RESEARCH

Predicting missed delirium diagnosis in a tertiary care center: the Consultation-Liaison at the American University of Beirut (CLAUB) analysis

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Abstract

Background Delirium is a very common occurrence in hospital settings and is frequently missed by the primary care team. It remains, however, poorly studied in the Middle East despite abundant global reports. In this study, we aimed to estimate the prevalence of missed delirium diagnosis in a tertiary care center in Lebanon and investigate potential predictors of this missed diagnosis. This was a retrospective study of adult patients admitted to the American University of Beirut Medical Center between March 2019 and December 2019 and assessed by the consultation-liaison psychiatry (CLP) team. The primary endpoint was the rate of missed delirium diagnosis among CLP consultations. Relevant statistical tests were performed to assess the association between the missed diagnosis of delirium and characteristics of patients.

Results Five hundred fifty-three patients were included with a mean age of 69.19 $\pm$ 14.79 years. 86.13% of the patients received a delirium diagnosis by the CLP team that had been missed prior to the CLP referral. A missed delirium diagnosis was more likely to be found in patients with a history of depression (OR = 24, $p < 0.01$) and a longer hospital stay [in days] (OR = 1.04, $p = 0.04$).

Conclusion The alarmingly high prevalence of missed delirium diagnosis is the first evidence of its kind in the Middle East. This urges the implementation of educational interventions to increase the detection of delirium among healthcare providers and ultimately improve patient outcomes.

Keywords Delirium, Missed delirium diagnosis, Consultation-liaison, Psychiatry, Beirut, Lebanon

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Background

Within consultation-liaison circles, delirium has often been termed "the condition of the subspecialty" [1]. The literature has evolved from defining it to creating different screening tools, identifying risk factors, and most recently finding novel management modalities [2–5].

Delirium is a neuropsychiatric syndrome marked by a sudden onset of attentional and cognitive impairments [3, 6]. These symptoms fluctuate in presence and severity and may be accompanied by psychosis and mood changes [3]. Importantly, despite its transient nature, sequalae

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may persist even after the resolution of the underlying cause in nearly 30% of patients [7].

In the West, delirium is considered the most common psychiatric syndrome found in general hospital settings, with an incidence ranging between 25 and 30% among critical care patients [3, 8]. Yet, it is often undetected or misdiagnosed, with missed diagnosis rates ranging between 42% and 64% [9–12]. With its high prevalence globally, the paucity of any evidence addressing delirium prevalence, risk factors, or management in the Middle Eastern region is alarming. The available evidence is mainly based on a few studies that assessed the prevalence of delirium and its correlates among hospitalized patients in samples from Saudi Arabia [13–15]. Unlike the West, the majority of hospitals in the Middle East do not have an electronic health record system where screenings may automatically flag patients at high risk for delirium. The identification of delirium is thus dependent on the initial assessment done by the primary medical team. This inherently prompts us to look at factors that may preclude the medical and surgical teams from recognizing delirium.

The urgency of this research is heightened by the detrimental sequelae of a delayed or missed detection of delirium. The association of worsened mortality rates with delirium has been widely documented, with such rates reaching up to 65%. Even those with an accurate diagnosis may have a 2- to 4-fold increase in mortality [16, 17]. Adding to that, delirium duration has been reportedly linked to this increased mortality [18]. Among those who recover, a longer delirium has also been associated with increased morbidity across all domains including physical functional disability and long-term cognitive decline [19–22]. Multiple studies have identified the development of delirium in-hospital as an independent risk factor for poor outcomes and mortality, even after adjusting for other confounders such as baseline differences in age, illness severity, comorbid illness, and dementia [17, 23, 24]. As such, the burden of delirium, both in terms of healthcare costs and patient functioning, is vast [25, 26]. This calls for an aggressive and early management of delirious states to improve overall outcomes, including the resolution of symptoms or, at the very least, shortening of delirium duration.

Prompted by the scarcity of delirium research in Lebanon and the region and the clinical importance of this diagnosis, this study aimed to determine the characteristics of consultation-liaison psychiatry (CLP) referrals diagnosed with delirium at the American University of Beirut Medical Center (AUBMC). Secondarily, it aimed to identify the rates and potential predictors of missed delirium diagnosis on referral in our specific patient population.

