

REVIEW ARTICLE

Prevalence of Delirium and Its Related Factors in Burn Patients; a Systematic Review and Meta-Analysis

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Abstract: Introduction: Considering the importance of delirium disorder in burn patients and its complications, the present systematic review and meta-analysis aimed to determine the prevalence of delirium and its related factors in burn patients. Methods: A comprehensive, systematic search was performed in different international electronic databases, such as Scopus, PubMed, and Web of Science, as well as Persian electronic databases such as Iranmedex, and Scientific Information Database (SID) using keywords extracted from Medical Subject Headings such as "Prevalence", "Delirium", and "Burns" from the earliest to the 17th of July, 2023. Results: In total, 2,710 burn patients participated in ten original studies. Among the participants, 64.6% were male. In the ten studies, the reported pooled prevalence of delirium among burn patients was 20.5% (95% CI: 10.9% to 35.0%; I2=96.889%; P<0.001). Also, factors such as total body surface area, duration of hospitalization, mortality, days on ventilator, alcoholism, benzodiazepine dose, methadone dose, age, male gender, ICU days, operation days, wound care under anesthesia, and opioid dose had a significant correlation with the prevalence of delirium in burn patients. Conclusion: Health managers and policymakers can reduce the prevalence of delirium in burn patients by eliminating or reducing factors associated with it.

Keywords: Prevalence; Delirium; Burns; Risk factors; Mental disorders

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1. Introduction

Delirium is one of the acute brain disorders that are diagnosed through a simultaneous disorder in attention, awareness, and cognition.

This disorder is a costly and unknown condition that affects

mostly the elderly (1, 2). The prevalence of this disorder is low in people who are not hospitalized, but in hospitalized patients, this number increases significantly. When these patients are hospitalized in the intensive care unit, this prevalence reaches its peak (3, 4). This disorder is caused by non-modifiable and modifiable predisposing factors, including age and surgery (5).

Recently, recognition and treatment of delirium disorder have been noticed in patients suffering from burns. Patients suffering from burns usually have severe injuries that require more care such as surgery, wound care, mechanical ventilation, and the use of sedatives (6-9). This special care is provided in intensive care units, and severe injuries cause patients to stay longer in this unit and receive care such as seda-

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tives and ventilators (10). This long stay in the hospital, especially in the intensive care unit, and receiving special care in this unit increases the prevalence of delirium in burn patients (11). A study showed that in Sweden, the prevalence of delirium in burn patients was 19.47%. It also showed that old age, the provision of special care, and the number of interventions under anesthesia were the related factors for delirium (12). Another study reported that in the Netherlands the prevalence of delirium in burn patients was 13.33%. It also reported that old age, physical impairment, and the use of anticholinergic drugs during admission were related factors for delirium in burn patients (13).

The prevalence of psychiatric disorders is high in people with burn injuries (14). Therefore, high-risk disorders such as delirium should be diagnosed and treated earlier or its occurrence and complications should be prevented with special strategies (15).

Considering the importance of delirium disorder in burn patients and its complications, as well as various factors related to this disorder in previous studies, this study was conducted to investigate the prevalence of delirium and its related factors in burn patients.

2. Methods

2.1. Study design and setting

This systematic review and meta-analysis utilized the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline as a means of conducting the study (16). The PEO framework was used to clarify the aim of this research. Accordingly, population (burn patients), exposure (delirium), and outcome (prevalence and related factors), were included in the systematic review and meta-analysis.

2.2. Search strategy

A comprehensive, systematic search was performed in different international electronic databases, such as Scopus, PubMed, and Web of Science, as well as Persian electronic databases such as Iranmedex, and Scientific Information Database (SID) using keywords extracted from Medical Subject Headings such as "Prevalence", "Delirium", and "Burns" from the earliest to the 17th of July 2023. For example, the search strategy in PubMed/MEDLINE database was (("Prevalence") OR ("Epidemiology")) AND (("Delirium") OR ("Delirium") OR ("Cognitive disorder")) AND (("Burn") OR ("Burn patient")). To combine terms, "OR" and "AND" Boolean operators were used, and Iranian electronic databases in Persian were also explored in this study. Additionally, two researchers performed a comprehensive search. However, this systematic review did not consider gray literature, such as conference presentations, expert commentary, research and committee reports, theses, and ongoing research, which was not officially published by a commercial publisher (17).

