalia, South Africa, Sierra Leone, South Sudan, Sudan, Togo, Tanzania, Tunisia, Zambia, Uganda, and Zimbabwe]. The accumulated articles were further screened to ensure that they met the required eligibility criteria. This systematic review has been registered with PROSPERO (registration ID CRD42021270604).

2.1 Data retrieval strategies

Based on the inclusion criteria, the process of article identification began with a complete screening of the main databases by three independent authors (AG, SS and SM): PsycINFO, Scopus, PubMed/MEDLINE, ProQuest for English articles, and the Al–Manhal database for Arabic articles. A final search of up to 10 pages on Google Scholar was also performed to ensure the inclusion of any remaining articles (including grey literature) that may have been missed. This aforementioned search strategy did not include a search based on a specific

timestamp, implying that any and all articles (including those that were published or in press) as of August 20, 2021 were included in the search.

The full versions of the articles were downloaded when their titles and abstracts met the inclusion criteria. After further exclusion of articles that did not meet the inclusion criteria, the three independent authors (AG, SS, and SM) for any articles that may have been missed during the initial search process, producing a final total of 52 articles for quality review using the Joanna Briggs Institute (JBI) guidelines - the prevalence checklist - for the evaluation of scientific research articles.[36] In case disagreement arose between the three main reviewers, the third, fourth, and fifth authors (SA, MS, and MFC) were consulted for discussion until a consensus was achieved.

2.2 Inclusion and exclusion criteria

Regarding the types of studies included in this systematic review, the characteristics of the included articles comprised of (1) original research (newly conducted studies or studies that use secondary data), (2) samples included civilian populations, (3) studies that measured some form of psychiatric or cognitive impairment after a single traumatic brain injury using standardised diagnostic procedures or self-reported measures, regardless of the time interval following the TBI event, and (4) prospective or retrospective cross-sectional, cohort, or case–control studies, (5) studies written in English or Arabic, and (6) samples from western Asia, South Asia, and Africa.

Studies were excluded if (1) the samples included military personnel and war veterans, (2) the participants reported a TBI that had not been diagnosed in a medical setting (reported based on nonstandardised measures and methods), or (3) the participants had a history of psychiatric illness, cognitive impairment, intellectual disability, or other neurological events (4) reviews, case studies, case reports, brief reports, brief communications, or any other type of article that was not original research, (5) they reported only average scores for psychometric measures but not prevalence.

The population included in this study was civilians who had been appropriately diagnosed with a TBI, as gleaned through the guidelines of the *Federal Interagency Traumatic Brain Injury Research Informatics System for TBI Research (2015)*, the *American Congress of Rehabilitation Medicine (1993), Department of Veterans Affairs and the Department of*

Defence (2009), and the *International and Interagency Initiative toward CDE for Research on TBI and Psychological Health (2010)*.[1,2,3,4]. Although there was no homogeneous agreement on the exact evaluative procedures used for the diagnosis of TBI, the condition generally involved damage or infarction of brain tissues attributable to an external mechanical force, as evidenced by loss of consciousness, posttraumatic cognitive and behavioural changes, or any other objective neurological finding.[37]

2.3 Evaluation of the quality of studies reports

According to the standardised items listed in the JBI checklist for prevalence studies, the three reviewers independently carried out an independent evaluation of the title, abstract, methods, results, discussion, and other sections of each included study was carried out independently by the three reviewers.[38] The resulting interrater reliability of the three independent authors of the current quality measure was strong, with an intraclass correlation coefficient (ICC) of 0.88. After a complete evaluation of all articles using the JBI checklist, the next stage was to decide which articles were of sufficient quality to include in the systematic review and data extraction. There is no single approach that is considered best practise. Porritt et al[39] suggested a mutual agreement between the members of the research team to be ideal. Since the JBI checklist consists of 9 questions, each article was scored on a scale of zero to nine points. It was decided among the team of authors that the articles that earned a score equal to or above 7 would be included in the systematic review and data extraction process.

2.4 Data extraction

Three independent authors (AG, SS and SM) extracted relevant information from identified studies, including information such as the name of the first author, the year of publication, the year(s) of study conduct, the country in which the study was conducted, sampling methods, the median, mean and standard deviation of the age of participants along with the age range, the characteristic of the sample (university student, patient, etc.), sample size, the sex distribution of the sample, the assessment tools, the reliability of the said tools, the disorder screened, the total number of positive cases and the duration after which neuropsychological tests were administered (post–TBI duration).

2.5 Patient and Public Involvement

There was no direct patient or public involvement or recruitment for the purposes of this study.

2.6 Statistical analysis

The acquired data were analysed using the MedCalc 12 statistical software. In this review, six main psychological outcomes of patients with TBI were identified: depression, anxiety, post–traumatic stress disorders (PTSD), obsessive–compulsive disorders (OCD), TBI–related sleep disturbance (TBI-SD) and cognitive impairment. In the meta-analysis, the estimated pooled prevalence for each outcome was calculated (Petrie et al[40]). The statistics I2 and Q were used to assess heterogeneity between articles with the same outcome.[41] The 95% CI of each study was estimated using the binomial method available in the MedCalc software. For the heterogeneity test, a random effects model was used to interpret the results if the I^2 statistic was greater than 50% and the Q statistic was < 0.1; otherwise, we used the fixed effects model. [42, 41].

