Delirium Research in India: A Systematic Review

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Abstract

Delirium is the most common psychiatric diagnoses encountered in patients with various medical-surgical illnesses, in all the treatment set-ups, with relatively higher incidence and prevalence in the intensive care units. As delirium is encountered in multiple specialties, it is important to understand the research on this diagnosis. This study aims to assess the research output involving patients of delirium from India. A comprehensive search was undertaken using Medline (PubMed) and other databases. Search words included were "delirium," "delirious," "delirium tremens" AND "India." No filters were used. Internet and hand searches yielded 305 articles. Out of these articles, 151 had the terms "delirium," "delirious," "delirium tremens" in the title and these were included for the review. Additionally, 14 articles were included for the review, although these did not have these terms in the title, but delirium was one of the major outcome parameters in these studies. Majority of the papers were original articles (n = 81), and these were followed by, case reports (n = 58), review articles (n = 10), letter to the editor (not as case reports but as a communication; n = 13), editorials (n = 2) and one clinical practice guideline. Most of the original papers have either focused on epidemiology (incidence, prevalence, outcome, etc.), symptom profile, with occasional studies focusing on effectiveness of various pharmacological interventions. There is a dearth of research in the field of delirium from India. There is a lack of studies on biomarkers, evaluation of nonpharmacological interventions, and evaluation of prevention strategies. It is the need of the hour to carry out more studies to further our understanding of delirium in the Indian context.

Keywords
- delirium
- India
- outcome

Introduction

Delirium is an acute medical emergency, with psychiatric manifestations, which is seen across different treatment settings, with higher prevalence in intensive care units (ICUs) and palliative care setting. It is characterized by poor attention, disturbances in other cognitive functions, motoric alteration, disturbance in sleep, and psychotic symptoms. The prevalence of delirium varies across different settings, with rates as high as 80% among patients admitted in intensive care units (ICUs) and palliative care setting.[1] From an organ failure point of view, delirium represents acute brain failure, occurring due to various causes.[2,3] The various contributing factors for delirium can be broadly categorized as risk or predisposing and the precipitating or etiological factors.[4] It is the combination of the risk and the precipitating factors which determine the manifestation of delirium.[5] Patients, who are at high risk, may require minor precipitating factors for the development of delirium, whereas those who have lower risk factors may require more or severe precipitating factors

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for the development of delirium.[5] As a disorder, delirium is associated with significant negative consequences for the patients and their families in terms of increased mortality, longer duration of ICU and inpatient stay, higher treatment cost, long-term cognitive deficits, a higher risk of developing dementia, and high level of distress to the patients and caregivers.[6]

Although it is seen across all the medical-surgical settings, it is often underrecognized and undertreated. Some of the developed countries have recognized the importance of early identification and prevention of delirium in various treatment settings.[7,8] Many authors have developed bedside assessment instruments to detect delirium at the earliest and have also developed various intervention packages, such as the Hospital Elder Life Program (HELP)[9] and Assess, Prevent, and Manage Pain, Both Spontaneous Awakening Trials (SAT) and Spontaneous Breathing Trials (SBT); choice of analgesia and sedation; and the Delirium: Assess, Prevent, and Manage Early mobility and Exercise, and Family engagement and empowerment (ABCDEF)[10] bundle for early detection, prevention, and management of delirium.

Considering its ubiquitousness across all clinical specialties and underrecognition, it is important to understand awareness about delirium. One of the ways to address the issue is to look at the research outcome on the topic. Till today, there is no systematic review focusing on the research output on delirium from India. Evaluating the research output can help in understanding the current level of research and deficits in research. This can help in planning future research on the topic. Accordingly, this systematic review attempted to evaluate the research on delirium from India.

Methodology

For this systematic review, literature was searched in various search engines, that is, PubMed and Google Scholar, by using the following terms: "delirium," "delirious," "delirium tremens," "India," and "organic brain syndrome" in different combinations in December 2019. No filters were used. Additional searches were performed by doing hand searches of the reference list of the published articles to identify more articles. Additionally, the table of content of online issues of various psychiatric and anesthesia journals (irrespective of the indexing status) published from India, were specifically searched for studies focusing on delirium.

To be included in the review, the published papers were required to have the words "delirium," "delirious," or "delirium tremens" in the title. However, if the studies did not include these terms in the title but the primary focus of the study was delirium, then these papers were included in the review. Studies describing the psychiatric referral pattern, but which did not focus on the delirium, but in general described the prevalence of delirium in psychiatric referrals, were excluded. Data published only as abstracts of the national conferences were also excluded.

Internet and hand searches yielded 305 articles. ►**Fig. 1** shows the selection of the articles. Full manuscripts of these articles were reviewed by D.D. and S.K. Out of these articles, 151 had the terms "delirium," "delirious," "delirium tremens" in the title and these were included for the review (►**Fig. 2**). Additionally, 14 articles were included for the review, although these did not have these terms in the title but had delirium as one of the major outcome parameters. A majority (n = 144; 87.3%) of these articles were available in the PubMed search (►**Fig. 2**).

Results

Out of the 165 articles, it was seen that the majority (85.5%, n = 141) of the papers were published in the last one decade (2011–2019), and this was followed by 23(13.9%) articles published during the year 2001 to 2010. There was only one article (0.6%) on delirium before 2001, arising from India. Again, in the years 2011 to 2019, there were at least 10 articles published every year (►**Fig. 3**). A majority (87.3%) of the articles were published in the PubMed indexed journals and about one-third (31.5%) of these articles had nonpsychiatrist as an author. In terms of the type of papers, majority of the papers were original articles (n = 81, one of which was in the form of a letter to the editor),[11-91] and these were followed by, case reports (n = 58),[92-149] review articles (n = 10),[4,150-158] letter to the editor (not as case reports but as a communication; n = 13),[81,159-170] editorials (n = 2),[171,172] and one clinical practice guideline.[173] In terms of the institutes, most (37.6%, n = 62) of the articles were from the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, and this was followed by National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru (n = 6).

In terms of the original paper, out of the 81 papers, a majority (n = 50; 61.7%) of these were published in journals published from outside India. About two-fifths (n = 33; 40.7%) of the original articles had nonpsychiatrists as an author and about one-fourth (n = 19; 23.5%) of these studies focused on ICU patients or ICU health care workers.

As across the globe, the prevalence and incidence of delirium, in studies from India have also varied depending on the study setting (►**Table 1**).[11-36] Majority of the studies have assessed the incidence and prevalence of delirium have relied on the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV)/DSM-IV text revision (TR) criteria.[15,17,19,20,23-27,29-31] However, some of the studies have used confusion assessment method (CAM)/CAM-ICU.[13,14,16,18,33,34] The prevalence rates in various ICUs have varied from 16.1 to 68.2%.[15-17,19,20,23] Similarly, the incidence of delirium in various ICUs ranges from 8 to 59.6%.[15,17-22]

One of the studies evaluated delirium in general medical inpatients and reported the prevalence rate to be 19%,[11] whereas another study that focused on postoperative patients reported a prevalence rate of 4%.[32] One study reported a prevalence of delirium in referrals of consultation liaison psychiatry (CLP) setting and estimated the prevalence to be 33.96%.[12] The same study extrapolated the prevalence to all the inpatients and estimated the prevalence to be 0.44%.[12] However, this could be an

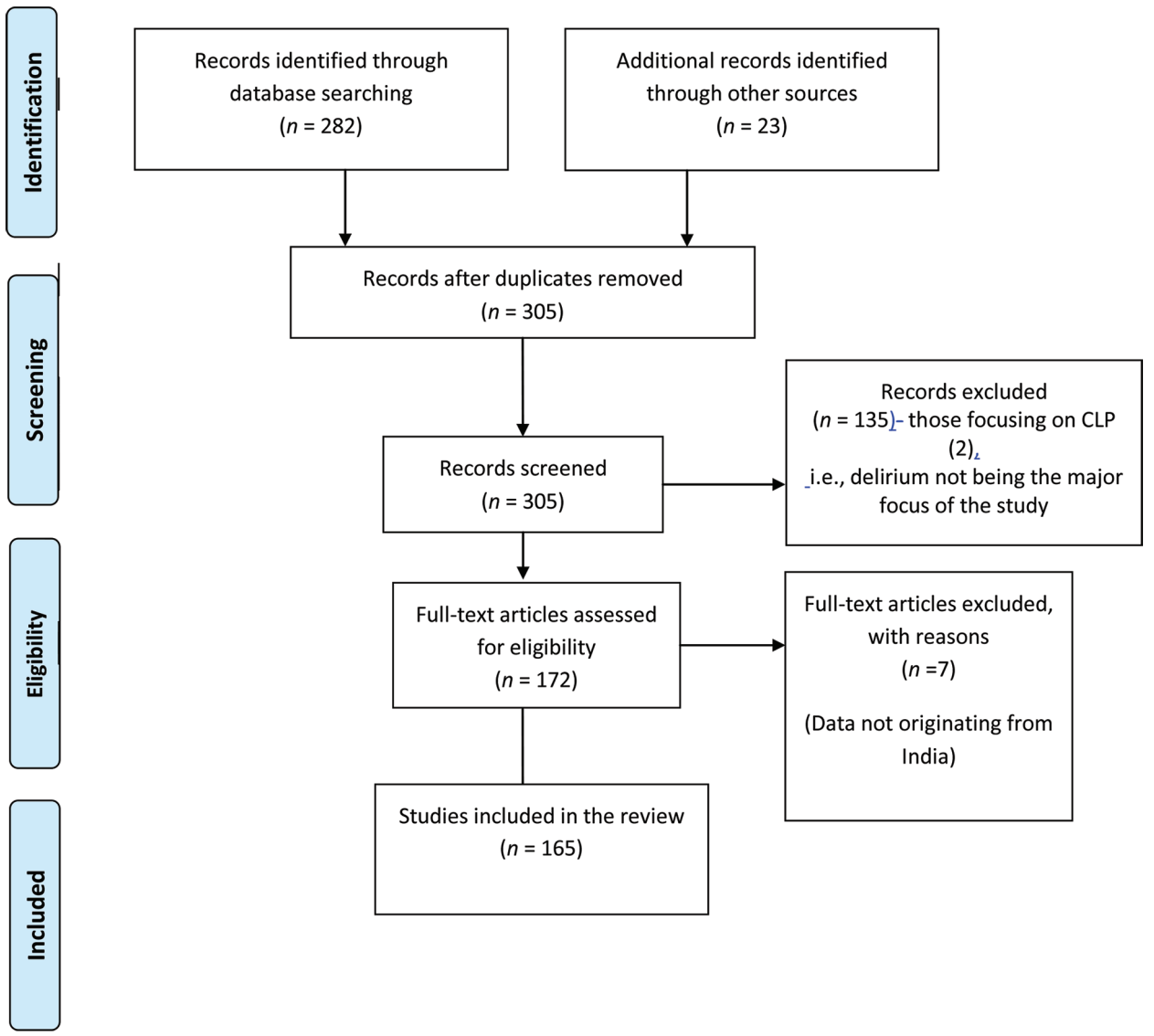

Fig. 1 PRISMA diagram showing selection of studies. PRISMA, preferred reporting items for systematic reviews and meta-analyses.