Methods
Study design and population
This was a single-center retrospective record review study of all adult patients who were admitted to AUBMC and referred to the CLP service between March 2019 and December 2019. AUBMC is a tertiary care center and is recognized as one of the leading medical centers in Lebanon and the Middle East and North Africa region. The CLP service at AUBMC was first established in February 2019. This study was part of the Consultation-Liaison at the American University of Beirut (CLAUB) analysis that included a total of 1475 patients (from both floor and emergency department consults) evaluated by the CLP team at AUBMC. The study was approved by the Institutional Review Board of the institution (BIO-2020-0180).

In this study, 533 patients (older than 16 years of age) admitted to the floor and evaluated by the CLP team, which consisted of an attending psychiatrist, psychiatric residents, and medical students, were eligible for inclusion. Each referred patient received a consultation diagnostic interview by the CLP team. After the interview, referred patients who met the criteria for a delirium diagnosis, based on diagnostic evaluation using the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5), were classified as either accurately diagnosed or missed diagnosed according to the primary care team's reason for consult. The diagnosis of delirium was further assessed through screening methods such as month of the year backwards (MOTYB), "lunch" spelled backwards, and the Montreal Cognitive Assessment (MoCA) [27]. An accurate diagnosis is considered when the patient's reason for consultation consisted of the word delirium or any of its other medical synonyms: altered mental status, encephalopathy, metabolic encephalopathy, acute encephalopathy, acute confusional state, acute brain failure, and acute brain dysfunction. Missed diagnosis was defined as a diagnostic discrepancy in which a patient who met DSM–5 criteria for delirium received a different label by the admitting physician at the time of the consultation, whether a symptom of delirium or a different diagnosis. These labels included: low mood, depression, agitation, irritability, anxiety, panic attack, medication management, suicidality, substance use, psychosis, catatonia, sleep disorder, medication seeking, and unclear or general psychiatric assessment.

The primary endpoint was the rate of missed delirium diagnosis among CLP consultations. The secondary endpoints included the rate of delirium among CLP consultations, the rate of delirium subtypes, the associations with delirium diagnosis and missed diagnosis (patient demographics and characteristics, service of admission, intubation requirement during hospitalization, intensive care unit (ICU) need during hospitalization, neurology

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consult prior to referral, restraint use prior to referral, the use of precipitating drugs, length of hospital stay, information about psychiatric consultation and implemented psychiatric interventions), and the reasons for psychiatric consultation in the settings of delirium.

Data extraction

The data collection sheet was standardized and anonymized. The information was extracted from the patients' electronic medical records present on the EPIC system at AUBMC. The variables collected included patient demographics and characteristics (age, gender, marital status, education status, employment status, pertinent medical comorbidities, and past psychiatric history), service of admission, intubation requirement during hospitalization, ICU need during hospitalization, neurology consult prior to referral, restraint use prior to referral, the use of precipitating drugs (anticholinergics medications, steroids, antihistamines, narcotics, and GABAergic agents), length of hospital stay, information about psychiatric consultation (time of consultation, reason for referral, and diagnosis according to DSM-5), and CLP implemented psychiatric interventions (non-pharmacologic and pharmacologic such as antidepressants, mood stabilizers, benzodiazepines, antipsychotics, melatonin, and others). It is noteworthy to mention that the extraction of data also included a full chart review of the written daily progress notes to avoid an inflation of the missed diagnosis. These notes usually include the teams' assessments and their differential diagnoses. All patients in whom delirium or any of its potential synonyms (altered mental status, encephalopathy, metabolic encephalopathy, acute encephalopathy, acute confusional state, acute brain failure, acute brain dysfunction) were noted, were considered as an accurate delirium diagnosis.

Statistical analyses

Descriptive statistics were represented by mean and standard deviations for continuous variables, while categorical variables were represented by frequencies and percentages. Associations were tested between all our predictor variables and the outcome of delirium diagnosis using the appropriate statistical tests. Chi-square analysis or Fischer's exact test were used for categorical predictors. Regarding the continuous predictors (age, length of hospital stay, and days until the CLP team was consulted), visual inspection of the distribution of graphical plots was used for assessing normality of the variables. For normally distributed data, an independent samples t test was used. Otherwise, Mann-Whitney U test was utilized. All significant results were entered into a multivariable binary logistic regression model to adjust for confounders and evaluate the predictors of delirium diagnosis.

Similarly, the associations between the predictor variables and the outcome "missed diagnosis of delirium" were tested using the appropriate statistical tests. Significant results were entered into a multivariable binary logistic regression model with the variable "type of delirium" and the product variable "type of delirium * predictor" to test for confounding and moderation effects, respectively. A p value of less than 0.05 was used to indicate statistical significance. Statistical analysis was conducted using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, N.Y., USA).