Results

An initial search of the databases yielded a total of 166 usable articles. Subsequently, duplicates (9), inaccessible (3) and articles that did not meet the inclusion criteria (104) were removed, leaving the team with a total of 56 articles **(Supplementary Figure 1)**.
Of the 56 unduplicated original studies identified by the initial search, 27 articles (earning a score equal to or above 7 according to the JBI criteria) were considered eligible for the systematic review **(Supplementary Table 1)**.[37, 43-68] Four studies were further excluded because it was not possible to group them into any of the categories based on symptoms, each study covering a singularly unique disorder by itself (i.e., post–concussive syndrome or symptoms, aggression, and posttraumatic amnesia). A final total of 23 studies were used for the meta-analysis **(Supplementary Figure 1)**.[37, 43-64]

Although the initial search of existing databases included 83 countries, a total of 27 studies from the following ten countries were finally included in this study: Israel, Iran, Oman, Morocco, India, Nepal, Tunisia, Ethiopia, Nigeria and Uganda **(Supplementary Figure 1 and Table 1)**. The highest number of studies came from India, accounting for 12 studies, followed by Iran with five studies. While both Oman and Israel produced two studies each, the remaining countries of Morocco, Nepal, Tunisia, Ethiopia, Nigeria and Uganda produced only one study each. The various neuropsychological symptoms reported were as follows:

depression (16 studies), anxiety (11 studies), PTSD (3 studies), OCD (3 studies), TBI - SD (4 studies), and cognitive impairment (8 studies).

The estimated prevalence of depression for 16 studies is shown in **Figure 1**. The pooled prevalence of depression in the total sample of 1882 was 35.35% (95% CI=24.64–46.87%), based on the random effects model (I^2=96.20%, Q=394.96, p< 0.001).

The estimated prevalence of anxiety for 11 studies is shown in **Figure 2**. The pooled prevalence of anxiety in the total sample of 1211 was 28.64% (95% CI=17.99–40.65%) based on the random effects model (I^2=94.92%, Q=196.91, p< 0.001).

The estimated prevalence of PTSD for three studies is shown in **Figure 3**. The pooled prevalence of PTSD in the total sample of 426 was 19.04% (95% CI=2.35–46.37%) based on the random effects model (I^2=97.28%, Q=73.46, p< 0.001).

The estimated prevalence of OCD for three studies is shown in **Figure 4**. The pooled prevalence of OCD in the total sample of 313 was 19.48% (95% CI=0.23–58.06%) based on the random–effects model (I^2=97.84%, Q=92.44, p<0.001).

The estimated TBI–SD for four studies is shown in **Figure 5**. The pooled prevalence of SD in the total sample of 562 was 26.67% (95% CI=15.63–39.44%) based on the random effects model (I^2=90.27%, Q=30.83, p< 0.001).

The estimated prevalence of cognitive impairment for eight studies is shown in **Figure 6**. The pooled prevalence of cognitive impairment in the total sample of 941 was 49.10% (95% CI=31.26–67.07%) based on the random–effects model (I^2=96.85%, Q=222.41, p<0.001).

Discussion

To lay the groundwork for the possible evolution of healthcare systems in the global south to address ‘silent epidemics’ such as TBI, alongside programmes such as WHO's Rehabilitation 2030, the current systematic review and meta-analysis aimed to critically evaluate the prevalence of cognitive and psychiatric sequelae of TBI, specifically in Western Asia, South Asia, and Africa.[20 33] High TBI prevalence leads to significant mortality and disability rates, amplified by healthcare challenges and limited resources. Despite rising non-communicable

diseases, healthcare priorities often favour communicable diseases. TBI improvements in the global north due to specialized care contrast with the resource limitations in the global south. Demographic shifts and distinct TBI epidemiology contribute to a higher burden. TBI burden persists with inadequate research and statistics in the global south, necessitating tailored management approaches.

The current analysis suggests that the prevalence of depressive symptoms derived from 16 studies is 35·35%. Of the studies used to assess the prevalence of depression, a distinction needs to be made between those studies that used self-report measures versus standardised diagnostic procedures to induce the presence of depressive symptoms and depressive disorders, respectively. Most relevant studies employed tools such as self–report measures that tap into subthreshold depressive or negative symptoms, often providing spurious results (Supplementary **Table 1)**. A study by Osborn et al. [69] compares the influence of the type of diagnostic measures used on the prevalence rates of depression in an Australian sample. In this study, 27% of people were formally diagnosed using standardised procedures, while 38% reported clinically significant depressive symptoms when using self-report measures.[69] The prevalence rate of the current study, 35.35%, falls in the middle of these two figures. Furthermore, in a systematic review, Scholten et al.[70] reported that the pooled prevalence estimates of depressive disorders were 17% in the first year after TBI and a higher long-term prevalence of 43%. These results suggest that the expression of depressive symptoms fluctuates in a complex way depending on whether they were diagnosed using self–report measures or standardised diagnostic procedures, and the time interval between the TBI event and diagnosis. More studies are needed to establish a clear demarcation between depression and negative symptoms, such as psychomotor retardation, fatigue, apathy, anhedonia, or abulia.[71]