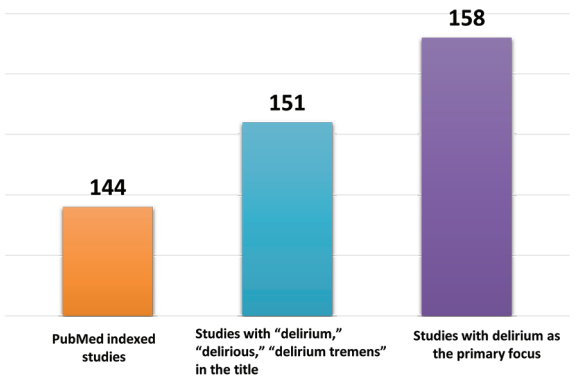

Fig. 2 Number of articles in PubMed search, having the word delirium and related terms in the title, and studies with delirium being the primary focus of the study.

underestimation, as many patients who develop delirium are not referred to the CLP services.

Studies have also reported the inpatient mortality rates for patients with delirium and the same has varied from 6.6 to 30.7%.[12,14,17-20,24-31] However, only occasional studies have compared the mortality data with all the inpatients, who did not develop delirium. One of the studies reported that the inpatient mortality rate for patients with delirium was 12.1% and was higher compared with those patients who were not referred to the CLP services for delirium.[27] Occasional studies have reported long-term mortality in patients of delirium, after 1 to 6 months of inpatient care and the rates have varied from 15.9 to 34.6%.[13,18,27]

A total of 23 studies (►**Table 2**)[15,24-29,31,37-51] have evaluated the symptom profile of delirium and most of these studies have relied on the Delirium Rating Scale Revised-1998 (DRS-R-98). The majority of these studies have focused on patients

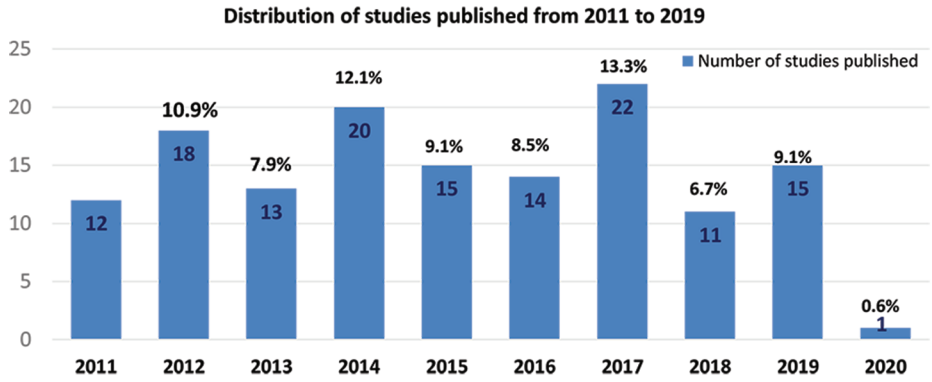

Fig. 3 Number of articles published in each year in last one decade.

seen by CLP services, with occasional studies focusing on ICU patients. Some of the studies have also specifically focused on children,[25,49] elderly,[37,41,44,46] and those with alcohol-withdrawal delirium (AWD).[31] In general, these studies suggest that disturbance in attention, disorientation, and other cognitive functions are present in a majority of the patients. In terms of specific items of DRS-R-98, studies that have been done in CLP setting, in general, report higher frequency of motor agitation, whereas studies in ICUs suggest a higher frequency of motor retardation. The studies which have compared people of different age groups suggest that there are minor variation in the symptom profile of delirium in children, adult, and elderly.[25,37,41,44,46,49]

Many studies have evaluated the factor structure of the symptom profile of delirium (►**Table 3**).[15,22,28,31,37-39,41,42,52] As with the symptom profile, most of these studies have again relied on DRS-R-98,[15,28,31,37,39,41,52] with some of the studies using the Memorial Delirium Assessment Scale (MDAS)[22,52] and Intensive Care Delirium Screening Checklist ICDSC scales.[38] One study combined items of DRS-R98, CSE, and MDAS.[52] Most of these studies have consistently recognized a three-factor solution,[15,28,31,37,39,41,42] with some differences in the distribution of symptoms across different factors. In the majority of these studies, the cognitive symptoms load on one factor, the motoric and psychotic symptoms load on to the same factor, and the third factor consists of language and thought process abnormalities. The motoric- and psychotic-symptom factors more consistently load on to the same factor across different studies. One study which compared the patients of pure alcohol withdrawal and those with alcohol withdrawal along with some other etiologies contributing to delirium reported subtle differences in the factor structure between the two groups.[31]

Studies have also evaluated motoric subtypes of delirium and have come up with different prevalence rates, which are mostly influenced by the study setting and the assessment scales (►**Table 4**).[14,15,18,23,25,29,38,44,47,51,53-55] Most of the studies have relied upon the Delirium Motor Symptom Scale (DMSS)/amended DMSS.[15,25,29,44,47,51,53] The prevalence rate of hypoactive delirium in ICUs[15,18,23,51] has varied from 26 to 65%, for mixed subtype, ranges from 10.2 to 29%, and for hyperactive subtype, ranges from 15.7 to 56.8%. The prevalence rate of hyperactive delirium is significantly more in studies evaluating the patients in CLP services setting and medical-surgical wards with prevalence varying from 25 to 70% and the prevalence of hypoactive delirium range from 7.3 to 65%.[14,25,29,38,44,47,53-55] Occasional studies have reported no subtype for approximately 5% of cases.[29,51]

Studies Evaluating other Aspects of Delirium in ICU Patients

Besides focusing on the incidence, prevalence, symptom profile, factor structure, and mortality in patients with delirium, studies involving ICU patients have also evaluated the risk factors and have validated scales such as ICDSC, MDAS, and CAM-ICU (►**Table 5**).[18-20,22,23,52,56,57] These studies suggest that these scales have good psychometric properties in ICU patients for detecting delirium.[22,23,52] The cut-off score of 3 or more for ICDSC and a cut-off score of 10 or more for MDAS have been found to have good psychometric properties for delirium.[22,52] One study which compared CAM-ICU and ICSDC suggests that compared with ICDSC, CAM-ICU has higher sensitivity and diagnostic odds ratio (84%, 86.1).[23] One of the studies evaluated the incidence and prevalence of delirium in patients admitted to ICU and compared these figures with the psychiatric referral rates and reported a wide gap in the actual incidence and prevalence of delirium in ICU patients and those referred to psychiatry CLP services.[56] Studies that have evaluated the risk factors, have, in general, reported mechanical ventilation to be an important risk factor for delirium.[18,19] Some of these studies also suggest that compared with those who do not develop delirium, those with delirium have higher mortality rate and significantly longer duration of ICU stay.[18-20]

Studies Focusing on Patients with Alcohol-Withdrawal Delirium

Five studies have primarily focused on patients with AWD (►**Table 5**).[30,31,58-60] One study evaluated the service model for patients with AWD and reported that compared with

Table 1 Prevalence and incidence of delirium

Study (year)	Treatment setting	Diagnostic system used	Sample size	Prevalence	Incidence	Inpatient mortality	Mortality at follow-up
Inpatient setting							
Khurana et al (2002)[11]	General medical inpatients	ICD-10	100, elderly	19%	8%		
Grover et al (2009)[12]	Inpatient	ICD-10	238,777 3,092[a]	0.44% 33.96%[a]		6.6%[a]	
Rai et al (2014)[13]	Neurology inpatient	CAM	52				34.6% (1–3 months of F/U)
Khurana et al (2011)[14]	Inpatient, elderly	CAM	400	27.47%		14.75%	
ICU setting							
Grover et al (2018)[15]	ICU	DSM-IVTR	66	68.2%	59.6%		
Kumar et al (2016)[16]	ICU	CAM-ICU	31	16.1%	–	–	
Grover et al (2014)[17]	CCU	DSM-IVTR	152 elderly	24.34%	13.4%	19.2%	
Jayaswal et al (2019)[18]	Medical ICU	CAM-ICU RASS	280		31.4%	9.9%	15.9 (1-month F/U)
Sharma et al (2012)[19]	RICU	DSM-IV	140	53.6%	24.4%	30.7%	
Lahariya et al (2014)[20]	CCU	DSM-IV	309	18.7%	9.3%	27%	
Bamalwa et al (2016)[21]	Cardiac ICU		50		16%		
Shyamsundar et al (2009)[22]	Medical/cardiac ICU		120		10.3%		
Barman et al (2018)[23]	Multidisciplinary ICU	DSM-IVTR	310	45%			
Consultation liaison setting							
Grover et al (2013)[24]	CLP	DSM-IV TR	331	–	–	12.4%	
Grover et al (2014)[25]	CLP	DSM-IVTR	49, CAP			10%	
Grover et al (2019)[26]	CLP	DSM-IVTR	103			10.7%	
Grover et al (2012)[27]	CLP	DSM-IVTR	97			12.1% 6.79%[b]	27.83% (6 months of F/U)
Grover et al (2012)[28]	CLP	ICD-10	109, elderly			16.5%	
Grover et al (2014)[29]	CLP	DSM-IV TR	321			10.3%	
Grover et al (2013)[30]	CLP, AWD	DSM-IVTR	112			13.4%	
Grover et al (2016)[31]	CLP, AWD	DSM-IVTR	112			13.4%	
Surgery and postoperative setting							
Dhakharia et al (2017)[32]	Postoperative setting		824	4%			
Kumar et al (2017)[33]	Postoperative (cardiac surgery)	CAM-ICU			17.5%		
Chrispal et al (2010)[34]	Delirium in patient undergoing hip fractures surgery	CAM	81		21%		

(*continued*)

Table 1 (*continued*)

Study (year)	Treatment setting	Diagnostic system used	Sample size	Prevalence	Incidence	Inpatient mortality	Mortality at follow-up
Miscellaneous							
Khanna et al (2018)[35]	Pediatric patients undergoing ophthalmic examination under sevoflurane	PAED scale	100	24%			
Sethi et al (2013)[36]	Pediatric patients undergoing cataract surgery under sevoflurane and desflurane	PAED scale	88	18.18% in the sevoflurane group 20.45% in the desflurane group			

Abbreviations: AWD, alcohol withdrawal delirium; CAM, confusion assessment method; CAP, children and adolescents; CLP, consultation liaison psychiatry; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, fourth edition; DSM-IV TR, DSM-IV text revision; F/U, follow-up; ICD, International Classification of Disease; ICU, intensive care unit; PAED, pediatric anesthesia emergency department.
[a]Prevalence of delirium in psychiatric referrals.
[b]Inpatient mortality rate of patients not referred to CLP services for delirium.

the emergency services treatment group alone, emergency services plus comprehensive inpatient addiction treatment group had fewer relapses.[59] Other studies have focused on risk factors associated with AWD,[58] symptom profile of delirium,[30] and factor structure of symptom profile.[31] One study evaluated the genetic variations associated with the development of delirium tremens and reported that delirium tremens was significantly associated with presence of T allele (GT and TT; [rs1824024]) of muscarinic cholinergic receptor 2 (CHRM2).[60]