2.3. Inclusion and exclusion criteria

The focus of this systematic review and meta-analysis was to investigate English or Persian original studies that addressed the occurrence rate of delirium and its associated factors in burn patients. However, qualitative studies, case reports, experimental studies, conference proceedings, reviews, and letters to the editor were not considered.

2.4. Study selection and data extraction

For this systematic review, EndNote 20 was utilized to organize the data. To select studies based on the predetermined inclusion and exclusion criteria, the following steps were followed: 1) Reviewing the title and abstract of each study; 2) Conducting electronic and manual searches to identify and remove duplicate papers, and 3) Carefully reading the complete contents of the publications. If any disagreements arose between the first two researchers during the study selection process, the third researcher was consulted to resolve them. Finally, the references were thoroughly reviewed to ensure that no pertinent data was overlooked. The information extracted in this review by the researchers includes the name of the first author, year of publication, location, sample size, male/female ratio, age, single/married ratio, burn degree, total body surface area (TBSA), prevalence of delirium, and related factors.

2.5. Quality assessment

The AXIS tool was employed to assess the quality of cross-sectional studies included in the analysis. The tool consists of 20 items and uses a two-point Likert scale (yes/no) to evaluate report quality (7 items), study design quality (7 items), and the potential introduction of biases (6 items). The quality of the studies was rated at three levels based on the percentage of correct responses: high (70-100%), fair (60-69.9%), and low (0-59.9%) (18). Two independent researchers extracted and evaluated the quality of the study data.

2.6. Statistical analysis

The analysis was performed using the CMA program, version 3. The sample size and frequency of delirium for each study were collected, and the overall effect size was calculated based on these results. The level of heterogeneity was determined using the I2 statistics, where values of 25%, 50%, and 75% indicate mild, moderate, and high heterogeneity, respectively. Due to the significant variability in the results, a random effects model was employed.

2.7. Sensitivity analysis

A sensitivity analysis was conducted to evaluate the impact of excluding each study on the overall prevalence of delirium in burn patients.

2.8. Publication of bias

To evaluate the potential for publication bias, the Egger's test results and a Funnel plot were utilized.

3. Results

3.1. Study selection

As shown in Figure 1, a search conducted across electronic databases retrieved a collective count of 1,995 articles. Following an initial analysis of the research and the removal of duplicate studies, 1,089 relevant studies remained. Subsequently, a comprehensive assessment of the titles and abstracts of these remaining papers was performed based on inclusion and exclusion criteria. This process led to the selection of 70 studies for a thorough full-text evaluation. Ultimately, ten studies (11-13, 19-25) were deemed suitable for inclusion in this systematic review.

3.2. Study characteristics

As mentioned in Table 1, in total, 2,710 burn patients participated in ten original studies (11-13, 19-25). Among the participants, 64.6% were male. The average TBSA in burn patients was 9.75%. Studies were conducted in the USA (n=3) (11, 20, 24), Turkey (n=2) (23, 25), Japan (n=1) (21), India (n=1) (19), Finland (n=1) (22), Netherland (n=1) (13), and Sweden (n=1) (12).

3.3. Methodological quality of included study

As shown in Figure 2, nine studies (11-13, 20-25) were of high quality and one study (19) was of fair quality. Three studies (19, 20, 23) did not report limitations and four studies (19-21, 23) did not report conflicts of interest or funding.

3.4. Prevalence of delirium

As shown in Figure 3, in the ten studies, the reported pooled prevalence of delirium among burn patients was 20.5% (95% CI: 10.9% to 35.0%; I2=96.889%; P<0.001).

3.5. Factors influencing the prevalence of delirium in burn patients

As shown in Table 1, there was a significant positive association between the prevalence of delirium in burn patients and TBSA (n=3) (12, 20, 22), duration of hospitalization (n=3) (12, 21, 24), mortality (n=2) (12, 20), days on the ventilator (n=2) (13, 24), alcoholism (n=1) (20), benzodiazepine dose (n=1) (20), methadone dose (n=1) (20), age (n=1) (12), male gen-

der (n=1) (20), ICU days (n=1) (24), operation days (n=1) (12), and wound care under anesthesia (n=1) (12). Also, there was a significant negative relationship between the prevalence of delirium in burn patients and opioid dose (n=1) (11).