In the present review, the estimated prevalence of anxiety–related disorders in 11 studies stood at 28·64%. Anxiety disorders were used most commonly using self–report measures, and it is important to consider the possible inflation of the reported prevalence rate (Supplementary **Table 1)**. A meta-analysis by Osborn et al.[72] that compared the outcome measures used and the time since the injury intervals reported that when using standardised diagnostic procedures, 11% were diagnosed with general anxiety disorders (GAD), while self–report measures revealed 37% had GAD. Scholten et al.[70] conducted a systematic review of the prevalence of anxiety symptoms in which they reported that the pooled prevalence estimates

of anxiety were 21% in the first year following TBI. Therefore, it is likely that factors that impact depressive symptoms also play a role in the expression of anxiety symptoms. Furthermore, Gould et al.[73] reported the importance of a pre–injury diagnosis of anxiety–related disorders that results in an increased probability of having a post–TBI anxiety disorder, the prevalence of which progressively increased each month after trauma. Therefore, demographic variability in the general prevalence of anxiety–related disorders is likely to also have an impact on the post–TBI diagnosis of GAD as well.[74 75] Concerted efforts are needed to establish robust data collection that account for such confounders in this region.

Statistics related to PTSD in populations of interest are often considered controversial due to inaccurate reporting or interpretation of responses using self–reporting questionnaires, as well as questionable cross–cultural applicability of the concept of PTSD featured in the *DSM* and *International Classification of Diseases (ICD)*.[76 77]
In the present study, the estimated prevalence derived from the three articles was 19·04%. A systematic review and meta-analysis by Van Praag et al.[78] reported a prevalence of PTSD after TBI ranging between 0% and 36%, with a pooled prevalence rate of 15.6%. Another systematic review and meta-analysis by Iljazi et al.[79] captured the longitudinal fluctuation of PTSD symptoms after TBI, reporting that the prevalence rate was 2·2% after three months, 16·3% after six months, 18·6% after 12 months, and 11·0% after 24 months. Such an analysis is better equipped to demarcate between acute types of adjustment disorder and full–fledged PTSD. The present studies reported a prevalence of 19.04% falls in the midrange of the studies mentioned above. However, not all the selected studies accrued in the present systematic review revealed the 'time since TBI' and the presentation of symptoms of PTSD, making it impossible to assess the longitudinal relationship between these two factors.

The pooled prevalence of OCD from the three relevant studies in the present review stood at 19·48%. In the general population, OCD has been shown to have a prevalence rate of about 2·3%, a number that is supposed to transcend ethnicity and geography.[80 81] Unlike other psychiatric disorders that are likely to be stigmatised in many traditionally religious societies that subscribe to scriptural teachings, a high level of care seek behaviour has been observed for OCD in both biomedical and traditional healing settings.[82 83] It has been hypothesised that the focus on purity, cleanliness, thought control, morality and sexuality could pose as trigger factors toward the development of OCD.[84] In the general population, the presence of OCD has been associated with frontostriatal abnormalities, an anatomical region that often also

undergoes microstructural damage due to TBI as well.[85 86] Rydon–Grange & Coetzer[87] have suggested that OCD secondary to TBI tends to be'masked' as cognitive impairment, and conversely, memory impairment and executive dysfunction are often incorrectly diagnosed as OCD.[88] Given this context, more studies are needed to discern whether OCD and the other sequelae

The present study revealed a prevalence estimate of TBI-related sleep disorder (TBI-SD) of 26·67% from the four existing studies. TBI–SD can hamper the recovery process, as well as potentially increase various comorbidities, including the post–TBI spectrum of neuropsychiatric impairment.[89-91] Reciprocally, mood and anxiety disorders can also contribute to the development of sleep disturbances, along with more direct factors such as the degree of injury to regions of the brain involved in sleep, namely the hypothalamus, brainstem, and reticular activating system.[92] Mathias & Alvaro[93] have identified hypersomnia, insomnia, narcolepsy, obstructive sleep apnea, and periodic limb movements as the most common sleep problems encountered after TBI. A systematic review and meta-analysis by Montgomery et al.[94] reported a pooled prevalence of insomnia disorder to be 27·0%, which closely resembles the prevalence rate in the present study. Given that TBI-SD are considered to be one of the most prevalent and persistent sequelae, more studies with larger samples are required to explore the complex interconnections between post–TBI sleep–wake patterns and other neuropsychiatric complications.

In the present review, the estimated prevalence of cognitive impairment from eight studies was 49·10%. Unlike posttraumatic psychiatric disorders, cognitive impairments that affect memory, sensorimotor, and functional status have been widely established to be strongly associated with damage to specific areas of the brain. Impaired cognition is associated with difficulties in information processing, resulting in problems with attention and concentration, learning and remembering, executive functioning, and other higher–order functions that fall under the rubric of neuropsychological impairment. A meta-analysis of the rate of cognitive deficits after TBI reported a pooled prevalence of cognitive decline ranging from 18% to 57%.[95] This wide variation probably stemmed from the excessive heterogeneity of the time of cognitive assessment (acute vs. chronic) and the severity of injury (moderate vs. severe). The prevalence rate attained in the current review falls within this range of the meta-analysis. The presence of cognitive decline has the potential to negate self-sufficiency, creating subtle but intransigent disability and dependency.[96]

4.1. Limitations:

A study by Kim et al.[97], exploring whether published studies on post–TBI neuropsychiatric sequelae met the criteria of the American Academy of Neurology for the classification of articles on diagnostic methods, identified that a limitation of their study was that articles on this subject that employed a robust methodology with usable data were rare. Similar conclusions were also made when analysing the articles included in this study. It was unfortunate that certain high–quality articles had to be excluded from the meta-analysis, as many of them reported prevalence data as continuous measures (i.e. reporting scores as means). Furthermore, as is often the case, systematic reviews and meta–analyses tend to have their own intrinsic conceptual and methodological limitations. These potential limitations will be discussed along with a critical appraisal of the studies emanating from the regions of interest. West and South Asia and Africa.

