

Prevalence of delirium in gastroenterology/hepatology units: A cross-sectional study

Delirprävalenz in der Gastroenterologie/Hepatology: Querschnittstudie zur Erhebung der Prävalenz stationärer Patient*innen



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ABSTRACT

Prevalence rates of delirium amount to 22.0 % within acute-care settings. In contrast, 30–40 % of patients with liver cirrhosis may develop hepatic encephalopathy, a condition that has been classified as a syndrome of delirium, based on recent pathophysiology findings. However, the prevalence of delirium in gastroenterology and hepatology units is unknown.

The aims of the study were (i) to identify delirium prevalence rates in inpatients of gastroenterology/hepatology wards, (ii) to analyze the delirium motor subtype, and (iii) to assess associations between delirium and patient characteristics.

In this monocentric, cross-sectional, epidemiological study, point prevalence was assessed at six time points in three gastroenterology/hepatology units within a German university hospital. Delirium was assessed using the 4 'As' Test (4AT) and delirium subtype by the delirium motor subtype scale. Patient characteristics were collected from patient charts.

The sample consisted of 188 patients, aged 18 to 98 years (mean age 64, n = 110 male). Of them, 18.1 % of patients showed delirium symptoms (61.8 % hypoactive, 29.4 % mixed, and 8.8 % hyperactive). For the participants aged ≥ 65 years (n = 96), prevalence of delirium amounted to 26.0 %. Significant associations were observed between delirium and the following characteristics: age (p = 0.001), length of hospital stay until assessment (p = 0.043), cerebrovascular disease (p = 0.002), dementia (p = 0.010), diabetes mellitus with chronic complications (p = 0.012), and gender (nonsignificant trend, p = 0.050), while no association was detected between moderate or severe liver disease and delirium (p = 0.414).

In conclusion, overall prevalence rates of delirium were rather low and did not increase in patients with liver disease.

ZUSAMMENFASSUNG

In Akutkrankenhäusern wird von einer Delirprävalenz von ca. 22 % ausgegangen. In der Gastroenterologie/Hepatology werden höhere Prävalenzen erwartet, da 30–40 % der Patient*innen mit Leberzirrhose im Verlauf ihrer Erkrankung eine Hepatische Enzephalopathie entwickeln, die als delirantes Syndrom verstanden werden kann.

Ziele dieser Studie waren (1) die Ermittlung der Delirprävalenz stationärer Patient*innen in der Gastroenterologie/Hepatology, (2) die Analyse des motorischen Delirsubtyps sowie (3) die Zusammenhänge von Delir mit patientenbezogenen Charakteristika zu erfassen.

In einer monozentrischen Querschnittstudie wurde zu sechs Zeitpunkten die Prävalenz auf drei gastroenterologischen/hepatologischen Normalstationen einer Universitätsklinik erho-

ben. Das Delir wurde anhand des 4-,A'-Tests (4AT) erfasst, der Motor Subtyp mit Hilfe der ‚Delirium Motor Subtype Scale‘, patient*innenbezogene Charakteristika wurden den Patient*innenakten entnommen.

Die Stichprobe umfasste 188 Patient*innen im Alter von 19–98 Jahren (Durchschnitt 64 Jahre, $n = 110$ männliche Teilnehmer). 18,1 % wiesen Symptome eines Delirs auf (61,8 % hypoaktiv, 29,4 % gemischt, 8,8 % hyperaktiv). Die Prävalenz eines Delirs in der Altersklasse ≥ 65 Jahre ($n = 96$) betrug 26,0 %. Es konnten signifikante Zusammenhänge zwischen Delir und folgenden Charakteristika nachgewiesen werden:

Alter ($p = 0,001$), Länge des Aufenthalts bis zur Erhebung ($p = 0,043$), zerebrovaskuläre Erkrankungen ($p = 0,002$), Demenz ($p = 0,010$), Diabetes mellitus mit Endorganschäden ($p = 0,012$), sowie eine Tendenz bezüglich des Geschlechts ($p = 0,050$). Im Gegensatz dazu bestand kein Zusammenhang zwischen moderater bis schwerer Lebererkrankung und dem Auftreten eines Delirs ($p = 0,414$).