3.6. Sensitivity analysis

As shown in Figure 4, by removing one study at a time, sensitivity analyses were performed to determine how each one influenced the summary results and between-study heterogeneity.

3.7. Publication of bias

The use of a funnel plot asymmetry was suggested to evaluate the likelihood of publication bias (Figure 5). However, the findings from the Egger's test did not reveal any significant evidence of publication bias (t=1.18, P=0.27).

4. Discussion

This systematic review and meta-analysis sought to explore the occurrence of delirium among burn patients. The findings revealed that approximately 20.5% of these patients experienced delirium. Also, factors such as TBSA, duration of hospitalization, mortality, days on ventilator, alcoholism, benzodiazepine dose, methadone dose, age, male gender, ICU days, operation days, wound care under anesthesia, and opioid dose had a significant relationship with the prevalence of delirium in burn patients.

Healthcare professionals must grasp the prevalence of delirium in burn patients to deliver suitable care and implement effective management strategies. Also, identifying risk factors linked to delirium in burn patients offers valuable insights for implementing preventive measures and targeted interventions (11, 26).

The findings of a systematic review and meta-analysis focusing on the occurrence of delirium among ICU-admitted patients revealed that approximately 31% of those in the ICU experience various forms of delirium (27). The study's outcomes indicate a clear correlation between the prevalence of delirium and both the length of ICU stay and the utilization of ventilator support among burn patients. In light of these observations, forthcoming research endeavors should delve further into the factors influencing delirium prevalence in burn patients undergoing ICU hospitalization, and also explore potential strategies for its management.

Based on the findings derived from this systematic review and meta-analysis, burn TBSA was a significant factor affecting the occurrence of delirium (12, 20, 22). Burn injuries, particularly those encompassing extensive TBSA, initiate a notable inflammatory reaction within the body. This systemic inflammation has the potential to affect the brain, thereby playing a role in the onset of delirium.

The liberation of pro-inflammatory cytokines and various immune agents can interfere with regular brain function, giving rise to cognitive alterations characteristic of delirium (28-30).

The duration of hospitalization emerged as a significant influencer of delirium prevalence among burn patients. The findings extracted from the studies incorporated into this systematic review and meta-analysis demonstrated a clear trend: individuals with burns who underwent extended hospital stays exhibited a higher propensity for the onset of delirium (12, 21, 24). Extended stays in the hospital subject patients to a range of stress-inducing factors, including pain, disturbances in sleep patterns, and alterations to their daily routines. These stressors can play a role in fostering the emergence of delirium, particularly when endured over a prolonged timeframe.

4.1. Limitations

The significant heterogeneity observed across the studies included constitutes a notable limitation. Particularly in prevalence meta-analyses, substantial heterogeneity often presents a significant challenge. The outcomes of the assessment of publication bias emphasize the necessity for further investigations to accurately establish the prevalence of delirium among burn patients. It is plausible that despite an exhaustive search across multiple databases, not all pertinent studies on this subject were identified. Lastly, this review's focus on studies published in English or Persian may result in potential language barriers, potentially excluding relevant data in other important languages from the analysis.

4.2. Implications for healthcare workers

Healthcare professionals, particularly those working within burn care environments, need to be well-informed about the prevalence of delirium in burn patients. They should integrate routine delirium screening protocols into their practice, enabling the swift identification and management of delirium cases, particularly in patients displaying risk factors. Additionally, these professionals should undertake the responsibility of educating burn patients and their families regarding the potential occurrence of delirium and the associated risk factors.

Furnishing information encompassing the early signs, symptoms, and the significance of timely intervention can effectively encourage reporting and foster active involvement of both patients and their families in the care process. Lastly, healthcare practitioners should identify pertinent risk factors, including prolonged hospitalization and the extent of burn injuries; thereby, facilitating a comprehensive patient assessment and implementation of preventive strategies.

4.3. Implication for future research

Subsequent investigations might delve deeper into elucidating the fundamental mechanisms that link recognized risk factors (such as extended hospitalization and burn severity) with the emergence of delirium in burn patients. Enhanced comprehension of these intricate pathways and interplays could pave the way for precise interventions. Additional research endeavors could prioritize the assessment of different intervention strategies to mitigate and handle delirium in burn patients. These strategies might encompass addressing pain, mitigating sleep disturbances, managing psychological distress, and tackling other risk factors in a concerted manner.