Studies Involving Patients Seen in Medical-Surgical Consultation Liaison Setting

Maximum numbers of studies done in the medical-surgical setting (►**Table 5**)[12,13,24,25,29,40,41,44-46,48-50,54,55,61-68] have not been limited to any one particular ward. Available data suggest that delirium is the most common diagnosis made by the CLP team,[12,62] diagnostic concordance of delirium between psychiatrists and physicians is low,[62] and mortality of patients with delirium is more than those without delirium. The most common reason for referral of patients with delirium to CLP teams is abnormal behavior or patient's noncooperation for treatment.[12]

Factors that predict a delay in referral of patients with delirium include prevalent delirium at admission, sleep–wake disturbance, the specialty of referral, presence motor retardation, being admitted to medical ward/medical ICUs, and absence of comorbid axis-1 psychiatry diagnoses. In terms of symptom/clinical profile, available data suggest that there are subtle differences between patients seen in medical-surgical wards and emergency setting.[61] Available data also suggest subtle differences in the symptom profile of patients with different subtypes of delirium,[25,44] patients of different age groups (children, adult, and elderly),[41,43,49,63] and those with and without premorbid cognitive deficits.[46] In terms of symptom profile, available data also suggest that attention deficit is the core symptom of delirium.[40] One study showed a prevalence of catatonic symptoms in about one-third of the patients with delirium. Inpatient mortality in patients with delirium is associated with lower age (<65 years) and more frequent use of restraining before the development of delirium.[24] Many studies have focused on the risk factors of delirium, and these studies have come up with some of the common risk and etiological factors,[13,54,63,68] and other factors specific to treatment setting.[24] One study validated the DMSS[64] and other amended the DMSS.[65] Another study evaluated the concordance between DSM-IV and DSM-5 criteria and reported considerable variability depending on how the criteria are interpreted, with very strict adherence to the text detailing DSM-5, leading to a reduction in the number of cases diagnosed with delirium; however, when a more "relaxed" approach is used, DSM-5 criteria is comparable to DSM-IV criteria.[66]

Studies Focusing on Postoperative Patients

Studies that have focused on postoperative patients (►**Table 5**)[32,34,35] have mainly attempted to identify the risk factors for delirium in patients of cancers undergoing surgery,[32] patients undergoing surgery for hip fracture,[34] and children undergoing ophthalmic examination under general anesthesia with sevoflurane.[35]

Studies Focusing on the Health Care Professionals

Studies evaluating the opinion of the health care professionals (►**Table 5**)[69-71]suggest that most of the ICU clinicians do not assess patients for delirium on regular basis, consider the prevalence rates of delirium, especially among those patients on mechanical ventilation to be lower than what is reported in the literature. In terms of assessment, those ICU clinicians, who assess patients for delirium, mostly rely on the CAM-ICU scale and use haloperidol for the management of delirium.[69] Data also suggest that most of the ICU clinicians are aware of the importance of early mobilization of ICU patients but are not able to practice the same due to lack of support staff and safety concerns. One study, which evaluated the practice of ABCDEF bundle across the globe and

Table 2 Frequency (%age) of DRS-R-98 items in various studies

Study (year)	Sample size and setting	Sleep–wake cycle disturbances	Perceptual disturbance	Delusions	Lability of affect	Language	Thought process abnormality	Motor agitation	Motor retardation	Disorientation	Attention deficits	Short-term memory	Long-term memory	Visuospatial ability
Grover et al (2012)[28]	151, CLP	100	76.2	27.8	77.5	76.8	69.5	94	39.1	100	100	97.4	93.4	96.7
Grover et al (2011)[37]	109, CLP, elderly	97.2	78.9	35.8	62.4	79.8	74.3	89.0	32.1	95.4	97.2	91.8	65.1	63.3
Jain et al (2011)[38]	86, CLP	100	76.7	37.2	59.3	73.3	89.5	89.5	31.4	100	97.7	97.7	40.7	98.8
Mattoo et al (2012)[39]	100, CLP	99	35	14	94	90	92	94	9	100	100	91	97	93
Arya et al (2013)[40]	84, CLP	100	80.9	60.7	94	92.8	76.2	86.9	53.6	98.8	98.8	97.6	48.8	76.2
Grover et al (2012)[27]	97, CLP	96.7	80	33.3	90	73.3	73.3	93.3	33.3	100	100	93.3	53.3	60
Grover et al (2014 and 2013)[29,41]	321 CLP, adult vs. elderly	98.1	79.4	45.2	85.7	87.5	84.7	90.3	50.8	98.8	99.7	95.6	52.6	63.2
Grover et al (2016)[31]	112, CLP, AWD	100	75	48.2	87	85.7	87	94.6	25	99.1	100	92.9	65.2	68.8
Sharma et al (2017)[42]	75, RICU	94.7	5.3	0	73.3	90.6	100	46.6	53.3	81.3	100	73.3	57.3	58.6
Grover et al (2018)[15]	66, ICU	100	48.9	37.8	64.4	42.2	53.3	73.3	80	84	97.8	64.4	40	33.3
Dhoble and Vankar (2009)[43]	100, CLP	92	74	67	62	46	62	72	58	84	95	90	94	90

(*continued*)

Table 2 (*continued*)

Study (year)	Sample size and setting	Sleep–wake cycle disturbances	Perceptual disturbance	Delusions	Lability of affect	Language	Thought process abnormality	Motor agitation	Motor retardation	Disorientation	Attention deficits	Short-term memory	Long-term memory	Visuospatial ability
Grover et al (2014)[44]	98 CLP, elderly	96.8	66.3	32.7	81.6	82.7	76.5	83.7	52	98	100	86.7	55.1	51
Grover et al (2014)[25]	49, CAP	91.8	71.4	28.5	73.4	5	69.3	83.6	34.6	91.8	93.8	87.7	59.2	65.3
Grover et al (2013)[24]	331, CLP	97.8	57.7	31.7	59.2	52.6	65.3	88.8	36.2	93.6	96.4	91.8	69.1	81.2
Grover et al (2014)[45]	255, CLP	98	65.9	37.6	53.7	68.3	82.9	93.2	40	98.5	99.5	99.5	83.4	92.2
Grover et al (2015)[46]	107, CLP, elderly	75.7	55.1	49.1	71	88.8	95.3	68.2	54.2	98.1	98.1	89.7	92.5	96.3
Grover et al (2012)[47]	53, CLP	100	81.2	20.7	83	81.1	79.2	94.3	34	100	100	98.6	94.6	93.1
Grover et al (2014)[48]	461, CLP	95.4	71.6	33	61.6	74.8	74	90.9	29.7	96.1	94.8	83.1	52.5	56.6
Grover et al (2012)[49]	30, CAP	96.1	80.3	40.8	78.9	85.8	76.3	90.8	50.0	97.4	100	98.7	51.3	57.9
Grover et al (2016)[50]	76, CLP	100	73.7	34.2	82.9	96.1	96.1	98.7	1.3	96.1	97.4	97.4	93.4	94.7
Grover et al (2019)[26]	59, CLP	100	50.5	62.1	98.1	98.1	100	97.1	73.8	100	99	98.1	88.3	85.4
Lahariya et al (2016)[51]	309, CCU	100	70	22	100	59	90	73	40	94	100	100	86	66
Range		75.7–100	5.3–81.2	0–67%	59.2–100	5–98.1	53.3–100	46.6–98.7	1.3–80%	81.3–100	93.8–100	64.4–100	40–97%	40–97%

Abbreviations: AWD, alcohol withdrawal delirium; CAP, children and adolescents; CCU, coronary care unit; CLP, consultation liaison psychiatry services; ICU, multispecialty intensive care unit; RICU, respiratory ICU.

Table 3 Factor analytic studies of delirium from India

Study (year)	Sample size	Treatment setting	Scales used	Percentage of variance explained (%)	Factor structure
Shyamsundar et al (2009)[22]	120	ICU	MDAS	62.7	Factor I ("cognitive disturbance"): impaired digit span, short-term memory impairment, disorientation, and inattention Factor II ("behavioral abnormality"): altered psychomotor activity, perceptual disturbances, delusions, disorganized thinking, sleep–wake cycle disturbances, and reduced awareness
George et al (2011)[52]	53	ICU	ICDSC	56.2	Factor-I (altered sensorium/psychopathology): altered level of consciousness, inattention, disorientation, hallucination/delusion/psychosis, psychomotor agitation, and inappropriate speech or mood Factor-II (sleep–wake cycle problems): sleep–wake cycle disturbances and fluctuation of symptoms
Jain et al (2011)[38]	86	CLP	DRS-R-98 separately and DRS-R-98, MDAS, and CSE combined	47.8	Factor I ("cognitive"): abnormalities of language, thought process, orientation, attention, short-term memory, long-term memory, visuospatial ability, reduced level of consciousness (awareness), and perseveration or prolonged latency Factor II ("behavioral"): sleep–wake cycle disturbances, delusions, perceptual disturbances including hallucinations, motor agitation, inverse of motor retardation, lability of affect, distractibility, irritability, and temporal onset of symptoms
Grover et al (2011)[37]	151	CLP, drug naive	DRS-R-98	47.32	Factor I (cognitive): attention, orientation, short-term memory, long-term memory, and visuospatial ability Factor II (sleep and motoric disturbances): sleep–wake cycle disturbances, delusions, perceptual disturbances, lability of affect, motor agitation, and inverse of motor retardation Factor III (thought, language, and fluctuations): language, thought process abnormality, temporal onset of symptoms, and fluctuations
Grover et al (2012)[28]	109	CLP, elderly	DRS-R-98	43.5	Factor I (cognitive): thought disturbance, short-term memory, long-term memory, and visuospatial disturbance Factor II (cognitive and diagnostic factor): disturbance of attention and concentration and the three items of diagnostic significance (temporal onset, fluctuation, and presence of physical disorder) Factor III (psychotic and motoric symptoms): perceptual disturbances, delusions, and the motoric disturbances
Mattoo et al (2012)[39]	100	CLP, mixed adult and elderly	DRS-R-98	48.5 59	2-factor model Factor I (cognition and thinking): delusions, language disturbances, thought process abnormality, attention, orientation, short-term memory, long-term memory, visuospatial ability, and temporal onset of symptoms Factor I (circadian): motoric disturbances and fluctuations 3-factor model Factor I (cognition): attention, orientation, short-term memory, long-term memory, visuospatial ability, and fluctuation Factor II (circadian and psychosis): sleep disturbances, delusions, hallucinations, and motoric disturbances Factor III (higher order thinking): language disturbances, thought process abnormality, and temporal onset of symptoms
Grover et al (2013)[41]	321	CLP, mixed adult and elderly	DRS-R-98	45.8	Factor I (psychotic and motoric disturbances): sleep–wake cycle disturbances, delusions, perceptual disturbances, lability of affect, motor agitation, inverse of motor retardation, and fluctuation Factor II (cognitive): language, thought process abnormality, short-term memory, long-term memory, and visuospatial ability Factor III (diagnostic factor): attention, orientation, temporal onset of symptoms, and physical disorder
Grover et al (2013)[41]	245	CLP, adult	DRS-R-98	46.75	Factor I (psychotic and motoric disturbances): sleep–wake cycle disturbances, delusions, perceptual disturbances, lability of affect, motor agitation, inverse of motor retardation, and fluctuation Factor II (cognitive): language, thought process abnormality, short-term memory, long-term memory, and visuospatial ability Factor III (diagnostic factor): attention, orientation, temporal onset of symptoms, and physical disorder

(*continued*)

Table 3 (*continued*)