Zusammenfassend wies die hier untersuchte Stichprobe eine geringe Delirsymptomatik auf. Die Prävalenz eines Delirs bei Patient*innen mit Lebererkrankungen war nicht erhöht.

Introduction

Delirium represents the most common cause of acute cognitive dysfunction in older inpatients [1]. The prevalence of delirium may vary according to setting, data collection methods, and patient population [1]. In general, the prevalence of delirium in inpatients within medical departments of acute-care hospitals is assumed to be approximately 22 % [2, 3], while in different inpatient settings point prevalence rates of delirium range between 9.0 % and 32.0 % [4]. Patients with delirium, their caregivers, and relatives report additional distress, helplessness, frustration, and fear while being hospitalized [5, 6, 7, 8]. For affected patients, delirium is a critical complication associated with prolonged hospitalization, permanent cognitive impairment, and continued need for additional care services [1, 7, 9, 10, 11, 12]. In addition, there are economic consequences associated with delirium during a hospital stay [13, 14, 15, 16]. The economic expenditure for the treatment of patients with hyperactive delirium in a German hospital has been analyzed by Weinreb and associates [15]. The additional costs per year in an internal medicine unit were estimated at approximately 948 000 €. For each patient with hyperactive delirium, an average of an additional 1200 € were incurred during the hospital stay as a result of additional staff and therapeutic efforts. Each case required an average of 240 additional personnel minutes. In addition, the average length of hospital stay was 4.2 days longer compared to patients without delirium [15].

Maldonado and associates summarized the different theories of the pathophysiology and causes of delirium within the system integration failure hypothesis (SIFH) [17]. The boundaries between different theories are fluid, so that a common hypothesis can be achieved. According to the SIFH, a combination of different risk factors with physiological characteristics of the individual can lead to changes in the processes and structure of the central nervous system (CNS) [17, 18]. Subsequently, the SIFH and its implications may lead to a new understanding of classifying delirium forms, like hepatic encephalopathy (HE).

HE is a frequent complication of liver cirrhosis affecting 30–40 % of patients over the course of their disease [19]. The overlap of symptoms of HE and the definition of delirium according to the International Statistical Classification of Diseases and Related Health Problems (ICD-10) may lead to conflicting conclusions

[20, 21, 22, 23, 24]. According to the ICD-10, a delirious state is to be understood as HE if it is solely due to liver failure. In relation to SIFH [17], however, HE was seen as a possible pathophysiological pathway of delirium in this study.

Studies on delirium prevalence focus mainly on older patients, leaving younger patients with liver cirrhosis unnoticed [4]. Furthermore, the prevalence of delirium in gastroenterological/hepatological inpatients could be higher than the reference value of 22.0 % [2, 3] because of the patients with liver diseases. No study on delirium prevalence in acute-care gastroenterology/hepatology settings has been identified so far.

Thus, the overall aim of this study was to determine the delirium prevalence in inpatients within gastroenterology and hepatology wards. The secondary aims were to analyze delirium motor subtype and to identify associations between delirium and relevant patient characteristics.