4.1.1. Heterogeneity of outcome measures

For logistical reasons, it was not feasible to demarcate articles based on outcome measures used due to the excessive heterogeneity of tools used. Thus, the ideal model of lumping prevalence rates according to whether they used self-report measures or standardised diagnostic procedures was not feasible in the present review. On the one hand, to avoid 'comparing oranges and apples', it is often ideal to calculate the prevalence rate using specific outcome measures. However, the method of lumping itself has limitations. As is often the case, self–report measures or standardised diagnostic procedures tend to reveal wide differences in prevalence rate, with standardised diagnostic procedures tilting towards more conservative figures. Therefore, the present review has the confounder of not being able to separate apples and oranges, so caution is needed when interpreting the statistics reported in this review. Related to this, it would have been ideal if the studies in the presently considered region quantified psychiatric symptoms that are part of international psychiatric nosology. For example, some studies have used the Self–Reported Questionnaire (SRQ). While this has been specifically designed by the WHO for non–western populations, SRQ only detects nonspecific psychological distress, although Bangirana et al.[60] used it to tap into depressive symptoms. In addition to the SRQ, other instruments such as the General Health Questionnaire, Apathy Evaluation Scale, and Brief Symptom Inventory appeared to be used to tap into psychological problems and symptoms of psychopathology that are not commonly used for rigorous neuropsychological evaluation. However, such measures have various

subscales that measure distresses featured in the DSM and ICD, such as the study by Devi et al.[44] utilizing the Neuropsychiatric Inventory–Questionnaire, which is an informant–based instrument.[98] Therefore, a demarcation is needed in terms of whether these instruments are capable of measuring specific functional outcomes, psychiatric symptoms, and cognitive symptoms.

4.1.2. Problems related to the assessment of cognition

While cognitive impairment after TBI is a common complication, there is currently no widely accepted unified process of quantifying it. Of the articles reviewed for this study, the tools used to assess cognition are those considered to be 'bedside' global cognitive tests, rather than conventional neuropsychological batteries.[99] They frequently produce false positives depending on the patient's education status, as well as false negatives depending on the anatomical region of the brain injury.[100] Related to this, important confounders of cognitive functioning such as language proficiency, premorbid IQ, and mood status have not been adequately addressed in studies accumulated from the regions of interest.–

4.1.3. Relationship between cognitive symptoms and psychiatric symptoms

Some emotional distresses and affective symptoms are likely to have a reciprocal relationship with cognitive symptoms. Similarly, premorbid functioning and level of education have been widely established to influence cognitive status. These relationships were not explored significantly in articles from the considered region.

4.1.4. Time since the injury

It has been widely established that longitudinal studies show fluctuating prevalence rates of secondary conditions following TBI.[79 101] However, the majority of articles that met the inclusion criteria did not explicitly mention the time since the injury, making it impossible for the current study to categorise and evaluate the results depending on the time since the injury.

4.1.5. Diversity in language

The regions considered are known for their diversity in languages spoken, some of which include Hindi, Farsi, Hebrew, Urdu, Arabic, and Swahili. Although attempts were made to access the TBI literature in Arabic through the Al Manhal database (to no avail), the present critical review could not evaluate any non-English-language articles that may have existed.

4.1.6. Heterogeneity of inclusion and exclusion criteria

Most of the articles used in the present critical evaluation did not indicate the specifics of the diagnostic criteria of TBI within the inclusion and exclusion criteria. What constitutes TBI is sometimes wrongly equated with perinatal trauma, hypoxia–ischemia events, cerebral edema, toxic and metabolic insult, primary ischemic or hemorrhagic strokes, seizure or its aftermath, intracranial surgery, cerebral neoplasms, skull fracture, or intracranial haematoma without concurrent cerebral injury.

4.1.7. Regions of Conflict

It must be noted that quite a few of the countries included in the current critical appraisal currently are, or have been, settings of major military conflicts. Although studies involving sustained TBI in military personnel were excluded, there were no internal mechanisms to rule out combat or war–related incidents in non–military samples. For example, blast-induced TBI is a unique diagnosis that has been referred to as a characteristic cause of injury due to conflicts in Iraq and Afghanistan due to different physical attributes and biological consequences that make it significantly different from other modes of injury.[102]

4.1.8. Potential duplication of data

In any given region, many of the studies on this topic have been performed by a similar set of authors using data from the same one or two healthcare settings in the region. Therefore, it was often not possible to account for the potential duplication of data in research articles analysing various psychiatric and cognitive symptoms.

4.1.9. Data pollution

Unlike data poisoning, which refers to "intentional attempts to feed inaccurate data into models", data pollution is the unintentional corruption of data due to various reasons such as poor measurement reliability, amorphous or heterogeneous definitions of key concepts, and selection bias, to name a few.[103] There is a likely chance that data pollution may have affected current data given the heterogeneous nature of data, lower quality of sample selection procedures of included studies and the use of self–reported measures.