Results

Characteristics associated with delirium diagnosis

Among the 533 consultations, 25.70% (137) cases were diagnosed with delirium. The demographic and medical characteristics of the patient sample are listed in Table 1. Age, days till psychiatry consult, length of hospital stay, intubation, ICU admission, restraint use, unemployment, cardiac disease, pulmonary disease, endocrinological disease, neurological disease, liver disease, dementia, chronic kidney disease (CKD), and steroid use were all significantly associated with delirium diagnosis (Table 2). The multivariable binary logistic regression model ($\chi^2 = 143.12$, df = 17, $p < 0.001$) explained 40.30% of the variance in the outcome variable of delirium. After controlling for all other variables, older age (OR = 1.06 95% CI 1.04, 1.08), ICU admission (OR = 1.99 95% CI 1.02, 3.90), and the application of restraints prior to psychiatric consultation (OR = 10.52, 95% CI 1.61, 71.4) remained significant.

Characteristics associated with missed diagnosis of delirium

86.13% (118/137) of the cases diagnosed as delirium by the CLP team were initially mislabeled by the medical team. Delirium was instead reported as depression (29.93%), agitation (26.28%) anxiety (11.68%), suicidality (4.38%), medication side effects (4.38%), psychosis (2.92%), substance use (2.92%), catatonia (1.46%), sleep disorder (1.46%), and medication seeking (0.73%) as a reason for consultation (Supplemental Table S1). Regarding delirium subtypes, 83.02% (44/53) of the cases of hypoactive delirium were not identified as delirium, as compared to 90.62% (58/64) and 80.00% (16/20) for hyperactive and mixed delirium, respectively. Hypoactive delirium was significantly mislabeled and had depression as a reason for consultation instead ($\chi^2 = 48.28$, $p < 0.001$) with an OR of 19.68 (95% CI 7.56, 51.20). Depression was significantly associated with a missed diagnosis of delirium with an OR of 24 (95% CI 1.41, 404). In a multivariable regression model, the total

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Table 1 General demographics of all cases diagnosed with delirium

Characteristics	Number/percentage
Age (in years)	69.19 ± 14.79
Sex (male)	62 (45.52%)
Education	
No formal education	0 (0%)
Highschool	1 (8%)
University and higher degrees	11 (92%)
Marital status	
Single	10 (7.6%)
Married	93 (70.4%)
Divorced/separated/widowed	29 (22%)
Employment status	
Employed	95 (86%)
Total length of hospitalization (in days)	35.96 ± 53.68
Admitting service	
Internal medicine	117 (85.40%)
Surgery	20 (14.60%)
Time to consult psychiatry (in days)	16.47 ± 26.56
Reason for psychiatry consult	
Low mood/depression	41 (29.93%)
Others[a]	36 (26.28%)
Agitation	23 (16.79%)
Delirium	17 (12.41%)
Anxiety/panic attack	16 (11.68%)
Psychosis	4 (2.92%)
Past medical history	
Cardiac	114 (83.21%)
Endocrinological	98 (72.53%)
Pulmonary	73 (53.28%)
Renal	54 (39.42%)
Neurological (excluding dementia)	51 (37.23%)
Oncological	40 (29.20%)
Hepatic	24 (17.52%)
Dementia	12 (8.76%)
Past psychiatry history	62 (45.26%)
Reason for admission	
Infectious	46 (33.58%)
Cardiac	23 (16.79%)
Pulmonary	16 (11.68%)
Oncological	12 (8.76%)
Gastrointestinal	11 (8.03%)
Orthopedic	11 (8.03%)
Neurological	9 (6.57%)
Surgical	6 (4.38%)
Renal	2 (1.46%)
Endocrinological	1 (0.73%)
Intensive care unit admission	64 (46.72%)
Intubation	28 (20.44%)

Table 1 (continued)

Characteristics	Number/percentage
Prescription of medications that worsen delirium	
Steroids	40 (29.20%)
Narcotics	24 (17.52%)
Anticholinergics	17 (12.41%)
Benzodiazepines/GABAergic	7 (5.11%)
Antihistamines	5 (3.65%)
Psychiatry recommendation	
2nd generation antipsychotic	56 (40.88%)
Melatonin	50 (36.50%)
Nonpharmacological intervention only	32 (23.36%)
Antidepressant	29 (21.17%)
Other medication	20 (14.60%)
1st generation antipsychotic	12 (8.76%)
Mood stabilizer	7 (5.11%)
Restraints applied prior to consult	7 (5.11%)
Type of delirium	
Hyperactive	64 (46.71%)
Hypoactive	53 (38.69%)
Mixed	20 (14.60%)

[a] Medication management, suicidality, substance use, catatonia, sleep disorder, medication seeking, and unclear or general psychiatric assessment

length of hospital stay (OR = 1.04, 95% CI 1.00, 1.08) was significant (Table 3).