Material and Methods

Design

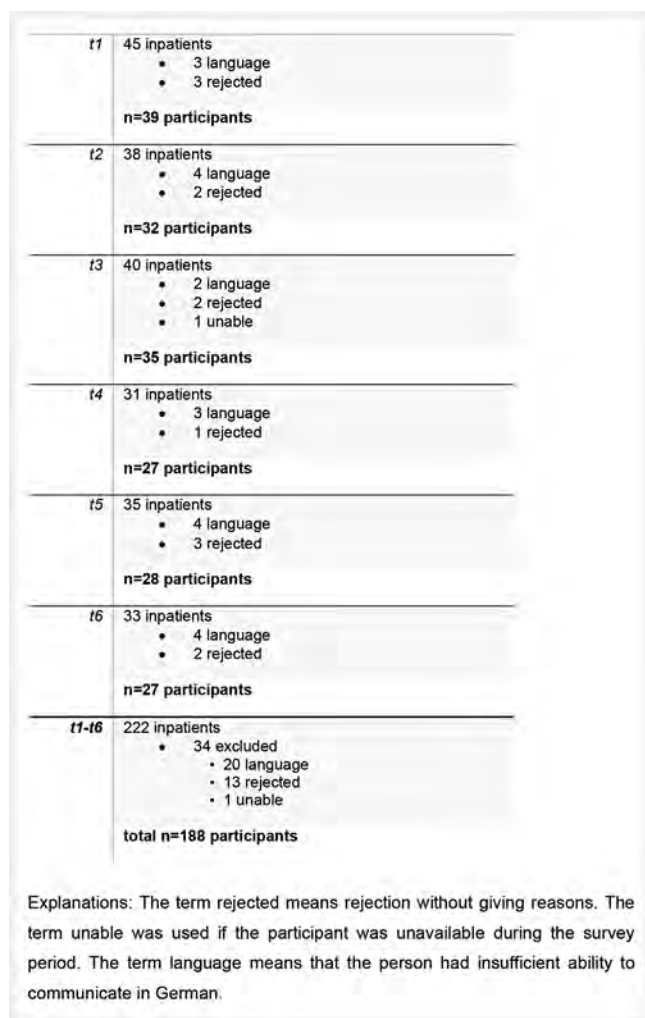
In this monocentric cross-sectional study, the overall prevalence was assessed by six point-prevalence assessments over a period of two months (► Fig. 1).

Patients who had already been assessed through previous surveys were excluded from further assessments and are not listed as inpatients in ► Fig. 1. The study protocol was approved by the institutional review board of the host institution (approval no. 95/18). The Universal Trial Number (UTN) is U1111-1209-1444; registration at the German Register of Clinical Studies (DRKS) was performed (DRKS00014804).

The findings of this study are reported in concordance with the ‘strengthening the reporting of observational studies in epidemiology’ (Strobe) statement for observational studies [25].

Sample and Setting

All patients who were inpatient 24–72 hours prior to one of the six days of the scheduled assessment measures were screened for inclusion and exclusion criteria. Those meeting the inclusion criteria were invited to participate. Inclusion criteria were age ≥ 18 years and inpatient status in one of the gastroenterological/hepatological units. Exclusion criteria were insufficient ability to communi-



► **Fig. 1** Flow chart of included and excluded participants in the study (with reasons) at times t1–t6.

cate in German and patients in a critical pre-final health state or in coma. The required sample size was calculated according to Nanning, Winn, and Rusli [26]. Based on the literature analysis, a delirium prevalence of 20.0–30.0% was expected in the population of interest. The power analysis resulted in a required sample size of $n = 211$ for a representative prevalence survey.

The study was carried out at the gastroenterological/hepatological units of the University Hospital Freiburg. These units are comprised of 59 beds and focus on the diagnostics and therapy of digestive tract and liver diseases.

Data Collection

For reaching the calculated sample size, six point-prevalence assessments were carried out during a two-month period over intervals of twelve days. On these six assessment days, the surveys were carried out between 8 a.m. and 4 p.m. Presence or absence of delirium was recorded. If a delirium was present, motor subtype (hyperactive/hypoactive/mixed form/no subtype) was determined. In addition, for each participant, comorbidities were captured using the Charlson comorbidity index (CCI) [27]. Further-

more, clinical data (admission to gastroenterology/hepatology unit, length of hospital stay) and demographic data (age, gender) were obtained from the patients' records.

Instruments

The 4 'A' Test

Presence or absence of delirium was assessed with the 4 'A' Test (4AT), a validated test for assessing delirium and cognitive impairment [28, 29]. The 4AT consists of four items measuring alertness, orientation, attention, and fluctuation. A total of 12 points can be assigned. Delirium is prevalent with four or more points; 1–3 points indicate a cognitive impairment. A score of zero makes delirium unlikely, although it cannot be completely ruled out because of fluctuation.