4.1.10. Publication bias

It is recommended that a publication bias assessment be done to account for any potential outliers, and this was taken into account by implementing a search of the all-inclusive

database Google Scholar for any grey literature. Aside from this, avoidance of publication bias also requires that studies included in a high–quality meta-analysis be better–powered. However, the majority of papers in the region of interest that met the inclusion criteria of the meta-analysis did not provide a proper explanation for the calculation of the sample size. This may be likely due to the adherence to reporting guidelines, such as the 'Strengthening the Reporting of Observational Studies in Epidemiology' (STROBE) guidelines, which is generally suboptimal in research from the regions under consideration.[104] Given the limited availability of existing research on the current topic, we did not wish to exclude articles that provided prevalence rates relevant to our study. Therefore, this particular aspect of publication bias had to be overlooked.

4.1.11. Overrepresentation of certain regions

Among the studies in the region of interest, two countries (India and Iran) were over-represented, accounting for 17 of the 27 included studies. Although Western Asian countries did produce a reasonable amount of research publications, unfortunately, several fell short of the standards of the JBI guidelines. Concerted efforts are needed for traumatic brain injury research to thrive in these regions, especially since their populations are known to be at higher risk.[33]

4.1.12 Specificity of the presenting symptoms

Survivors of TBI frequently exhibit a range of neuropsychiatric symptoms, often encompassed by the term "postconcussion syndrome." This syndrome is marked by a confluence of cognitive, emotional, behavioural, and even physical issues. This amalgamation of symptoms contributes to the intricate nature of their diagnosis. However, the intricate nature of this diagnostic spectrum introduces intricacies to comprehending these conditions. The labels and classifications applied to these conditions are significantly influenced by the specific screening tools used for assessment. Consequently, these variations in labelling can substantially affect the estimated prevalence rates attributed to these conditions. In essence, the diverse array of symptoms and the dependence on varying screening tools intertwine to create a landscape of uncertainty in the study of these conditions, casting potential shadows on the precision of prevalence estimates.

4.2. Theoretical Implications for Future Research:

While acknowledging the possible limitations of the current design, it is relevant to take into account the theoretical implications of the current findings and how they can be applied towards the designing of future research into this subject. Although the present article reviewed is not necessarily representative of the global south in its entirety, the resulting prevalence rates, as documented in the regions of interest, can probably be generalised for other populations in the global south.

First, the very fact that neuropsychiatric sequelae such as depression, anxiety, PTSD, and OCD have significant prevalence rates in the global south challenges the previous narrative around the populations of these regions. Due to sociocultural views and the resultant idioms of distress, psychiatric disorders in this region are sometimes considered to be expressed differently compared to data obtained using diagnostic tools derived from international titles, such as the DSM and ICD. If these distinctions do indeed exist, their symptoms are likely to be considered 'atypical' and diagnosed as an indistinct 'not otherwise specified' subtype of the disorder.[105] While it is clear that the existing literature challenges this perspective, concerted efforts are needed to develop disease–specific and culturally adaptive tools to identify post–TBI psychiatric disorders. Furthermore, more studies that use standardised clinical interviews would result in better comparability and reliability of results, in contrast to self-report measures.

Second, despite the large population residing in West Asia, South Asia, and Africa, the normative data for different populations in the global south have not yet to be charted.[106] Future studies from the global south should attempt to employ conventional and validated neuropsychological batteries to diagnose cognitive impairment. However, these high–power cognitive tests do not appear to be widely accessible to clinicians and researchers in regions of interest, as most of them are not available in the public domain or, if available, require exorbitant fees that are not feasible for clinicians in certain resource–depleted regions.[107] Thus, the allocation of resources for complications related to TBI is yet to receive the due attention. Neuropsychological tests that are frequently used in the global south in the context of TBI are often not supported by relevant literature on their cross–cultural validity.[108] Efforts are needed to unravel the relationship between cognitive symptoms and critical neural substrates involved in cognition. This has the potential to lay the groundwork for the establishment of demographically valid and disease–specific measures for cognition without running into a race norming discourse in cognitive testing.[108]

Third, there is a global increase in interest in developing evidence-based rehabilitation and remediation for post–TBI secondary conditions. There is evidence to suggest the efficacy of pharmacotherapy and psychotherapeutic interventions for post-TBI neuropsychiatric sequelae that are being examined in the present review.[109-112] Proper attention must be paid to adapting rehabilitation services for the TBI population in the global south.

Fourth, some of the articles that met the inclusion criteria were not necessarily featured in dominant search engines such as PsycINFO, Scopus, PubMed/MEDLINE, and ProQuest**.** It is not clear whether more inclusive criteria would entail the potential consideration of articles published in journals that are sometimes labelled as being 'predatory.' Despite such a caveat, such articles appear to perform well with the inclusion criteria and screening using the JBI guidelines, which was set to be greater than 75%, which, though adequate, falls in the lower range of quality control scores. However, such a threshold constitutes the best compromise to accumulate enough articles from the presently defined region for a proper meta-analysis. In this regard, it appears that the North-South divide in the quality and quantity of articles is evident in the research on the neuropsychiatric sequela of TBI.[31] The hope is that the present critical appraisal of the literature from the following regions within the global south, western Asia, South Asia, and Africa, would be catalytic in addressing the existing tribulations of unmet needs of those who sustain brain injuries.