Discussion

To the best of our knowledge, this is the first study to assess delirium characteristics and missed diagnosis by a CLP service in Lebanon and the Arab world. This study suggests that the referring teams of medical and surgical specialties face difficulty in identifying delirium in most cases, with some missing the diagnosis and others reporting symptoms rather than the disorder. Hence, we highlight various patient characteristic variables that may impede a correct diagnosis of delirium by the treating team.

The overall prevalence of delirium among the studied population, referred to the CLP team, was 25.70%. This comes in line with the range found in the literature [12, 28, 29]. Higher or lower prevalence reported in other studies may be explained by the type of population studied (medical, surgical, or critical), diagnostic tools used, and knowledge of the medical hospital staff. When looking into delirium risk factors, the findings of our study replicate those reported in various major international studies [7, 30, 31]. At one out of four of our psychiatry consults being delirious, this only reinforces the need for increased national and regional efforts into detecting and treating this condition.

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Table 2 Significant associations with the diagnosis of delirium

Risk factor	Chi-square value	P value	OR with 95% CI
Categorical variables			
Unemployment	12.16	< 0.001	2.71 (1.52, 4.83)
Intensive care unit admission	38.52	< 0.01	3.61 (2.38, 5.49)
Intubation	29.65	< 0.01	4.86 (2.63, 8.96)
Cardiac history	44.22	< 0.001	4.90 (2.98, 8.06)
Pulmonary history	27.93	< 0.001	2.89 (1.93, 4,32)
Endocrinology history	27.93	< 0.001	3.049 (1.99, 4.65)
Dementia	11.41	< 0.001	4.15 (1.71, 10.08)
Neurology history (other than dementia)	8.07	0.004	1.81 (1.20, 2.75)
Liver disease	7.91	0.005	2.20 (1.25, 8.86)
Chronic kidney disease	34.16	< 0.001	3.53 (2.28, 5.48)
Steroids	7.60	0.006	1.87 (1.19, 2.93)
Restraints[a]	8.57	0.004	5.30 (1.53, 18.41)
Continuous variables			
Risk factor	Mann-Whitney *U* standardized test statistic		P value
Age (in years)	9.40		< 0.001
Days till psychiatry consult	6.71		< 0.001
Length of hospital stay (in days)	6.64		< 0.001

[a] Fisher's exact test was used to test the association

Table 3 Significant associations with missed diagnosis of delirium

	OR	Upper 95% CI	Lower 95% CI	P value
Predictors of delirium diagnosis				
Age (in years)	1.06	1.04	1.08	< 0.001
ICU admission	1.99	1.02	3.90	0.029
Restraint application	10.52	1.61	71.4	0.006
Predictors of missed diagnosis				
Age (in years)	0.99	1.03	0.96	0.882
ICU admission	0.656	1.83	0.24	0.656
Total length of hospital stay (in days)	1.041	1.08	1.0	0.042

This gap in practice is highlighted as this study observed a higher rate (86.13%) of missed delirium cases by the medical team prior to CLP team referral compared with those in existing reports (30–60%) conducted in other countries [12, 28, 32]. We hypothesize that the higher rate of missed delirium diagnosis may be attributed by poor documentation of the primary team especially in busy clinical settings. These numbers reinforce that delirium is a very common occurrence among admitted patients yet continues to be under recognized by the medical team.

Moreover, our results showed that there are two significant predictors of delirium missed diagnosis: history of depression and length of hospitalization. Having a history of depression is a common predisposing factor for developing delirium. Depression is also a common consequence of delirium [40]. That being said, the interconnected nature of these two disorders may contribute to the missed diagnosis of delirium. Although the two neuropsychiatric conditions have overlapping clinical manifestations such as lethargy, diminishing activity, agitation, and cognitive decline, the distinction between both is necessary to provide patients with optimal health care outcomes [40, 41]. Therefore, educational training for delirium detection should focus on highlighting the variations in the clinical presentation of delirium and differentiating it from other psychiatric disorders.