The 4AT is a clinically established screening tool with a pooled sensitivity of 0.88 (95.0% CI 0.80–0.93) and a pooled specificity of 0.88 (95.0% CI .82–0.92) [29].

In the present study, the 4AT was used without further standard diagnostics. A value from ≥ 4 when a trained healthcare professional uses the 4AT was defined as presence of delirium for this study. All screening procedures were performed by the same trained healthcare professional. In this study, the internal consistency of the 4AT was calculated with Cronbach's $\alpha = 0.792$.

Delirium Motor Subtype Scale (DMSS-G)

If a participant had a 4AT value of ≥ 4 , the motor subtype of the delirium was determined by applying the validated German version of the delirium motor subtype scale (DMSS-G) [30]. By applying the DMSS-G, symptoms in the period of 24 hours prior to the survey are to be analyzed. Data were collected using patient documentation, as well as from interviews with the nursing and medical staff.

Data Analysis

Data were analyzed using IBM SPSS 22. For descriptive analyses, absolute and percentage frequencies were calculated. For metric data, mean values (M) and standard deviation (SD) were calculated. Age dichotomization using M provided prevalence rates for both age groups, in addition to the overall prevalence of delirium.

A subgroup analysis was used to examine correlations of delirium with liver disease, age, duration of inpatient stay, and gender. Group differences were analyzed using the Mann–Whitney U-test. Correlations between dichotomous variables were checked by means of the χ^2 -test. Odds ratios (OR) were calculated for reporting the strength of association. The degree of correlation was calculated for metric and dichotomous variables using point biserial correlation measures; for non-normally distributed data, the correlation was given by Kendall-t-b. To determine the correlation of dichotomous variables, Phi-coefficient (ϕ) or Fisher's exact tests were used. Fisher's exact test was conducted if cells had expected values < 5 . The significance level was set at 95.0% ($p \leq 0.05$). The internal consistency of the 4AT was calculated using Cronbach's α .

Ethical Considerations

Within this study, the vulnerable group of patients with delirium were considered with the highest sensitivity possible, and the additional diagnostic procedure offered a direct benefit. If delirium symptoms were detected by the 4AT assessment, ward-standard diagnostics and interventions could be initiated. The risk of the assessment for the participant was considered to be low.

Written informed consent had to be given before participation, and results of the assessment were communicated to each participant after the performance. Patients with delirium must be regarded as unable or partially able to give consent. In these cases, the Declaration of Helsinki in § 28 provides the opportunity that informed consent is provided on behalf by the legal representative [31]. If a participant regained a mental state allowing informed consent to be given within a 28-day follow-up observation, the person had the right to decide independently how the collected data be handled. Refusing consent resulted in deletion of the entire dataset for the individual patient. The participants did not receive any incentives.

Results

Participants

Overall, 222 patients were accessible at six consecutive assessment points (t1–t6) (► **Fig. 1**). Of those 222 potential participants, 188 persons (84.7 %) provided consent and were included in the study.

Descriptive Data

Mean age was 64 ± 16 years (range 19–98 years); 51.1 % ($n = 96$) were 65 years or older; length of hospital stay until the assessment was on average 5 ± 4 days (range 1–32 days). ► **Table 1** shows gender distribution and comorbidities by CCI with absolute and percentage values. Multiple comorbidities per patient could be recorded, and there were no missing data.

Delirium Prevalence

A delirium prevalence of 18.1 % ($n = 34$) was calculated. ► **Table 2** shows the point prevalence at individual survey measurement points (t1–t6) and the overall prevalence. Dichotomized at the

► **Table 1** Descriptive data of the 188 participants: Gender Distribution and Comorbidities structured by the Charlson Comorbidity Index.