Fifth, this study has employed the Joanna Briggs Institute guidelines to evaluate the quality of the studies, which helped the present study select studies that adhered to more standardised methodologies. However, in future research, it is recommended to promote the use of more standardised assessment tools and methodologies to improve the comparability and reliability of the findings in different studies. In the global South, it is known to have limited access to healthcare resources, varying levels of awareness of neuropsychiatric sequelae, and differences in reporting practises. These factors could contribute to the observed prevalence rates. Therefore, to better understand these influences, more research could involve qualitative investigations or sub-analyses that explore the relationship between healthcare disparities and prevalence rates. Finally, it should be noted that this study highlighted substantial prevalence rates of depression, anxiety, PTSD, OCD, sleep disturbance related to TBI and cognitive impairment following TBI in the specified regions. While existing studies lacked homogeneous data, the consistency of these prevalence rates suggests a notable

burden of neuropsychiatric sequelae in the 'global south.' These findings underscore the need for targeted interventions, remedial services, and neurorehabilitation, and the importance of increasing awareness in the global south is paramount. As an avenue for future research, it might be prudent to investigate potential socioeconomic, cultural, and contextual factors that could contribute to the observed patterns, helping in the development of more tailored strategies for prevention and management.

Conclusions

To date, this is the first critical review that has examined the spectrum of post–TBI neuropsychiatric sequelae in the specified regions. The observed prevalence rates are significant and comparable to statistics from the global north. This challenges the existing narrative on the existence and presentation of neuropsychiatric symptoms among the populations of the regions under consideration and can help lay the foundation for the adaptation of rehabilitation services for patients with TBI in the global south. Future studies should prioritise uniform assessment tools and methodologies for enhanced comparability. Limited access to healthcare care, variations in awareness and reporting disparities in the global south could influence prevalence rates, warranting qualitative investigations. The consistent rates of neuropsychiatric sequelae in the study highlight their significant burden despite the heterogeneity of the data. This emphasises the need for targeted interventions, neurorehabilitation, and increased awareness in the global south. Future efforts should explore socioeconomic, cultural and contextual factors to shape tailored prevention and management strategies.

Authors' Contribution

AG, SS, SM, DTB, MS and SA contributed to the conceptualization and design of the study or involved in data collection, and MFC, SA provided data analysis, interpretation, and statistical expertise. The initial draft was prepared by AG, SS and SM, and was revised critically by MFC, DTB, KR, MS, and SA. Approval of the final version prior to submission was done by AG, SS, SM, MFC, DTB, KR, MS and SA. All authors agree to be held accountable for all aspects of the work and its accuracy and integrity. All authors approved the final version of the manuscript.

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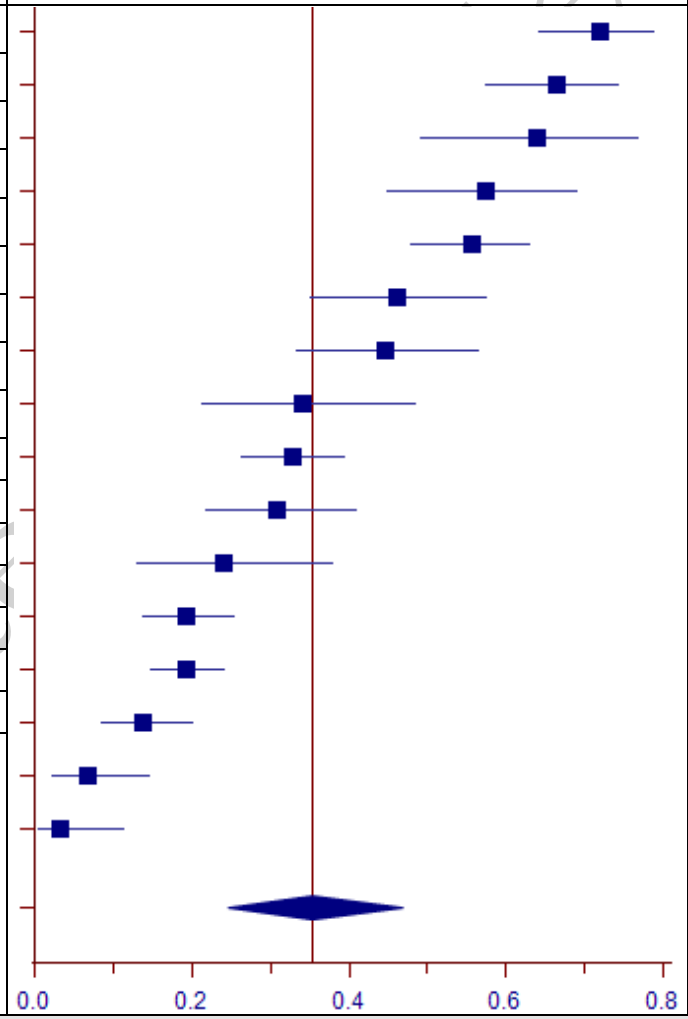
Figure 1. Prevalence estimates of depression