A prolonged length of hospital stay was a significant predictor of missed delirium diagnosis; a longer hospitalization period was associated with a lower delirium detection rate. The latter finding is novel as, to our knowledge, it has never been reported in the literature. One hypothesis behind the association of delirium with prolonged hospital stay may be that chronic patients with no acute issues have often longer follow-up intervals allowing delirium to go undetected. It is important to note that patients with delirium have a longer hospitalization period, higher mortality and higher rates of institutional care making length of hospitalization both a predictor and a sequela of delirium [31]. Thus, it is necessary to implement a thorough screening routine which includes an initial screening test, a regular re-assessment

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at every shift in order to detect new onset delirium or follow-up on previous diagnosis, an interval screening test in case primary care providers have missed the diagnosis or were unable to assess the patient regularly and finally an aggressive intervention once delirium is diagnosed. The following findings could provide a new prototype of individuals prone to missed diagnosis of delirium and therefore should be included in the screening process for the disorder itself.

Due to its high prevalence and its susceptibility to time, educating the primary care team in identifying delirium is a key component in the sequence of treatment provision and patient care. Once the diagnosis has been made, it is vital for the primary care team to consult psychiatry due to the nature of the disease and its impact on overall disease progression and quality of life. In fact, as previously mentioned, time is a key factor in limiting impairment; the longer the duration of delirium, the more the deterioration in cognitive and physical function [19–22]. By sequence, a longer duration of delirium signifies a longer hospital stay and therefore also adds a financial burden on the patient. That being said, early detection and consultation of the CLP service may improve the patient's quality of life by tackling causes of disease burden. Thus, it is essential to train primary care providers to regularly screen patients with a history of depression as well as long hospitalization periods for delirium.

This study has some limitations. It has a small sample size limiting its statistical power. As recruitment was done at one institution and from cases referred to the CLP team only, there is a risk of sample bias, and the generalizability of the results is decreased. This study was retrospective, and the data was derived from electronic clinical records. Therefore, detection of missed delirium diagnosis was based on the primary care team's report. One of the factors that could affect the accuracy of our results is the primary team's definition of delirium: detection could have been influenced by their inability to encompass synonyms of delirium or other relative words that fall under our umbrella of selected key words describing delirium. Longitudinal studies assessing the predictors of missed delirium diagnosis are warranted. Another factor could be the absence of a standardized method to measure delirium as the hospital, at the time of diagnosis, did not utilize the Confusion Assessment method for the ICU (CAM-ICU), the Brief Confusion Assessment Method (bCAM), or the Richmond Agitation and Sedation Scale (RASS) as screening tools. The assessors relied on the DSM-5 criteria for delirium as well as MOTYB and "lunch" spelled backward for screening instead.

Other factors impairing delirium reporting could be attributed to the primary care team's understanding of the disease itself. Although delirium is very prevalent in hospital settings, one could postulate that many primary care providers fail to report these cases to the CLP service due to the fact that delirium does not have a pharmacological treatment that is effective on its own. Therefore, many primary care providers dismiss the importance of its management through psychiatry, rendering the nature of the problem one of communication and consultation rather than missed diagnosis. However, treating delirium requires combining both pharmacological and non-pharmacological approaches best provided by specialized CLP teams. Also, since multiple comparisons were conducted, there is an increased risk of type I error [33]. We also did not assess the characteristics of the referring treating physicians or teams, such as their clinical specialty, knowledge, and level of training. Future studies looking into this might help identify further causes behind the missed diagnosis of delirium.

Conclusion

Critical challenges are often faced by the primary team to accurately identify and diagnose delirium. One of the most efficient means to enhance delirium prognosis is to increase its diagnostic efficacy. This calls for educational interventions and various training models for non-psychiatric staff to improve the outcomes of patients with or at high-risk of delirium through prevention and early detection. Training should focus on improving knowledge about delirium and its different presentations, enhancing the ability to differentiate it from other organic and non-organic diseases, and encouraging the use of delirium screening tools. This also requires validating international screening assessments in Lebanon and the Arab world. Implementing such proactive strategies rather than relying on a reactive CLP service is crucial to overcoming the burdening diagnostic inaccuracies of delirium.

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Declarations

Ethics approval and consent to participate
All procedures were revised and approved by the Institutional Review Board of the American University of Beirut (BIO-2020-0180).

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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