Study (year)	Sample size	Treatment setting	Scales used	Percentage of variance explained (%)	Factor structure
Grover et al (2013)[41]	76	CLP, elderly	DRS-R-98	48.53	Factor I (cognitive-1): delusions, language disturbance, thought process abnormality, long-term memory, and visuospatial ability Factor II (psychotic and motoric disturbances): sleep–wake cycle disturbances, perceptual disturbances, motor agitation, inverse of motor retardation, fluctuation, and physical disorder Factor III (cognitive-2): inverse of lability of affect, attention, orientation, short term memory, and temporal onset of symptoms
Sharma et al (2017)[42]	75	RICU	DRS-R-98	54.6–63.4	Factor I (cognitive factor): attention, orientation, short term memory, long-term memory, and visuospatial ability Factor II (motoric disturbances): motor agitation, inverse of motor retardation, and lability of affect Factor III (behavioral disturbances): language disturbance, thought process abnormality, temporal onset of symptoms, fluctuation
Grover et al (2018)[15]	66	ICU	DRS-R-98 and MDAS	56.3	Factor I: perceptual disturbance, delusion, lability of affect, language, thought process abnormality, orientation, short-term memory, long-term memory, visuospatial ability, and impaired digit span Factor II: motor agitation and inverse of motor retardation Factor III: sleep wake cycle disturbances, reduced level of consciousness, and reduced ability to maintain and shift attention
Grover et al (2016)[31]	112	CLP, AWD	DRS-R98	50.09–56.59	Whole sample Factor I (cognitive factor): attention, orientation, short-term memory, long-term memory, visuospatial ability, language, and thought process abnormality Factor II (psychotic): perceptual disturbance, delusion, fluctuation of symptoms, and presence of physical disorder Factor III (motoric–circadian disturbance): sleep–wake cycle disturbance, lability of affect, motor agitation, and inverse of motor retardation Pure AWD Factor I (psychotic): perceptual disturbance, delusion, language, thought process abnormality, lability of affect, long-term memory, and visuospatial ability Factor II (cognitive factor): attention, orientation, short-term memory, and physical disorder Factor III (motoric–circadian disturbance): sleep–wake cycle disturbance, motor agitation, inverse of motor retardation, and fluctuation of symptoms AWD with associated etiologies Factor I (psychotic): perceptual disturbance, delusion, fluctuation of symptoms, and presence of physical disorder Factor II (cognitive factor): attention, orientation, short term memory, physical disorder, language, thought process abnormality, long-term memory, visuospatial ability, and acute onset of symptoms Factor III (motoric–circadian disturbance): sleep–wake cycle disturbance, lability of affect, motor agitation, and inverse of motor retardation

Abbreviations: AWD, alcohol withdrawal delirium; CLP, consultation liaison psychiatry services; CSE, confusional state evaluation; DRS, delirium rating scale; DRS-R-98, DSR revised-1998; ICDSC, intensive care delirium screening checklist; ICU, intensive care unit; MDAS, memorial delirium assessment scale; RICU, RICU, respiratory ICU.

included the opinion of clinicians from India too, although did not provide India specific data, suggests that in Asia, 80% of the clinicians implement delirium monitoring, with CAM-ICU being the most common scale for assessment.[70] However, in terms of the prevalence of delirium, again the awareness was low, with only 2% of the clinicians from Asia believed that >60% of the patients in the ICU have delirium. One of the studies specifically focused on nurses.[71] In this study, the authors assessed the knowledge of the nurses before an education program for delirium and showed that providing knowledge about delirium to the nurses was associated with significant improvement in the knowledge and practice of nurses toward delirium.

Studies Focusing on the Experience of Patients with Delirium

Three studies (►**Table 5**)[26,53,72] have evaluated the patients' experience and distress after the resolution of symptoms of delirium. These studies suggest that about one-fourth (28.3%)[72] to one-third (35%)[53] of patients remember their experience of delirium. Those who could remember their experience reported moderate-to-severe levels of distress. Those who remembered their experience, in general,

Table 4 Prevalence of motoric subtypes in different studies

Study (year)	Treatment setting	Diagnostic system used	Sample size	Assessment of motoric subtype	Hypoactive (%)	Mixed (%)	Hyperactive (%)	No subtype (%)
Grover et al (2014)[25]	CLP	DSM-IV TR	98	DMSS	23.5	21.4	45.9	8.2
Grover and Shah (2012)[47]	CLP	DSM-IV	53	DMSS	17	18.9	58.5	5.6
Grover et al (2014)[44]	CLP, CAP	DSM-IV TR	49	DMSS	16.3	26.5	53	4
Grover et al (2018)[15]	ICU	DSM-IV TR	66	DMSS	47	29	24.5	–
Jayaswal et al (2019)[18]	Medical ICU	CAM-ICU	280	RASS	55.7	10.2	34.1	–
Barman et al (2018)[23]	Multidisciplinary ICU	DSM-IV	310	RASS	65	19.3	15.7%	–
Lahariya et al (2016)[51]	CCU	DSM-IV TR	309	Amended DMSS	26	11.1	56.8	5
Grover et al (2015)[53]	CLP	DSM-IV TR	203	Amended DMSS	7.3	36.1	56.6	–
Grover et al (2014)[29]	CLP	DSM-IV TR	321	Amended DMSS	19.93	24.61	50.15	5.29
Jain et al (2011)[38]	CLP	DSM-IV TR	86	DRS-R-98	10	21	69	–
Kumar et al (2015)[54]	General hospital	DSM-IV TR	80	MDAS	30	0	70	–
Khurana et al (2011)[14]	Inpatient elderly	CAM	400	Self-designed criteria	65	10	25	–
Mushtaq et al (2014)[55]	Medical-surgical wards	DSM-IV TR	80	Self-designed criteria	30	0	70	–

Abbreviations: CAM-ICU, confusion assessment method for the intensive care unit; CAP, children and adolescents; CCU, coronary care unit; CLP, consultation liaison psychiatry; DMSS, delirium motor subtyping scale; DRS-R-98, delirium rating scale revised-1998; DSM IV TR, diagnostic and statistical manual of mental disorders, fourth edition, text revision; ICU, intensive care unit; MDAS, memorial delirium assessment scale; RASS, Richmond agitation-sedation scale.

described it as a state of fearfulness, anxiety, confusion, and feeling strange.[72] One of the studies reported that the most common distressing themes which were recollected were fear and visual hallucination.[53] In terms of symptom profile, recall of delirium experience was associated with a higher prevalence of perceptual and language disturbances, and a higher severity of delirium. Those who could not remember their delirium experience also were distressed and more often reported moderate-to-severe distress. One of the studies evaluated the patient experience in terms of posttraumatic stress disorder (PTSD) and reported that 30.5% of the patients had substantial symptoms of PTSD, 22% (n = 13) had probable symptoms of PTSD, and 15.3% were considered to have partial symptoms of PTSD after the resolution of delirium. Again, the experience of PTSD was associated with higher severity of delirium and in terms of specific symptoms, it was associated with higher mean scores for the items of motor agitation and attentional deficits.[26]

Studies Focusing on Caregivers of Patients with Delirium

Two studies have focused on family caregivers.[47,73] According to one of the studies, symptoms of delirium are attributed to the nonorganic causes by about one-third of the caregivers.[47] Other paper based on the same cohort reported severe or very severe distress in about two-thirds of the caregivers.[73]

Effectiveness of Medications in the Treatment of Delirium

Few studies (►**Table 6**)[74-78] have evaluated the effectiveness of various antipsychotic medications in the management of delirium in CLP setting.[74-77] Three of these studies[74-76] suggest that the atypical antipsychotics like olanzapine, risperidone, and quetiapine are equally effective as haloperidol. One retrospective study also showed the effectiveness of risperidone.[77] One double-blind randomized controlled trial (DBRCT) compared the beneficial effect of melatonin with placebo in patients admitted to ICU with organophosphorus poisoning.[78] This study showed that the use of melatonin is associated with a lower prevalence of delirium after 3 days and patients receiving melatonin spend lower time in delirium when compared with a placebo group.

Prevention of Postoperative Emergence Delirium

It is well known that the use of flurane in anesthesia among children and adolescents is associated with a

Table 5 Findings reported in different studies done in different treatment settings

Study (year)	Setting	Findings
Studies focusing on ICU patients		
Grover et al (2017)[56]	ICU *n* = 66 (prospective arm)	• Wide gap in the actual incidence and prevalence of delirium in ICU patients and those referred to psychiatry consultation liaison services
Mohan et al (2015)[57]	Neuro ICU 30 patients divided into two groups	• Compared the severity of symptoms of delirium, as assessed by DRS-R-98, between patients with and without MRI changes • Those with neuroimaging changes had lower severity of delirium, compared with those without neuroimaging changes
Jayaswal et al (2019)[18]	Medical ICU *n* = 280	• Factors, which significantly predispose the persons to develop delirium include tobacco use, chronic liver disease, and past episodes of delirium • Factors which significantly precipitate delirium include mechanical ventilation, hypoxia, fever, raised levels of bilirubin and creatinine, and use of benzodiazepines • Delirium was significantly associated with longer ICU stay and 1-month postdischarge mortality
George et al (2011)[52]	Medical ICU *n* = 59	• A score of 3 or more on ICDSC, is an indicator of delirium • When the original cut-off of 4 was used, sensitivity and specificity were 75% and 74%, respectively; but a cut-off of 3 led to increase in sensitivity to 90%, but the specificity of 61.54% • The ICDSC had good internal consistency, with Cronbachα of 0.754 • The ICDSC had good internal consistency, with Cronbachα • The ICDSC had good internal consistency, with Cronbachα of 0.754
Sharma et al (2012)[19]	RICU *n* = 140	• Predisposing factors identified in univariate analysis: higher age, higher Glasgow coma scale score, increased APACHE II score, hyperuricemia, hypoalbuminemia, presence of acidosis, abnormal alkaline transferase levels, use of mechanical ventilation, higher number of total medication received and use of sedative, steroids and insulin • Compared with those without delirium, patients with delirium had significantly longer duration of ICU stay and higher mortality rates • Risk factors associated with mortality in patients with delirium: Age, multiple organ failure, hypoactive delirium and higher DRS-R-98 scores
Barman et al (2018)[23]	ICU *n* = 310	• Evaluated the diagnostic accuracy of CAM-ICU and ICDSC • The inter rater agreement (kappa coefficient) between nurse and intensivist was 0.86 (95% CI: 0.8–0.9) and 0.89 (95% CI: 0.83–0.96) for CAM-ICU and ICDSC respectively • Overall sensitivity and specificity were 84.4% (95% CI: 70.5–93.5%) and 94.6% (95% CI: 84.9–98.9%) for CAM-ICU, 77.8% (95% CI: 62.9–88.8%) and 94.6% (95% CI: 84.9–98.9%) for ICDSC. • CAM-ICU has higher sensitivity and diagnostic odds ratio (84%, 86.1) compared with ICDSC

higher rate of emergent delirium and agitation. Given the same, many studies (►**Table 7**)[79-91] have evaluated the beneficial effects of additional use of agents, like ketamine (low and high doses),[79] midazolam,[80,82,83,85] dexmedetomidine,[81-83,86,87,89,90] propofol,[81] glycopyrrolate,[82] and bupivacaine[84] in reducing the incidence of delirium. Some of the studies have also evaluated different doses of the same medications,[79,87] whereas others have evaluated the different techniques of administration of these drugs[86] and some of the studies have evaluated the different timing of giving these medications.[80] In general, available data suggest that the incidence of emergent delirium is lower with dexmedetomidine when compared with other agents (ketamine, midazolam, and clonidine) and placebo.[81-83,86,87,89,90] Compared with the use of bupivacaine only, the use of adjuvant ketamine along with bupivacaine is protective against emergence delirium in children.[84] It has