Study	N	Depression	Prevalence	Forest Plot	95% CI
Varghese et al. (2018)[62]	154	111	72.08		64.29 to 79.00
Groswasser et al. (2018)[51]	128	85	66.41		57.53 to 74.51
Sameh et al. (2021)[61]	50	32	64.00		49.19 to 77.08
Al–Adawi et al. (2007)[37]	68	39	57.35		44.77 to 69.28
Bangirana et al. (2019)[60]	171	95	55.56		47.78 to 63.14
Al–Adawi et al. (2004)[43]	80	37	46.25		35.03 to 57.76
Hoofien et al. (2001)[45]	76	34	44.74		33.31 to 56.59
Shafiei et al. (2016)[54]	50	17	34.00		21.21 to 48.77
Jain et al. (2014)[63]	204	67	32.84		26.45 to 39.75
Dhakal et al. (2021)[58]	97	30	30.93		21.93 to 41.12
Devi et al. (2020)[44]	50	12	24.00		13.06 to 38.17
Dade et al. (2019)[48]	187	36	19.25		13.86 to 25.64
Fakharian et al. (2015)[50]	286	55	19.23		14.83 to 24.28
Ramezani et al. (2018)[53]	146	20	13.70		8.57 to 20.36
Nuhu & Yusuf (2012)[59]	75	5	6.67		2.20 to 14.88
Keshavan et al. (1981)[55]	60	2	3.33		0.41 to 11.53
Total (random effects)	**1882**	**677**	**35.35**		**24.64 to 46.87**

Heterogeneity: I^2=96.20%, Q=394.96, p< 0.001

Figure 2. Prevalence estimates of anxiety

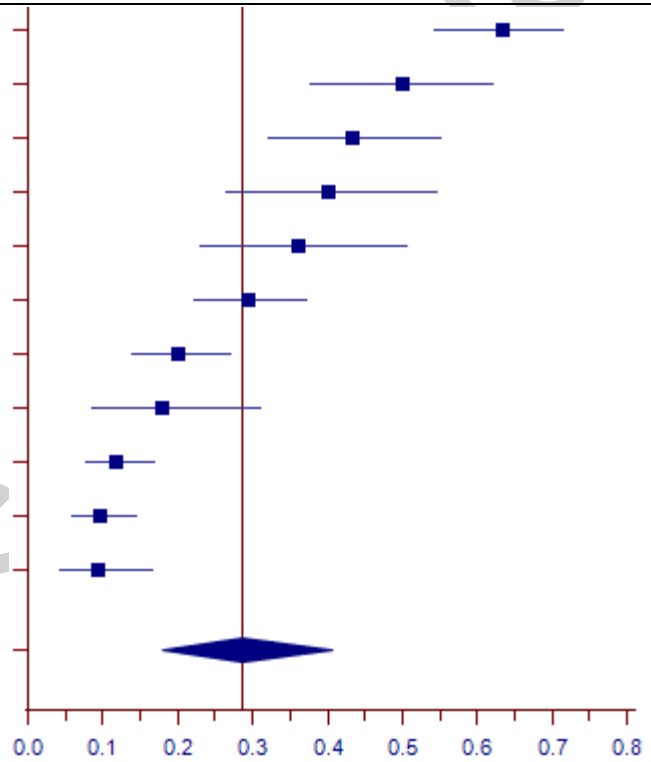
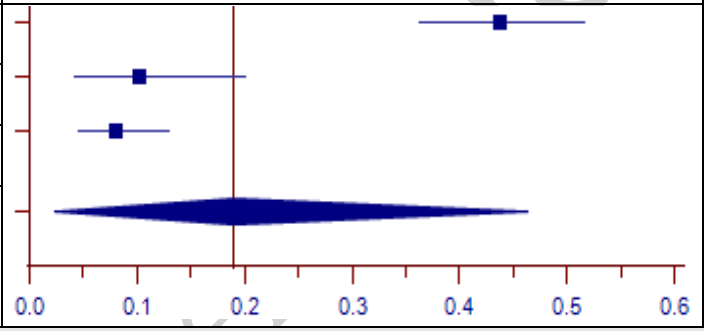
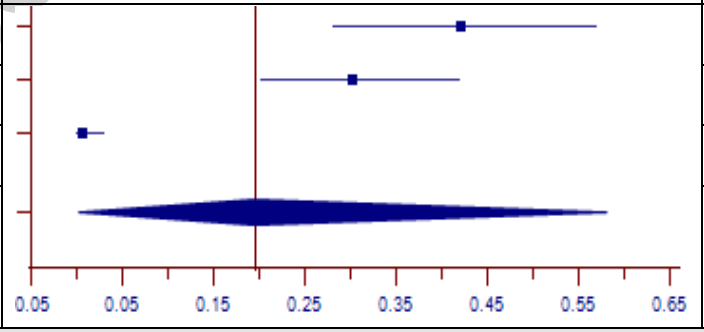
Study	N	Anxiety	Prevalence	Forest Plot	95% CI
Groswasser et al. (2018)[51]	128	81	63.28		54.31 to 71.62
Al–Adawi et al. (2007)[37]	68	34	50.00		37.62 to 62.38
Hoofien et al. (2001)[45]	76	33	43.42		32.08 to 55.29
Sameh et al. (2021)[61]	50	20	40.00		26.41 to 54.82
Shafiei et al. (2016)[54]	50	18	36.00		22.92 to 50.81
Ramezani et al. (2018)[53]	146	43	29.45		22.20 to 37.56
Rezaei et al. (2014)[52]	155	31	20.00		14.01 to 27.17
Devi et al. (2020)[44]	50	9	18.00		8.58 to 31.44
Sharma et al. (2015)[47]	204	24	11.77		7.69 to 17.00
Dade et al. (2019)[48]	187	18	9.63		5.81 to 14.79
Dhakal et al. (2021)[58]	97	9	9.28		4.33 to 16.88
Total (random effects)	**1211**	**320**	**28.64**		**17.99 to 40.65**
Heterogeneity: I^2=94.92%, Q=196.91, p< 0.001					