	N (%)	Delirium (%)	No Delirium (%)
Gender			
male	110 (58.5 %)	25 (22.7 %)	85 (77.3 %)
female	78 (41.5 %)	9 (11.5 %)	69 (88.5 %)
Acute myocardial infarction	11 (5.9 %)	3 (27.3 %)	8 (72.7 %)
Congestive heart failure	38 (20.2 %)	11 (28.9 %)	27 (71.1 %)
Peripheral vascular disease	13 (6.9 %)	2 (15.4 %)	11 (84.6 %)
Cerebrovascular disease	23 (12.2 %)	10 (43.5 %)	13 (56.5 %)
Dementia	6 (3.2 %)	4 (66.7 %)	2 (33.3 %)
Chronic pulmonary disease	33 (17.6 %)	7 (21.2 %)	26 (78.8 %)
Rheumatic disease	7 (3.7 %)	2 (28.6 %)	5 (71.4 %)
Peptic ulcer disease	26 (13.8 %)	7 (26.9 %)	19 (73.1 %)
Mild liver disease*	7 (3.7 %)	3 (42.9 %)	4 (57.1 %)
Diabetes without chronic complication	25 (13.3 %)	4 (16.0 %)	21 (84.0 %)
Renal Disease	21 (11.2 %)	7 (33.3 %)	14 (66.7 %)
Diabetes with chronic complication	16 (8.5 %)	7 (43.8 %)	9 (56.3 %)
Any malignancy without metastasis	53 (28.2 %)	12 (22.6 %)	41 (77.4 %)
Leukemia	5 (2.7 %)	0 (0.0 %)	5 (100.0 %)
Lymphoma	10 (5.3 %)	1 (10.0 %)	9 (90.0 %)
Moderate or severe liver disease*	40 (21.3 %)	9 (22.5 %)	31 (77.5 %)
Metastatic solid tumor	38 (20.2 %)	5 (13.2 %)	33 (86.8 %)
Total	188 (100.0 %)	34 (18.1 %)	154 (81.9 %)

N = number of participants with corresponding characteristics or comorbidities or preexisting disease. * = Mild liver disease is defined as chronic hepatitis or cirrhosis without portal hypertension; moderate or severe liver disease is defined as chronic hepatitis or cirrhosis with portal hypertension and with/without variceal bleeding history.

► **Table 2** Delirium prevalence and motor subtype at assessment points t1–t6.

Assessment point	n	Delirium (%)	Hyperactive Motor Subtype (%)	Hypoactive Motor Subtype (%)	Mixed Motor Subtype (%)
t1	39	10 (25.6%)	1 (10.0%)	8 (80.0%)	1 (10.0%)
t2	32	4 (12.5%)	0 (0.0%)	3 (75.0%)	1 (25.0%)
t3	35	5 (14.3%)	0 (0.0%)	3 (60.0%)	2 (40.0%)
t4	27	6 (22.2%)	1 (16.7%)	3 (50.0%)	2 (33.3%)
t5	28	3 (10.7%)	0 (0.0%)	1 (33.3%)	2 (66.7%)
t6	27	6 (22.2%)	1 (16.7%)	3 (50.0%)	2 (33.3%)
t1–t6	188	34 (18.1%)	3 (8.8%)	21 (61.8%)	10 (29.4%)

n = Number of participants at corresponding assessment points.

mean age, the delirium prevalence (t1–t6) for those ≥ 65 years ($n = 96$) was 26.0% ($n = 25$). Delirium prevalence was increased within the age group of ≥ 65 years (OR 3.247, 95% CI 1.423–7.411; $p \leq 0.004$). In participants < 65 years ($n = 92$), the delirium prevalence (t1–t6) was 9.8% ($n = 9$). For the entire sample, the most frequent motor subtype was hypoactive ($n = 21$; 61.8% of participants with delirium). Three participants (8.8%) with delirium showed a hyperactive motor subtype (► **Table 2**).

Subgroup Analysis

The subgroup analysis revealed the following associations between the occurrence of delirium based on the 4AT and descriptive variables.