Table 5 (*continued*)

Study (year)	Setting	Findings
Lahariya et al (2014)[20]	CCU *n* = 309	• Risk factors for delirium, identified in binary logistic regression analysis: hypokalemia, Sequential organ failure assessment score, presence of cognitive deficits, receiving more than three medications, sepsis, hyponatremia, presence of cardiogenic shock, having undergone coronary artery bypass grafting, left ventricular ejection fraction <30, currently receiving opioids, age more than 65 years, presence of diabetes mellitus, presence of uncontrolled diabetes mellitus, history of seizures, presence of congestive cardiac failure, having undergone angioplasty, presence of atrial fibrillation, ongoing depression, currently receiving/taking benzodiazepines, warfarin, ranitidine, steroids, nonsteroidal anti-inflammatory drugs, higher total number of medications, presence of raised creatinine, anemia, hypoglycemia, acute physiology, and chronic health evaluation II score and Charlson's comorbidity index score • Mortality rate (27%) was significantly higher among those with delirium, compared with those without delirium (1%) • The duration of ICU stay was significantly longer for those with delirium, compared with those who did not develop delirium • Risk factors for mortality among patient with delirium: uncontrolled diabetes mellitus, cardiogenic shock, sepsis, presence of diabetes mellitus, higher APACHE-II score, higher SOFA score, and higher Charlson's score
Shyamsundar et al (2009)[22]	Medical and cardiac ICU *n* = 120	• Validation of memorial delirium rating scale (MDAS) • The scale has good interrater agreement (0.92; 95% confidence interval,0.81–0.96) and test–retest reliability (0.93; 95% CI: 0.83–0.97) • The MDAS had good internal consistency (Cronbachα: 0.89) • The MDAS had good internal consistency (Cronbachα • The MDAS had good internal consistency (Cronbachα: 0.89) • A ROC showed that the optimal threshold for screening as MDAS total score of at least 10 • This cut-off has high sensitivity (100%), specificity (95.45%), positive predictive value (75%), and negative predictive value (100%)
Alcohol withdrawal delirium		
Sarkar et al (2017)[58]	Psychiatry setting *n* = 80	• Factors associated with development of alcohol withdrawal delirium include: Heavy drinking, continuous pattern of drinking, past history of delirium, alcohol induced psychosis, and presence of cognitive deficits
Baby et al (2017)[59]	Emergency and inpatient services Emergency (*n* = 111) Comprehensive inpatient addiction treatment (CIAT) (*n* = 107)	• Patients who received both emergency and comprehensive inpatient addiction treatment had better regular follow-up compared with patients treated in the emergency services alone at 6 months • Comprehensive inpatient addiction treatment also resulted in better combined follow-up (regular follow-up and telephonic follow-up) • Compared with emergency services treatment group alone, emergency services plus comprehensive inpatient addiction treatment group had fewer relapses
Grover et al (2016)[31]	*n*= 112, AWD	• Factor structure of pure AWD is different from AWD with associated etiologies
Grover et al (2013)[30]	CLP *n*= 112, AWD	• Compared with those with delirium due to medical-surgical causes, patients with delirium associated with alcohol withdrawal more often have delusions and thought process abnormality; and less often have motor retardation, long term memory deficits, and visuospatial ability
Malhotra et al (2018)[60]	*n*= 210 patients with alcohol dependence and 200 controls	• Delirium tremens was significantly associated with T allele carrying status (GT and TT [rs1824024]) of muscarinic cholinergic receptor 2 (CHRM2)

Table 5 (*continued*)

Study (year)	Setting	Findings
CLP setting		
Prinka and Sharma (2016)[61]	Emergency and CLP *n* = 100	• Compared clinical profile of patients of delirium seen in emergency and CLP set-up-Subtle differences noted between the two groups
Grover et al (2017)[62]	CLP *n* = 219	• Delirium is the most common diagnosis made by the CLP team • Diagnostic concordance between the diagnosis of delirium made by the psychiatrist and that made by the physicians/surgeons is low
Grover et al (2013)[24]	CLP *n* = 331	• Inpatient mortality rate 12.4% • In comparative analysis, inpatient mortality was associated with lower age(<65 years), high rate of alcohol dependence, more frequent use of restrain prior to development of delirium • In regression analysis lower age (<65 years) and more frequent use of restrain prior to development of delirium
Grover et al (2015)[46]	CLP *n* = 107 Elderly (≥60 years)	• Presence of premorbid cognitive deficits is more often associated with development of delirium prior to getting admitted to the hospital, compared with those without premorbid cognitive deficits • Those with and without cognitive deficits prior to onset of delirium do not differ in terms of frequency and severity of various symptoms of delirium, severity of delirium as assessed by using DRS-R98, DRS-R98 cognitive domain score, DRS-R98 noncognitive domain score, motoric subtypes, risk factors for development of delirium, various associated etiologies, mean number of risk factors for delirium, and mean number of associated etiologies
Grover et al (2014)[44]	CLP *n* = 98 Elderly ≥60 years	• Compared with hyperactive subtype, significantly higher proportion of patients with hypoactive subtype had thought process abnormality and motor retardation • When the hyperactive and mixed motoric subtype groups were compared, patients with mixed subtype group had significantly higher prevalence of thought process abnormality and motor retardation • When hypoactive and mixed subtype were compared, patients with mixed subtype had significant higher frequency of perceptual disturbances, delusions and motor agitation • The three motoric subtypes do not differ significantly, in terms of severity of cognitive symptoms, however, there was some difference in the severity of noncognitive symptoms across the various motoric subtypes
Grover et al (2016)[50]	CLP *n* = 76	• Attention deficits in patients with delirium influence the severity of cognitive and noncognitive symptoms of delirium • The mean HMSE score has significant correlation with DRS-R-98 severity score, DRS-R-98 cognitive subscale score, DRS-R-98 noncognitive domain subscale score, and DRS severity score without attention score.
Grover et al (2014)[48]	CLP *n* = 461 Retrospective	• Longer duration of psychiatric referral after the onset of delirium is associated with: older age, presence of and higher severity of sleep disturbance, presence of and higher severity of motor retardation, presence of visuospatial disturbances, presence of fluctuation of symptoms, being admitted to medical ward/medical intensive care units, and absence of comorbid axis-1 psychiatry diagnoses • In the regression analysis, longer duration of psychiatric referral after the onset of delirium is associated with presence of sleep disturbance, presence motor retardation, being admitted to medical ward/medical intensive care units, and absence of comorbid axis-1 psychiatry diagnoses

Table 5 (*continued*)

Study (year)	Setting	Findings
Grover et al (2013)[41]	CLP *n* = 321 (adult sample 245; geriatric 76)	• When the patients in the adult and geriatric group were compared, no significant difference was seen between the two groups, except for the adult group having statistically higher prevalence and severity scores for thought process abnormalities and lability of affect • The two groups were similar for the mean number of etiologies associated with delirium • When the two groups were compared for the etiological factors, patients in the adult group more often had hepatic derangement, substance intoxication, withdrawal, and postpartum causes; in contrast lung disease, and cardiac abnormalities were more common in the elderly group
Grover et al (2014)[25]	CLP *n* = 49, CAP	• Different subtypes of delirium do not differ from each other in terms of frequency and severity of various symptoms of delirium except for minor differences • Compared with those with hypoactive delirium, those with hyperactive and mixed subtype more often have hallucination
Rajlakshmi et al (2013)[40]	CLP *n* = 84	• Attention deficit is a core symptom of delirium • Cognitive deficits are quite prevalent in patients with delirium and correlate with overall severity of delirium
Grover et al (2014)[45]	CLP *n* = 205	• Two-fifths (*n* = 80; 39%) of patients with delirium have two or more catatonic symptoms • When the diagnosis of catatonic syndrome was considered, 32% and 12.7% were observed to have catatonia as per the Bush Francis Catatonia screening instrument and DSM-5 criteria, respectively • Catatonic syndrome was more common in women and in those who had onset of delirium prior to hospitalization • Among the delirium subtypes, hypoactive delirium was more commonly associated with catatonic syndrome
Grover et al (2012)[49]	CLP *n* = 30 CAP	• Compared with adults, children and adolescents had lower frequency of long-term memory and visuospatial disturbances • Compared with the elderly, children, and adolescents had higher frequency of lability of affect • In terms of severity of symptoms, compared with adults, the children and adolescents have lower severity of sleep–wake disturbances, abnormality of thought, motor agitation, orientation, attention, short-term memory, long-term memory, and visuospatial abilities • When compared with elderly, children and adolescents have higher severity of lability of affect and lower severity of language disturbances, short-term memory, and visuospatial abilities
Grover et al (2009)[63]	CLP *n* = 46 (retrospective) CAP	• The most common underlying pathology was various infections followed by neoplasms • Besides clouding of consciousness, all patients exhibited sleep–wake cycle disturbance and impaired orientation

Table 5 (*continued*)

Study (year)	Setting	Findings
Grover et al (2009)[12]	*n* = 3,092 Retrospective	• The prevalence of delirium in all inpatients ranged from 0.28 to 0.53% (mean = 0.44%), with higher prevalence among the elderly • Delirium forms the largest diagnostic category (30.77–38.95%) of all referred cases with a mean of 33.96% • In 80% of the cases, the referral for delirium was made for abnormal behavior or patient's noncooperation for treatment
Grover et al (2014)[29]	CLP *n* = 321	• When the hyperactive and hypoactive subtypes of delirium were compared, patients with hyperactive delirium had significantly higher prevalence of perceptual disturbances, delusions, lability of affect and motor agitation; however, patients with hypoactive delirium had higher prevalence of thought process abnormality and motor retardation • When hyperactive and the mixed subtype were compared, significantly higher prevalence of thought process abnormality and motor retardation were seen in the mixed subtype group • When the mixed and hypoactive subtype were compared, patients with mixed subtype had significantly higher prevalence of perceptual disturbances, delusions, lability of affect, and motor agitation • No significant differences emerged for the cognitive symptoms as assessed on DRS-R-98 across the different motoric subtypes
Grover et al (2013)[64]	CLP *n* = 100 (replication study)	• Validation of DMSS
Meagher et al (2014)[65]	CLP *n* = 487	• Development of abbreviated version of DMSS-4
Gupta et al (2010)[66]	CLP *n* = 80	• Factors which predict delayed diagnosis of delirium include prevalent delirium at admission, sleep–wake disturbance, and specialty of referral
Meagher et al (2014)[67]	CLP *n* = 768 Retrospective	• Evaluated the concordance between DSM-IV and DSM-5 criteria of delirium • The concordance between DSM-IV and DSM-5 criteria varies considerably depending on the interpretation of criteria • Overly strict adherence to the text detail, as described in DSM-5, can lead to reduction in the number of cases diagnosed with delirium; however, a more "relaxed" approach renders DSM-5 criteria comparable to DSM-IV criteria with minimal impact on their actual application and is thus recommended
Khurana et al (2002)[68]	Medical-surgical ward *n* = 100	• Risk factors for delirium: preexisting cognitive deficits, neurological illnesses, urinary tract infections, visual impairment, hearing impairment, current proteinuria, leucocytosis, raised blood ammonia, hyponatremia, and potassium level disturbances
Kumar et al (2015)[54]	*n* = 80	• Risk factors commonly associated with hyperactive subtype: alcohol and other substance use disorders • Risk factors commonly associated with hypoactive subtype: other psychiatric disorders such as schizophrenia and mood disorders, infection, and chronic medical conditions • Compared with hyperactive subtype, cognitive impairments were significantly higher among those with hypoactive subtype
Rai et al (2014)[13]	Neurology inpatient setting *n* = 52 Mean age = 65 years	• Factors frequently associated with delirium are leucocytosis and hyponatremia • Duration of hospital stay is longer and mortality rate is higher in patients of delirium in whom cause of delirium could not be ascertained