Figure 3. Prevalence estimates of post–traumatic stress disorder (PTSD)

Study	N	PTSD	Prevalence	Forest Plot	95% CI
Bangirana et al. (2019)[60]	171	75	43.86		36.30 to 51.64
Hoofien et al. (2001)[45]	68	7	10.29		4.24 to 20.07
Dade et al. (2019)[48]	187	15	8.02		4.56 to 12.89
Total (random effects)	426	**97**	**19.04**		**2.35 to 46.37**
Heterogeneity: I^2=97.28%, Q=73.46, p<0.001					

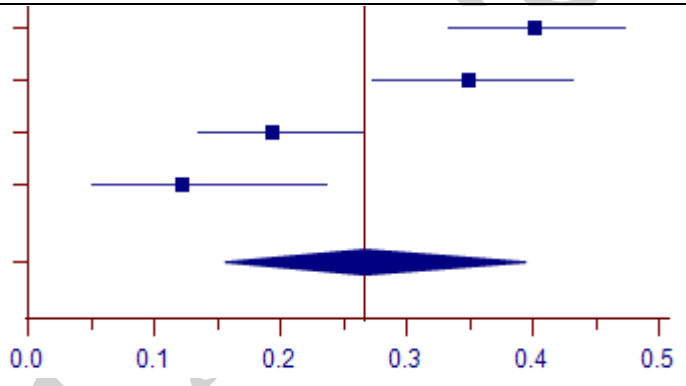
982

Figure 4. Prevalence estimates of obsessive–compulsive disorders (OCD)

Study	N	OCD	Prevalence	Forest Plot	95% CI
Shafiei et al. (2016)[54]	50	21	42.00		28.19 to 56.79
Hoofien et al. (2001)[45]	76	23	30.26		20.25 to 41.88
Dade et al. (2019)[48]	187	1	0.54		0.014 to 2.94
Total (random effects)	**313**	**45**	**19.48**		**0.23 to 58.06**
Heterogeneity: I^2=97.84%, Q=92.44, p<0.001					

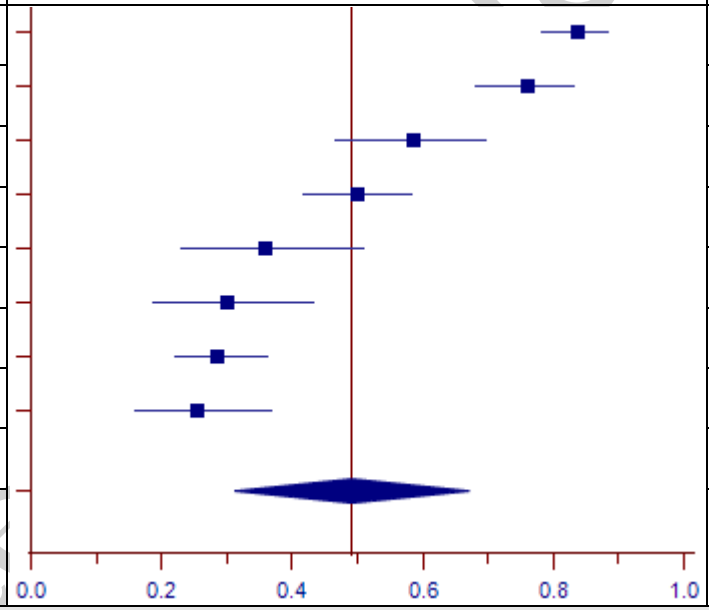
983

Figure 5. Prevalence estimates of TBI–related sleep disturbance (TBI-SD)

Study	N	TBI–SD	Prevalence	Forest Plot	95% CI
Jain et al. (2014)[63]	204	82	40.20		33.41 to 47.27
Ramezani et al. (2018)[53]	146	51	34.93		27.24 to 43.25
Rezaei et al. (2014)[52]	155	30	19.36		13.46 to 26.46
Madaan et al. (2021)[57]	57	7	12.28		5.08 to 23.68
Total (random effects)	**562**	**170**	**26.67**		**15.63 to 39.44**
Heterogeneity: I^2=90.27%, Q=30.83, p<0.001					

984

Figure 6. Prevalence estimates of cognitive impairment (CI)

Study	N	CI	Prevalence	Forest Plot	95% CI
Panwar et al. (2019)[46]	228	191	83.77		78.33 to 88.31
Singh et al. (2021)[64]	134	102	76.12		67.99 to 83.06
Sinha et al. (2013)[56]	77	45	58.44		46.64 to 69.57
Ramezani et al. (2018)[53]	146	73	50.00		41.62 to 58.38
Devi et al. (2020)[44]	50	18	36.00		22.93 to 50.81
Chabok et al. (2012)[49]	60	18	30.00		18.85 to 43.21
Bangirana et al. (2019)[60]	171	49	28.66		22.01 to 36.06
Nuhu & Yusuf (2012)[59]	75	19	25.33		15.99 to 36.70
Total (random effects)	**941**	**515**	**49.10**		**31.26 to 67.07**

Heterogeneity: I^2=96.85%, Q=222.41, p<0.001

985