Participants with delirium were significantly older (74 ± 13 years) than participants without delirium (61 ± 16 years; $U = -4.136$, $p < 0.001$). The point biserial correlation between age and delirium showed a mean effect with $r = 0.310$, $p < 0.001$. The age range of participants with delirium was 47–98 years.

Length of hospital stay was higher in participants with delirium ($m = 6$ days) than in participants without delirium ($m = 5$ days, $U = -2.025$, $p = 0.043$) at the time of data collection. The correlation according to Kendall- τ -b showed a small effect with $\tau = 0.127$, $p = 0.043$.

As shown in ► **Table 3**, a meaningful, albeit not significant, correlation was found between male sex and the presence of delirium (OR 2.255, 95% CI 0.988–5.148, $p = 0.050$). The calculation of ϕ indicated a small effect ($\chi^2(1df) = 3.857$; $\phi = 0.143$).

Discussion

In this study, inpatients with delirium symptoms were detected in gastroenterology and hepatology wards using the validated AT4 tool, and results revealed an 18.1% prevalence of delirium. Of those, 61.8% had a hypoactive subtype, 29.4% a mixed motor subtype, and 8.8% a hyperactive motor subtype. For participants aged ≥ 65 years, delirium prevalence was slightly higher (26.0%). Determinants associated with delirium were older age, longer length of hospital stay until survey, cerebrovascular disease, de-

mentia, diabetes mellitus with end organ damage, and a tendency toward male gender. No significant relationship was identified between mild or severe liver disease and the occurrence of delirium.

Clinical experience surmises an increase in delirium prevalence in gastroenterological/hepatological units *inter alia* because of the patients with liver disease. An HE diagnosis requires the presence of liver disease, especially liver cirrhosis [21]. However, within this study sample, no association between liver disease and delirium was detected. One might conclude, with caution, that the delirium detected in this study may be a result of other causes and not necessarily HE. Similar findings were confirmed by a recent study [32]. However, no further HE diagnostics or revision of a previous HE-treatment was performed for this sample. On the other hand, a systematic review showed a significant association between low albumin levels and the incidence of delirium, albeit no association with an underlying liver disease was reported [33].

In concordance with other studies, significant associations were detected between older age (≥ 65 years) and delirium [34, 35, 36]. However, as the number of participants aged ≥ 65 years was rather small, the analysis of this group of participants should be handled with caution. Here the maximum sample error is 7.84%. Likewise, the association between length of hospital stay until assessment point and the occurrence of delirium was significant. The first day of the survey showed moderate to extreme outliers in the number of days. The reason for this was that at t1 patients were included who had already been admitted to the hospital for more than 12 days. An association between the incidence of delirium and an increased length of hospital stay has also been identified in other studies, whereby the main focus on prolonged hospitalization was attributable to delirium [33, 37].

In line with other studies [38, 39, 40], significant associations of delirium and relevant comorbidities including dementia, cerebrovascular disease, and diabetes with chronic complications have been identified within our sample. The connection between delirium and cognitive impairment, dementia, and history of apoplexies or transient ischemic attacks (TIA) is mentioned several times in the literature [2, 32, 38, 39, 40, 41].

► **Table 3** Correlation of delirium, gender, and comorbidities structured by the Charlson Comorbidity Index.