Table 5 (*continued*)

Study (year)	Setting	Findings
Mushtaq et al (2014)[55]	Medical-surgical inpatients *n* = 40 (in the delirium group)	• Hypoactive delirium had more cognitive impairment compared with hyperactive delirium ($p = 0.001$)
Postoperative		
Dhakharia et al (2017)[32]	Postoperative stage after cancer surgery *n* = 824	• Postoperative delirium is significantly associated with older age, history of addiction, presence of respiratory complications, sepsis, ICU stay >24 hours ($p < 0.05$), and electrolyte impairment ($p < 0.05$)
Chrispal et al (2010)[34]	Delirium in patient undergoing hip fractures surgery *n* = 81 Elderly (≥ 60 years)	• Risk factors for delirium: presence of dementia, duration of surgery >2.5 and preoperative packed cell volume <25 (OR = 8.07) • Precipitating factors: postoperative infections, metabolic abnormalities and vascular events • Patients with delirium had longer hospital stays and poor ambulation at discharge
Khanna et al, (2018)[35]	*n* = 100	• Longer duration of preoperative fasting duration is a risk factor for postoperative emergence delirium in children undergoing ophthalmic examination undergeneral anesthesia with sevoflurane
Studies focusing on health professionals		
Chawla et al (2014)[69]	Survey of ICU clinicians *n* = 659	• Majority (65.6%) of the responders reported that they were not assessing delirium in the ICU regularly • About two-thirds of the responders (65%) considered that the incidence of delirium in mechanically ventilated patients is less than 10%; 31% responders reported incidence of delirium in mechanically ventilated patients was in the range of 10–50 and only 2% of the responders reported that more than half of their mechanically ventilated patients experience delirium • 73% responders responded when asked about use of delirium scale • Confusion Assessment Method-ICU (CAM-ICU) was the most preferred method of delirium assessment • Haloperidol was the most commonly used agent for delirium • Majority of the respondents were aware of the benefit of early mobilization, but lack of support staff, and safety concerns were the main obstacles to its implementation
Morandi et al (2017)[70]	*n* = 1,521 clinicians	• Worldwide ABCDEF (Assessing Pain, Both Spontaneous Awakening and Breathing Trials, Choice of Drugs, Delirium monitoring/management, Early exercise/mobility, and Family Empowerment) survey • Delirium monitoring was implemented in 70% of ICUs, but only 42% used a validated delirium tool. • Although India specific data are not available, in Asia 80% of the clinicians implemented delirium monitoring, with CAM-ICU being the most common scale for assessment • From Asia, only 2% of the clinicians believed that >60% of the patients in the ICU have delirium
Varghese et al (2014)[71]	*n* = 32	• Educational program for nurses • Providing knowledge about delirium to the nurses was associated with significant improvement in the knowledge and practice of nurses toward delirium among the nurses in the educational group.

Table 5 (*continued*)

Study (year)	Setting	Findings
Patient's experience of delirium		
Grover et al, (2019)[26]	CLP *n* = 103	• 30.5% of the patients had substantial symptoms of PTSD, 22% (*n* = 13) had probable symptoms of PTSD and 15.3% were considered to have partial symptoms of PTSD after resolution of delirium • When those with and without PTSD were compared, those with PTSD symptoms had significantly higher prevalence of fluctuation of symptoms, while experiencing delirium and had significantly higher mean scores for the items of motor agitation, attentional deficits, higher total severity score on the DRS-R-98 and higher DRS-R-98 total score. Higher severity of delirium was associated with higher severity of PTSD symptoms
Grover and Shah (2011)[72]	CLP *n* = 53, patients with delirium	• 28.3% of patients remembered themselves to be confused and rest had no recollection of the same • Those who could remember their experience had moderate (26.7%), severe (40.0%) and very severe (33.3%) level of distress • Of those who could not remember their delirium experience, most of them had moderate (44.7%) to severe (26.3%) distress. Those who remembered their experience in general described it as a state of fearfulness, anxiety, confusion and feeling strange
Grover et al (2015)[53]	CLP *n* = 203	• One-third (35%) of the patients were able to recollect their experiences during the delirium, and the majority (86%) of them were distressed by these experiences • About half of the patients who reported the experience to be distressing reported it to be of moderate level of distress • The most common distressing themes which were recollected were fear and visual hallucination. When the patients who could recall and who could not recall their experience of delirium were compared, recall of delirium experience was associated with a higher prevalence of perceptual and language disturbances and a higher severity of delirium
Studies focusing on caregivers		
Grover and Shah (2013)[73]	*n* = 72 caregivers of 53 patients with delirium CLP	• Symptoms of delirium that led to severe or very severe distress in more than two thirds of the caregivers included decreased sleep, increased motor activity, attempts to remove intravenous lines, tubings, and attempts to get out of bed when they were actually required to lie down
Grover and Shah (2012)[47]	*n* = 72 caregivers CLP	• About one-third of the caregivers (36.11%) attributed the symptoms of delirium to nonorganic causes like supernatural beliefs, emotional stress resulting from physical illness or various social factors, attention seeking behavior, or a result of religious disobedience

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; AWD, alcohol withdrawal delirium; CAM-ICU, confusion assessment method for the intensive care unit; CAP, children and adolescents; CCU, coronary care unit; CI, confidence interval; CLP, consultation liaison psychiatry; DMSS, delirium motor symptom scale; DRS-R-98, delirium rating scale revised-1998; ICDSC, intensive care delirium screening checklist; ICU, intensive care unit; MMSE, Mini Mental State Examination; MRI, magnetic resonance imaging; OR, odds ratio; PTSD, posttraumatic stress order; RICU, respiratory intensive care unit; ROC, receiver operating curve; SOFA, Sequential Organ Failure Assessment.

Table 6 Efficacy of various medications in management of delirium

Study (year)	Medications compared	Sample size	Diagnostic measure	Trial design	Setting	Outcome measure	Outcome
Jain et al (2017)[74]	Haloperidol (1–4 mg/day) vs. olanzapine (2.5–10 mg/day)	Haloperidol (n = 53) Olanzapine (n = 47)	DSM-IV	Open-label RCT	CLP	MDAS	• Both medications effective in management of delirium • Haloperidol ≈ olanzapine
Grover et al (2016)[75]	Haloperidol (0.25–1.25 mg/day) vs. quetiapine (12.5–75 mg/day)	Haloperidol (*n* = 32) Quetiapine (*n* = 31)	DSM-IV	Single-blind RCT	CLP	DRS-R-98 MMSE	• Both medications effective in management of delirium • Haloperidol ≈ quetiapine
Grover et al (2011)[76]	Haloperidol (0.25–10 mg/day) vs. olanzapine (1.25–20 mg/day) vs. risperidone (0.25–4 mg/day)	Haloperidol (*n* = 21) Olanzapine (*n* = 23) Risperidone (*n* = 20)	DSM-IV	Single-blind RCT	CLP	DRS-R-98 MMSE	• All the medications effective in management of delirium • Haloperidol ≈ olanzapine ≈ risperidone
Gupta et al (2005)[77]	Risperidone (0.5–2 mg/day)	Risperidone (*n* = 7)	–	Retrospective study	CLP	–	• Six out of the seven patients were either significantly improved or recovered at the last follow-up
Vijaykumar et al (2016)[78]	Melatonin (3 mg/day) vs. placebo	Melatonin (*n* = 26) Placebo (*n* = 26)	–	DBRCT	ICU Delirium in patients with organophosphorus poisoning	CAM-ICU	• Patients receiving melatonin had significantly lower time to be delirium free compared with placebo group • Prevalence of delirium was significantly lower in the melatonin group, compared with the placebo group after day 3

Abbreviations: ≈ No statistically significant difference; CAM-ICU, confusion assessment method for the intensive care unit; CLP, consultation liaison psychiatry; DBRCT, double-blind randomized controlled trial; DRS-R-98, delirium rating scale revised-1998; DSM IV, diagnostic and statistical manual of mental disorders, fourth edition; MDAS, memorial delirium rating scale; MMSE, mini metal state examination;

Table 7 Studies evaluating the efficacy of various measures in prevention of emergence delirium

Study (year)	Medications compared	Sample size	Trial design	Setting	Outcome measure	Outcome
Avidan et al (2017)[79]	Placebo (normal saline) vs. low-dose ketamine (0·5 mg/kg) vs. high dose ketamine (1·0 mg/kg)	Placebo (*n* = 222) Low-dose ketamine (*n* = 227); High-dose ketamine (*n* = 223)	Multicentric DBRCT	Postsurgical	CAM, CAM-ICU	• No decrease delirium in older adults after major surgery • Might cause harm by inducing negative experiences
Gonsalvez et al (2018)[80]	Midazolam at the induction (0.03 mg/kg) vs. midazolam (0.03 mg/kg) administered 10 minutes before the end of surgery	At Induction (*n* = 40) and 10 minutes before the end of surgery (*n* = 40)	DBRCT	Pediatric surgery	PAED scale	• No difference between the two groups in the incidence of emergence delirium in children undergoing sevoflurane anesthesia

Table 7 (*Continued*)