5. Conclusion

The evidence showed that approximately 20.5% of burn patients encountered episodes of delirium. Furthermore, variables including TBSA, hospitalization duration, mortality rate, duration of ventilator use, alcoholism, dosage of benzodiazepines and methadone, age, male gender, days spent in the ICU, days of operation, wound care administered under anesthesia, and opioid dosage exhibited notable associations with the prevalence of delirium in burn patients. Given these insights, it is recommended that healthcare practitioners seamlessly incorporate regular delirium screening protocols into their routine practice. This proactive approach facilitates prompt identification and effective management of delirium cases, particularly in patients who manifest these identified risk factors.

6. Declarations

6.1. Acknowledgments

None.

6.2. Conflict of interest

The authors declare no conflict of interest.

6.3. Funding and supports

None.

6.4. Authors' contribution

Study concept and design by all authors; Data acquisition by all authors; Data interpretation by all authors; drafting of the manuscript by all authors; Revision of the manuscript by all authors; the final version of the manuscript is approved by all authors.

6.5. Data availability

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

6.6. Using artificial intelligence chatbots

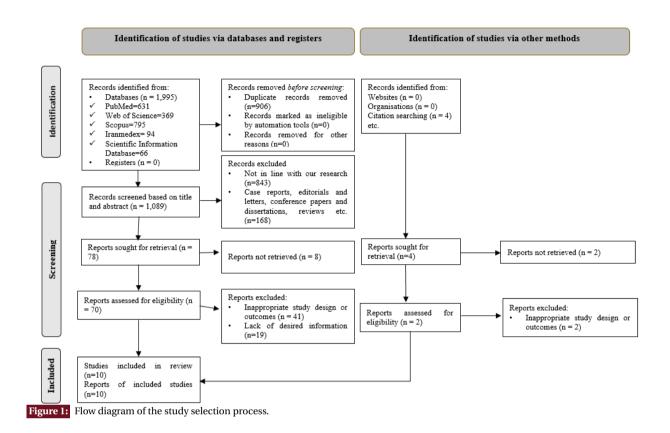
The authors declare that they have not used artificial intelligence chatbots.

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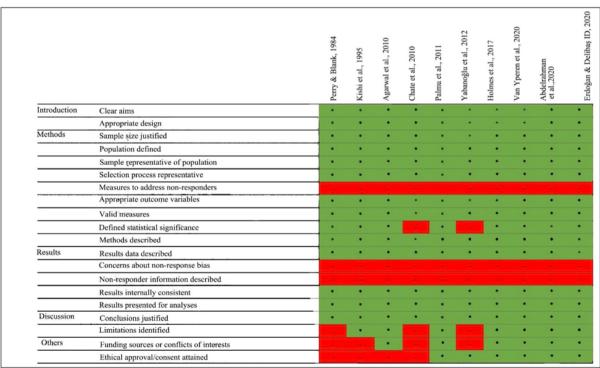


Figure 2: Assessment of the quality of the included articles.

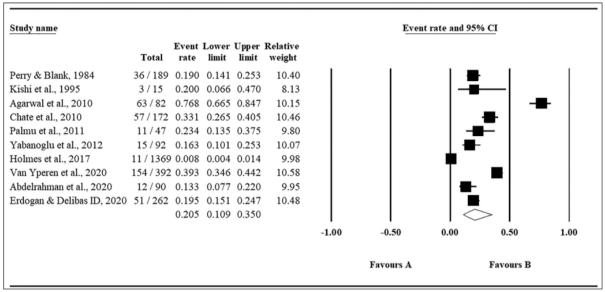


Figure 3: Forest plot of delirium prevalence in burn patients. CI: confidence interval.

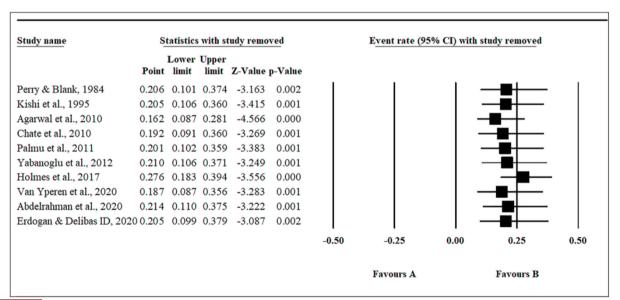


Figure 4: Sensitivity analysis of included studies. CI: confidence interval.