Correlation of delirium and ...	χ^2 (P)	ϕ (P)	OR and corresponding 95 % CI
Gender	3.857 (0.050)	0.143 (0.050)	2.255 0.988–5.148
Acute myocardial infarction	* (0.422)	0.060 (0.415)	1.766 0.443–7.037
Congestive heart failure	3.793 (0.051)	0.142 (0.051)	2.250 0.981–5.159
Peripheral vascular disease	* (1.000)	–0.019 (0.793)	0.813 0.172–3.846
Cerebrovascular disease	* (0.002)	0.246 (0.001)	4.519 1.781–11.467
Dementia	* (0.010)	0.229 (0.002)	10.133 1.775–57.846
Chronic pulmonary disease	0.264 (0.607)	0.037 (0.607)	1.276 0.503–3.242
Rheumatic disease	* (0.612)	0.054 (0.463)	1.863 0.346–10.030
Peptic ulcer disease	* (0.269)	0.092 (0.207)	1.842 0.705–4.811
Mild liver disease	* (0.113)	0.127 (0.083)	3.629 0.773–17.031
Diabetes without chronic complication	* (1.000)	–0.021 (0.771)	0.844 0.270–2.641
Renal Disease	* (0.070)	0.140 (0.054)	2.593 0.957–7.022
Diabetes with chronic complication	* (0.012)	0.203 (0.005)	4.177 1.433–12.174
Any malignancy without metastasis	1.034 (0.309)	0.074 (0.309)	1.503 0.683–3.309
Leukemia	* (0.587)	–0.078 (0.287)	0.815 0.760–0.873
Lymphoma	* (0.693)	–0.050 (0.495)	0.488 0.060–3.988
Moderate or severe liver disease	0.669 (0.414)	0.060 (0.414)	1.428 0.606–3.368
Metastatic solid tumor	0.780 (0.377)	–0.064 (0.377)	0.632 0.227–1.760

* = If cells had expected values < 5, the Fisher's exact test was conducted. Therefore, there is no value for χ^2 , but the exact significance is stated. 95 % Confidence Interval (CI), OR = odds ratio.

Limitations and Bias

First, as the detection of a delirium is limited to when the patient is assessed and is, thus, a fluctuating symptom, data collection

was not continuous. A survey conducted more regularly, for example day and night, could provide more accurate results, if not a better overview. Thus, an underestimation of the prevalence within this study cannot be excluded, which may be exacerbated by possible early treatment of HE symptoms because of the specification of the wards. Second, the absence of further diagnostic processes was a limitation. For this reason, over- or underestimation of delirium prevalence cannot be ruled out despite the sufficient sensitivity and specificity of the 4AT tool. Third, participation was refused by 13 patients without citing specific reasons. In particular, patients with hypoactive delirium tend to show a negative, lethargic behavior [42], which might have impacted the data presented herein. However, the study attrition rate of 84.7 % is comparable with rates in previously published studies on this topic [2, 3, 43].

A selection bias could have occurred because of the limited ability of patients in delirium to give informed consent. This bias should be avoided by the procedure described above under ethical considerations. An additional selection bias could result by conducting the survey on the same weekday and/or at a fixed time after patient admission to the hospital. To prevent this systematic error, the current survey was conducted every 12 days on different weekdays. Prevention of an information bias was achieved in the careful selection of validated assessment instruments. Systematic errors in the evaluation procedure were kept at a minimum because of the descriptive design. In addition, the variables already defined in the study design were intended to counteract this bias. Based on hospital patient registry data, the determined sample size was recalculated to ensure adequacy. The recommended number of participants was 163, so the sample size of $n = 188$ appeared to be sufficient. A research diary was utilized.

Generalizability

The number and discipline of the comorbidities or preexisting diseases show that the included patients do not have exclusively basic gastroenterological/hepatological diseases. ► **Table 1** illustrates the broad spectrum of diagnoses within an acute-care setting in internal medicine. For this reason, a cautious application within internal medicine could be justifiable. Wards with a focus on geriatrics, as well as intensive-care units, vary widely in the patients treated therein. A patient transfer between wards does need to be taken cautiously and within the context of the respective target setting and target patient population.

Conclusions

In this study, an 18.1 % prevalence of delirium symptoms in gastroenterological/hepatological inpatients was determined. Our findings may direct the utilization of easy-to-use validated screening tools like the 4AT instrument, particularly in specialty areas like gastroenterology/hepatology. Furthermore, our findings point to the need for multi-professional collaboration in an attempt to provide the best therapy possible for this vulnerable patient population, acknowledging scarce resources within the clinical setting.

Conflict of Interest

The authors declare that they have no conflict of interest.

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