Study (year)	Medications compared	Sample size	Trial design	Setting	Outcome measure	Outcome
Makkar et al (2015)[81]	Dexmedetomidine (0.3 µg/kg) vs. propofol (1 mg/kg) vs. saline 0.9%	Dexmedetomidine (*n* = 32) Propofol (*n* = 36) Saline (*n* = 32)	RCT	Pediatric surgery (infraumbilical surgery)	PAED scale	• Compared with normal saline, dexmedetomidine leads to significant reduction in the incidence of emergence delirium but this occurs at the cost of higher incidence of sedation in the recovery period
Trivedi et al (2016)[82]	Group K: premedication with inj. glycopyrrolate 0.01 mg/kg, inj. ketamine 2 mg/kg Group M: premedication with inj. glycopyrrolate 0.01 mg/kg and inj. midazolam 0.05 mg/kg, inj. ketamine 2 mg/kg, Group D: after premedication with inj. glycopyrrolate 0.01 mg/kg and inj. dexmedetomidine 0.5 µg/kg, ketamine 2 mg/kg	Group K (*n* = 30) Group M (*n* = 30) Group D (*n* = 30)	DBRCT	Surgical setting (patients undergoing laparoscopic ligation, skin grafting, dilatation and curettage, endoscopic procedures, and excision of small swelling)	MDAS	• Incidence of delirium was least with use of dexmedetomidine, and the difference was statistically significant compared with the ketamine only group • Incidence of delirium was also lower with use of midazolam compared with the ketamine only group
Prabhu and Mehandale (2017)[83]	Comparison of oral dexmedetomidine (4 µg/kg) vs. oral midazolam (0.5 mg/kg) as premedication to prevent emergence agitation after sevoflurane anesthesia in pediatric patients	Midazolam (*n* = 45) Dexmedetomidine (*n* = 45)	DBRCT	Postoperative	PAED scale	• Compared with midazolam, dexmedetomidine was associated with lower incidence of emergence agitation
Sinha and Sood (2012)[84]	Comparison of caudal block with bupivacaine (0.25% 0.5mL/kg)vs.bupivacaine (0.25% 0.5 mL/kg) and ketamine(0.5 mL/kg) and no caudal block in pediatric anesthesia with sevoflurane	*n* = 150 Children	DBRCT	Postoperative	PAED scale	• Compared with use of bupivacaine only, use of adjuvant Ketamine along with bupivacaine, is protective against emergence delirium children, following sevoflurane anesthesia

Table 7 (*Continued*)

Study (year)	Medications compared	Sample size	Trial design	Setting	Outcome measure	Outcome
Perumal et al (2015)[85]	Midazolam premedication (0.02 mg/kg iv) for ketamine-induced (1 mg/kg) emergence	*n* = 30 Adult	Observational study	Postoperative	Self-designed criteria (presence of purposeless and hallucinatory behavior)	• Mild emergence delirium was noted in 13.3% of patients at 30 minutes, incidence of which increased to 16.7% at 1 hour, which reduced to 13.3% at 2 hours
Mukherjee et al (2015)[86]	Intranasal dexmedetomidine (1 µg/kg) and clonidine (4 µg/kg) in patients receiving sevoflurane-based general anesthesia	*n* = 80	Double-blind parallel group study	Postoperative	PAED scale	• Incidences of emergence delirium were significantly lower in the dexmedetomidine group, when compared with clonidine up to the first 15 minutes; however, later the two groups were comparable • Overall compared with dexmedetomidine group, higher proportion of patients in the clonidine group had emergence delirium
Study (year)	**Medications compared**	**Sample size**	**Trial design**	**Setting**	**Outcome measure**	**Outcome**
Begum et al (2019)[87]	Bolus dexmedetomidine (0.4 µg/kg) vs. low-dose Infusion (0.4 µg/kg/h) in children undergoing sevoflurane anesthesia	*n* = 48	DBRCT	Postoperative	PAED scale	• Compared with children who received low dose infusion, those who received bolus dexmedetomidine had lower proportion of patients with PAED scale score of >10
Shenoy et al (2018)[88]	Transversus abdominis plane block supplementation during iliac crest bone graft harvesting Additional TAP block along with local infiltration Vs. wound infiltration only	*n* = 143	Simple random sampling	Postoperative	Watch a scale score of >2	• Compared with the control group, emergence delirium was lower among the patients who received TAP block (2.4 vs. 9.5%)

Table 7 (*Continued*)

Study (year)	Medications compared	Sample size	Trial design	Setting	Outcome measure	Outcome
Priye et al (2015)[89]	Dexmedetomidine as an adjunct in post-operative analgesia following cardiac surgery: 12-hour infusion of normal saline and group-B received a 12-hour infusion of dexmedetomidine 0.4 µg/kg/h	*n* = 64	Double-blind study	Postoperative	RASS	• Although the incidence of delirium with dexmedetomidine was less, both the groups did not differ statistically
Sharma et al (2019)[90]	Single dose of dexmedetomidine 1 µg/kg vs. volume matched saline for intraoperative hemodynamic and postoperative recovery profile in children undergoing adenotonsillectomy	*n* = 60 Children	Placebo-controlled study	Intra- and postoperative	PAED scale	• Compared with control group, decrease in postoperative EA without causing any excessive sedation, desaturation, or any other drug-related adverse events
Singh et al (2012)[91]	EA in pediatric patients under isoflurane, sevoflurane or desflurane anesthesia	*n* = 75 (3 groups of 25 each) Children	DBRCT	Postoperative	PAED scale	• Incidence and intensity of EA were comparable in all three groups

Abbreviations: CAM, confusion assessment method; CAM-ICU, confusion assessment method for the intensive care unit; DBRCT, double blind randomized controlled trial; EA, emergence agitation; Inj., injection; MDAS, memorial delirium assessment scale; PAED, pediatric anesthesia emergency department; RASS, Richmond agitation-sedation scale; TAP, transversus abdominis plane.

Table 8 Case reports focusing on delirium

	Study (year)	Findings
Medication associated delirium		
1	Kasim et al (2019)[92]	Levetiracetam associated delirium in an elderly
2	Ghoshal et al (2015)[93]	Levofloxacin induced anaphylaxis and acute delirium
3	Raj and Murthy (2013)[94]	Levofloxacin induced delirium
4	Chowdhry et al (2015)[95]	Fluoroquinolones: an underrecognized cause for delirium
5	Nasiruddin et al (2014)[96]	Acute delirium in an elderly woman following zoledronate administration
6	Kaur et al (2017)[97]	Delirium induced by albendazole–ivermectin combination
7	Mane and Angane (2019)[98]	Cyclopentolate 1% eye drops induced delirium in a Child
8	Sharma et al (2012)[99]	Bath salts-induced delirium
Delirium associated with psychotropics		
9	Das et al (2019)[100]	Delirium associated with discontinuation of sertraline in an elderly
10	Sharma and Aggarwal (2010)[101]	Delirium associated with olanzapine therapy in an elderly male with bipolar affective disorder
11	Dixit et al (2015)[102]	Valproate induced delirium due to hyperammonemia in a case of acute mania
12	Muraleedharan et al (2015)[103]	Valproate induced hyperammonemic delirium

Table 8 (*Continued*)

	Study (year)	Findings
Delirium associated with psychotropics		
13	Pradeep (2008)[104]	Valproate monotherapy induced-delirium due to hyperammonemia
14	Khanra et al (2016)[105]	Unusual case of delirium after restarting clozapine
15	Ghosh et al (2014)[106]	Mirtazapine-associated hyponatremia presenting as delirium
16	Manjunatha et al (2011)[107]	Delayed onset, protracted delirium and aspiration pneumonitis associated with use of a combination of clozapine and ECT
17	Kumar et al (2003)[108]	Delirium associated with combination of clozapine and ECT
18	Sadananda et al (2013)[109]	Delirium during the course of electroconvulsive therapy in a patient on lithium carbonate treatment
19	Selvaraj and Praharaj (2012)[110]	Delayed onset and prolonged interictal delirium following electro-convulsive therapy
20	Sarangula et al (2016)[111]	Post injection delirium/sedation syndrome associated with olanzap-ine depot injection
21	Garg et al (2019)[112]	Delayed onset post injection delirium/sedation syndrome associated with olanzapine pamoate a case report
22	Punnoose et al (2017)[113]	Low body mass index a risk factor for post-injection delirium/seda-tion syndrome with depot olanzapine
23	Upadhyay et al (2017)[114]	Post injection delirium/sedation syndrome with long-acting olan-zapine pamoate
24	Venkatesan et al (2019)[115]	Post-injection delirium/sedation syndrome after 31st long-acting olanzapine depot injection
Delirium associated with alcohol or opioid withdrawal		
25	Mattoo et al (2012)[116]	Refractory delirium tremens
26	Ram et al (2017)[117]	Lorazepam precipitated alcohol withdrawal delirium
27	Charan et al (2011)[118]	Genital self-mutilation in alcohol withdrawal state complicated with delirium
28	Saddichha et al (2008)[119]	Delayed-onset delirium tremens
29	Talikoti et al (2012)[120]	Delirium tremens with hollow viscus perforation
30	Das et al (2005)[121]	Naltrexone precipitating delirium in a patient with opioid dependence
31	Das et al (2017)[122]	Opioid withdrawal presenting as delirium
32	Sharma et al (2017)[123]	Opium withdrawal delirium
33	Raj et al (2017)[124]	Complicated opioid withdrawal in delirium without convulsions
34	Ghosh et al (2013)[125]	Acute delirium due to parenteral tramadol
35	Narayan et al (2015)[126]	Varenicline induced delirium in an alcohol and nicotine dependent patient
36	Mattoo et al (2011)[127]	Zolpidem withdrawal delirium
37	Sharan et al (2007)[128]	Intoxication delirium associated with zolpidem
Delirium associated with specific physical illnesses		
38	Padhy et al (2008)[129]	Delirium in a child with nephrotic syndrome
39	Manamohan et al (2017)[130]	Delirium in an elderly with chronic lymphocytic leukemia
40	Manappallil (2016)[131]	Delirium in a patient with Parkinson's disease

Table 8 (*Continued*)

	Study (year)	Findings
Delirium associated with specific physical illnesses		
41	Singh (2017)[132]	Pancreatic pseudocyst with delirium in an alcohol dependent male
42	Khanna (1988)[133]	Hypopituitarism presenting as delirium
43	Pappachan and Agrawal (2019)[134]	Postoperative delirium
44	Nag et al (2016)[135]	Sepsis associated delirium mimicking postoperative delirium as the initial presenting symptom of urosepsis in a patient who underwent nephrolithotomy
45	Jebaraj et al (2005)[136]	Tuberculous meningitis masked by delirium in an alcohol-dependent patient
46	Upadhyaya et al (2011)[137]	Delirium and catatonia in a person with alcohol dependence with tubercular meningoencephalitis
47	Raina et al (2019)[138]	Hyperactive delirium and bilateral ptosis: bilateral thalamic infarcts due to artery of Percheron occlusion
Prolonged or persistent delirium		
48	Sireesha et al (2013)[139]	Prolonged delirium secondary to hypoxic–ischemic encephalopathy following complete hanging
49	Grover et al (2014)[140]	Persistent delirium
50	Thukral et al (2013)[141]	Conundrum of prolonged delirium
51	Achalia et al (2018)[142]	Protracted delirium tremens
	Delirious mania	
52	Soni et al (2015)[143]	Delirious mania in elderly
53	Chawla et al (2018)[144]	Identification and management of "delirious mania": a rare clinical entity
54	Bipeta and Khan (2012)[145]	Delirious mania
	Management of delirium	
55	Gupta et al (2004)[146]	Olanzapine for delirium in Parkinsonism
56	Mahajan et al (2010)[147]	Use of propofol as an adjuvant therapy in refractory delirium tremens
57	Danivas et al (2010)[148]	Electroconvulsive therapy in the treatment of delirious mania
58	Narayanaswamy et al (2012)[149]	Successful use of oxazepam in the treatment of delirium tremens

Abbreviation: ECT, electroconvulsive therapy.

been reported that the incidence of emergence agitation is comparable across the use of most flurane anesthetic agents.[91]