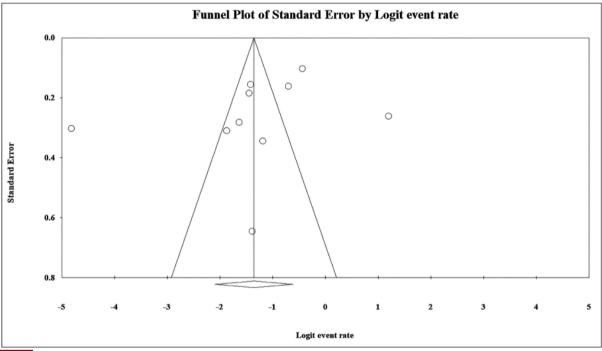


Figure 5: Funnel plot for evaluating the likelihood of publication bias.

 Table 1:
 Basic characteristics of the studies included in this systematic review

First Au- thor/year	Location	Sample size	M/F ratio (%)	Age (year) (Mean ±SD)	Single/ Married ratio (%)	Burn de- gree(%)	TBSA (%)	Preva- lence of delir- ium; n (%)	Related factors	Axis
Perry & Blank, 1984 (20)	USA	189	N/A	N/A	N/A	N/A	N/A	36 (19.05)	There was a significant relationship between gender and delirium (higher in males) (P<0.05). There was a significant positive relationship between TBSA and delirium (P<0.05). There was a significant positive relationship between alcoholism or drug abuse and delirium (P<0.01). There was a significant positive relationship between mortality and delirium (P<0.01).	High
Kishi et al., 1995 (21)	Japan	15	N/A	N/A	N/A	N/A	N/A	3 (20.00)	There was a significant positive relationship between duration of hospitalization and delirium (P=0.0001).	High
Agarwal et al., 2010 (11)	USA	82	65.85/ 34.15	N/A	N/A	I: 10 (12.20) II: 41 (50.0) III: 31 (37.80)	20	63 (76.83)	There was a significant positive relationship between benzodiazepine dose and delirium (P<0.001). There was a significant positive relationship between methadone dose and delirium (P<0.001). There was a significant negative relationship between opioid dose and delirium (P<0.001).	High
Chate et al., 2010 (19)	India	47	44.68/ 55.32	35.11 (SD= 16.17)	N/A	N/A	N/A	11 (23.40)	N/A	Fair
Palmu et al., 2011 (22)	Finland	92	69.57/ 30.43	46.30 (SD= 16.5)	45.65/ 54.35	N/A	N/A	15 (16.30)	There was a significant positive relationship between TBSA and delirium (P=0.004).	High
Yabanoğlu et al., 2012 (23)	Turkey	1369	N/A	N/A	N/A	N/A	N/A	11 (0.80)	N/A	High
Holmes et al., 2017 (24)	USA	392	66.58/ 33.42	N/A	N/A	N/A	7	154 (39.29)	There was a significant positive relationship between ICU days and delirium (P<0.001). There was a significant positive relationship between days on ventilator and delirium (P<0.001). There was a significant positive relationship between duration of hospitalization and delirium (P<0.001).	High
Van Yperen et al., 2020 (13)	Netherl- and	90	50.00/ 50.00	N/A	N/A	N/A	5	12 (13.33)	There was a significant positive relationship between days on ventilator and delirium (P=0.03).	High
Abdelrah- man et al., 2020 (12)	Sweden	262	68.70/ 31.30	N/A	N/A	N/A	7	51 (19.47)	There was a significant positive relationship between age and delirium (P<0.001). There was a significant positive relationship between mortality and delirium (P<0.001). There was a significant positive relationship between TBSA and delirium (P<0.001). There was a significant positive relationship between duration of hospitalization and delirium (P<0.001). There was a significant positive relationship between wound care under anesthesia and delirium (P<0.001). There was a significant positive relationship between wound care under anesthesia between under anesthesia and delirium (P<0.001).	High
Erdoğan & Delibaş ID, 2020 (25)	Turkey	172	77.33/ 22.67	N/A	55.23/ 44.77	N/A	N/A	57 (15.70)	N/A	High