Case Reports focusing on Delirium

A total of 58 case reports/series have focused on delirium as the primary outcome/issue (►**Table 8**).[92-149] Some of these case reports have reported association of delirium with medications such as levetiracetam,[92] levofloxacin,[93,94] fluoroquinolones,[95] zoledronate,[96] a combination of albendazole and ivermectin,[97] and use of cyclopentolate eye drops.[98] One report presented information about delirium associated with bath salts.[99] In terms of psychotropics, delirium has been reported with discontinuation of sertraline,[100] use of olanzapine,[101] valproate associated hyperammonemia,[102-104] restarting of clozapine,[105] mirtazapine associated hyponatremia,[106] use of a combination of clozapine and electroconvulsive therapy (ECT),[107,108] use of a combination of lithium and ECT,[109,110] and postinjection delirium/sedation syndrome associated with olanzapine depot injection.[111-115] Some of the case reports/case series focus on substance-related delirium,[116-128] either during the withdrawal phase or intoxication phase. The case reports also cover topics

like refractory delirium tremens,[116] delayed onset delirium tremens,[119] delirium tremens with hollow viscus perforation,[120] genital self-mutilation in alcohol withdrawal state complicated with delirium,[116] delirium during opioid withdrawal,[122] naltrexone precipitating delirium,[121] delirium due to use of parental tramadol,[125] varenicline-induced delirium,[126] and delirium associated with zolpidem withdrawal[127] or intoxication.[128] Delirium has also been reported in association with various physical illnesses such as nephrotic syndrome,[129] chronic lymphocytic leukemia,[130] Parkinson's disease,[131] pancreatic pseudocyst,[132] hypopituitarism,[133] postoperative state,[134] sepsis,[135] tuberculous meningitis,[136,137] and thalamic infarcts.[138] One case report has focused on long-standing delirium secondary to hypoxic–ischemic encephalopathy following complete hanging.[139] Some of the reports have primarily focused on persistent[140] or prolonged[141] or protracted delirium[142] and delirious mania.[143-145] Only four reports[146-149] talked about interventions for delirium, with one focusing on the use of oxazepam in the treatment of delirium tremens,[149] the use of olanzapine for delirium in Parkinsonism,[146] use of propofol as adjuvant therapy in refractory delirium tremens,[147] and ECT for management of delirious mania.[148]

Discussion

This systematic review suggests that there is a limited research on delirium from India. However, a good thing is that in recent times, delirium has received more research attention, compared with about a decade back. This review further suggests that although psychiatrists have performed the majority of research in the area of delirium, in the recent years, other specialists too, especially, anesthetists have also shown interest in delirium and some of the studies have focused on incidence/prevalence of delirium in ICUs, postoperative delirium,[32,33] and emergent delirium.[35,36] Another important aspect that is evident from the available literature is that most of the studies have been based on standard evaluation instruments.

Although there are methodological differences across different studies, available data from India suggest that the prevalence and incidence of delirium in various ICUs have varied from 16.1 to 68.2 and 8 to 59.6%, respectively. In terms of specific non-ICU setting, the prevalence rates vary, depending on the study setting. When one compares the incidence and prevalence figures with the available western literature,[174] it can be said that these figures from India are comparable to those reported from other parts of the globe. Although, no much information is available in terms of the practices to assess delirium and the knowledge about delirium of clinicians from various specialties, few studies which involved clinicians from India, suggest that most of the ICU clinicians do not assess patients for delirium on regular basis and consider the prevalence rates of delirium, especially among those patients on mechanical ventilation to be lower than what is reported in the literature.[175] Data also suggest that there is a low concordance rate between the diagnosis made by the psychiatrist and other clinicians[67] and most of the ICU clinicians are aware of the importance of early mobilization of ICU patients but are not able to practice the same due to lack of support staff and safety concerns.[69] A study, which focused on improving the knowledge of the nurses, showed that it was associated with significant improvement in the knowledge and practice of nurses toward delirium.[71] Taken together, it can be said that the incidence and prevalence of delirium in various treatment settings in India are high and comparable to the rest of the world. However, many times, clinicians do not focus on this entity due to lack of awareness and do not screen patients for delirium regularly. Accordingly, it can be said that there is a need to improve the knowledge base, awareness, and change in clinical practice to identify delirium and manage the same in the Indian context to reduce the negative impact of the same on the patients and their caregivers. In India, ICU facilities and ventilators are also a scarcity. Accordingly, prevention and early identification of delirium can reduce the duration of ICU stay and the number of days on ventilators. This would help more patients to utilize these scarce resources. Mental health professionals need to play an important role in improving the awareness of other clinicians about delirium. Mental health professionals can train the clinicians and nurses to identify the patients who are at higher risk of delirium, screen patients, if not all inpatients, then patients at high risk for delirium on day-to-day basis, institute reorientation cues, other behavioral measures, and environmental measures to improve the outcome of patients with delirium.

In terms of mortality, data from India suggest inpatient mortality in patients with delirium is 6.6 to 30.7%[12,14,17-20,24-31] and some data suggest that this mortality rate is more than that seen in patients without delirium. Postdischarge, over 1 to 6 months after discharge, the mortality increases to approximately 15.9 to 34.6%.[13,18,27] Considering these, it can be said that there is a need to improve the awareness of clinicians and other medical professionals about the negative impact of delirium on mortality rates. This may be an important motivating factor for clinicians to manage delirium in their patients.

One of the major areas of research on delirium from India is symptom profile and the factor structure of the symptoms. In general, studies involving the patients in the CLP setting suggest that the majority of the patients of delirium have symptoms of attention deficits, disorientation, sleep–wake cycle disturbances, and motor agitation. Studies that have focused on different subgroups suggest that there are minor differences in the symptom profile of patients belonging to different age groups[25,37,41,44,49] (elderly, adult, and children), different motoric subtypes,[29] and those with AWD.[31] Further, when one compares the symptom profile of those reported for patients in CLP setting and the ICUs, it is evident that patients in the CLP setting have a higher frequency of motor agitation, whereas studies in ICUs suggest a higher frequency of motor retardation.[15,42,51] These differences possibly actually reflect the differences in the study design than the actual difference in the symptom profile. Studies that have evaluated patients in ICUs have focused on all the patients in the ICUs and hence, they are more often able to include hypoactive patients too,

which form a small proportion of patients referred to the CLP setting. When one compares the data from India, the findings from India align with studies from other parts of the world.[176]

Studies that have evaluated the factor structure of symptoms of delirium suggest that symptoms cluster on to two to three factors. In the majority of these studies, various cognitive symptoms load onto the same factor, the motoric and psychotic symptoms load together, and the third factor consists of language and thought process abnormalities. In general, data suggest that the motoric and psychotic symptoms more consistently load on to the same factor across different studies. These findings are also supported by the existing literature from other parts of the world.[177]

In terms of other research endeavors, occasional studies from India have attempted to validate various instruments used for screening and diagnosing delirium.[22,23,52] The instruments which have been validated and evaluated for some psychometric properties in studies from India include ICDSC, MDAS, CAM-ICU, DMSS, and development of DMSS-4 item version. Accordingly, this area of research requires a major boost in the form of development of new instruments and validation of other existing instruments. This will possibly help to study delirium in a much better way.

Although alcohol dependence is reported to be one of the major substances of abuse in India, AWD has received limited research attention. In terms of AWD, available data suggest that compared with emergency services treatment only, emergency services plus comprehensive inpatient addiction treatment is associated with fewer relapses.[59] Based on this, it can be said that there is a need to develop service models, which will have the mechanism of transferring patients of AWD from emergency settings to inpatient settings after initial stabilization.

Available data also suggest that delirium is the most common diagnosis made by the CLP team.[62] Other studies from India, which have focused on the prevalence of various psychiatric disorders among patients seen in CLP setting, suggest that the prevalence of delirium ranges from 0.2 to 0.53% in all the admitted patients.[178] These findings suggest that delirium should form a major focus for CLP training. Further, it can be said that focusing on delirium in undergraduate training can lead to a reduction in stigma associated with psychiatry, in medical professionals.

Some of the available data from India suggest that symptoms of delirium are associated with significant distress in patients and their caregivers. Accordingly, there is a need to develop supportive intervention programs for these patients to minimize the negative impact of delirium on the sufferers and their caregivers.

In terms of intervention, almost all the studies have focused on one or the other pharmacological agents in the prevention and management of delirium.[74-78] These studies suggest that atypical antipsychotics, like olanzapine, risperidone, and quetiapine, are not inferior to haloperidol in the management of delirium. Data from other countries also support the same.[179] However, it is important to note that the trials evaluating these molecules are of small sample size and short duration. In terms of prevention, most of the studies have focused on reduction in the incidence of emergent delirium in children receiving flurane anesthesia and these studies suggest that additional use of agents, like ketamine (low and high doses), midazolam, dexmedetomidine, propofol, glycopyrrolate, and bupivacaine are of some benefit.

Limitations of the Literature and Future Directions

If one looks at the available literature, it is evident that although delirium occurs at the interface of psychiatry and other clinical specialties, in general, there is a lack of interdisciplinary research in this area. Further, there is a lack of multicentric studies on delirium and there are only occasional attempts at collaboration with researchers from other parts of the globe.[174] Further, only the Indian Psychiatric Society has come up with the management guidelines for delirium,[173] with none of the other professional associations from India, coming up with any other recommendations on the subject. Keeping this in mind, there is a need to develop collaborations at the institutional level to start multidisciplinary research and also develop collaboration across various institutes. This will not only lead to an improvement in the research output on the subject but will also help in developing intervention models which can be implemented in resource-constrained countries like India. Further, these collaborations will also help to develop instruments that may be more suitable for the Indian setting. Further, forming a multidisciplinary professional society for delirium, like the American Delirium Society and European Delirium Society, can provide a platform for further exchange of ideas and collaborative research.

If one closely examines the available literature from India, except for a few studies, most of the studies have been limited to approximately 100 participants or less. Accordingly, these studies can be considered as underpowered and collaborative research can address this issue further. One of the important examples of delirium research comes from Italy, in which like-minded researchers joined together for the "Delirium Day" research, which focused on point prevalence of delirium in 1,867 elderly patients across 108 acute and 12 rehabilitation wards.[180] In this study, delirium was assessed across all the centers on the same day. If researchers from India can take a lead from this, doing this kind of research can help in improving the data and understanding about delirium.

Across the globe, nonpharmacological measures are considered to be the first-line management for delirium and a lot of efforts have been made to evaluate various nonpharmacological treatment bundles, such as HELP program and ABCDEF bundle.[9,10] Available data suggest that these programs are very useful in the prevention, early identification, and management of delirium.[7,8] However, none of the studies have evaluated the various nonpharmacological measures for the prevention and management of delirium in the Indian setting. This area requires a major boost if we need to improve the outcome of delirium.

One of the major strengths of India is family system.[181] Whenever a person from the family falls ill, their family is always available to support the person. However, except

for the occasional study, there is no research from India, as to how we can utilize this asset to improve the outcome of patients with delirium.

One of the major areas of research, which has not caught the attention of researchers from India, is an evaluation of biomarkers of delirium. One of the major risk factors for delirium is dementia. However, this group of patients has also not received any major attention. As the elderly population is on the rise and India is already an aging country, we need to focus on understanding delirium in this group of patients.

Conclusion

To conclude, this systematic review suggests that although there is limited research on delirium from India, in recent years there is an increase in research output concerning delirium. Available data suggest that most of the studies have focused on the incidence, prevalence, and symptom profile of patients of delirium.

Conflict of Interest
None declared.

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