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Neurocognitive and psychiatric sequelae following traumatic brain injury in an Iranian forensic cohort: A longitudinal analysis of lesion localization and clinical outcomes

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Abstract

Background: Traumatic brain injury (TBI) is a well-established risk factor for neuropsychiatric disorders. However, the relationship between lesion localization and psychiatric phenotypes remains incompletely characterized, particularly in forensic contexts.

Objectives: This longitudinal study of an Iranian forensic cohort retrospective analysis of prospectively collected data aimed to investigate the frequency and pattern of psychiatric sequelae following TBI and explore associations between neuroanatomical injury sites and specific psychopathological outcomes.

Methods: A total of 113 patients with documented TBI (GCS ≤14, hospitalization ≥24 hours) were consecutively recruited from the Forensic Medicine Organization of Khorasan Razavi, Iran (2020–2022). Patients underwent psychiatric evaluation over a median follow-up of 13 months (IQR: 6–18 months). DSM-5 diagnoses were established using structured clinical interviews. CT scans were reviewed for lesion localization. Multivariate logistic regression and effect sizes (Cramér's V, Cohen's h, risk ratios) were employed.

Results: The cohort comprised 92 males (81.4%) and 21 females (18.6%), with a mean age of 36.5 ± 18.4 years. Traffic accidents predominated (84.1%). Notably, 41.6% of patients exhibited no focal parenchymal lesions on initial CT. The most prevalent diagnoses were neurocognitive Disorder (23.0%), major depressive Disorder (19.5%), personality change (13.3%), and post-concussion syndrome (13.3%). In this forensic cohort, 100% of participants received at least one psychiatric diagnosis, which reflects the medicolegal referral context and does not generalize to non-forensic TBI populations. Frontal lobe involvement showed a numerically higher frequency of personality change (29.4% vs. 10.5%; risk ratio = 2.80, 95% CI: 0.98–7.99; p = 0.078). Gender was not an independent predictor (adjusted OR = 1.24, 95% CI: 0.48–3.21, p = 0.66).

Conclusion: Neurocognitive Disorder and major depression are the predominant psychiatric sequelae in this Iranian forensic TBI cohort. A substantial proportion of patients developed significant psychopathology despite normal CT imaging—the "normal CT paradox"—underscoring the need for psychiatric surveillance regardless of neuroimaging findings. Findings are limited to forensic medicolegal populations and do not generalize to the general TBI population.

Keywords: Traumatic Brain Injury; Neurocognitive Disorders; Major Depressive Disorder; Forensic Psychiatry

1. Backgrounds

Traumatic brain injury (TBI) constitutes a major global public health challenge, representing a leading cause of mortality and long-term disability among individuals under 35 years of age (1). In the United States alone, approximately 1.5 million individuals sustain a TBI annually, resulting

in over 50,000 fatalities and leaving an estimated 80,000 to 90,000 survivors with enduring functional impairments (2). Globally, the age-standardized incidence rate of TBI is estimated at 369 per 100,000 person-years, with considerable regional variation attributable to differences in traffic safety infrastructure and occupational hazards (3). The most prevalent etiologies include motor vehicle collisions, falls from height, and interpersonal violence (4).

In the Islamic Republic of Iran, epidemiological surveillance data indicate that the incidence of road traffic injuries and TBI substantially exceeds global averages, positioning Iran among nations with the highest burden of trauma-related morbidity worldwide (5). Prior investigations have documented a male predominance in TBI incidence, with male-to-female ratios ranging from 2.2:1 to 3:1, and a peak incidence during the third and fourth decades of life—a demographic pattern with considerable socioeconomic ramifications (6).

The neuropsychiatric sequelae of TBI represent an increasingly recognized dimension of posttraumatic morbidity. Convergent evidence from large-scale epidemiological studies and longitudinal cohort investigations has established TBI as an independent risk factor for the development of diverse psychiatric disorders, including major depressive disorder, generalized anxiety disorder, posttraumatic stress disorder, substance use disorders, and aggressive behavioral dysregulation (7,8). Notably, a nationwide Danish register-based cohort study encompassing 113,906 individuals with head injury documented significantly elevated incidence rate ratios for schizophrenia (IRR = 1.65), depression (IRR = 1.59), bipolar Disorder (IRR = 1.28), and organic mental disorders (IRR = 4.39) relative to the general population (9). Critically, these psychiatric sequelae frequently manifest even in the absence of macroscopic structural brain injury detectable by conventional neuroimaging modalities (10).

Despite the burgeoning international literature characterizing post-TBI psychiatric morbidity, several critical knowledge gaps persist. First, the majority of extant studies have been conducted within Western sociocultural contexts, which may differ substantially from Middle Eastern populations with respect to family structure, social support networks, and stigma associated with mental illness (11). Second, the specific neuroanatomical correlates of distinct psychiatric phenotypes following TBI remain incompletely elucidated, with limited data addressing whether particular lesion localizations confer differential vulnerability to specific psychopathological outcomes (12). Third, forensic psychiatric cohorts—representing a distinct subpopulation of TBI survivors undergoing medicolegal evaluation—have received comparatively scant empirical attention, despite their unique clinical and psychosocial characteristics (13).

The present investigation was designed to address these lacunae in the literature. Specifically, we aimed to: (1) characterize the frequency and typology of DSM-5 psychiatric diagnoses in an Iranian forensic cohort of TBI survivors over an extended follow-up interval; (2) examine potential associations between neuroanatomical lesion localization (as determined by admission computed tomography) and specific psychiatric outcomes; and (3) evaluate sociodemographic and injury-related factors as potential predictors of post-TBI psychopathology. We hypothesized that Frontal lobe involvement would be associated with a higher frequency of trauma-induced personality change

(operationalized as ≥20% absolute difference). Also, temporal lobe involvement will be associated with a higher frequency of neurocognitive disorder (operationalized as ≥15% absolute difference). Furthermore, a substantial proportion of psychiatric morbidity will manifest independent of radiologically evident structural injury ("normal CT paradox").

2. Methods

2.1. Study Design and Setting

This investigation was designed as a longitudinal cohort study, utilizing retrospective analysis of prospectively collected clinical data from the forensic psychiatric service of the Khorasan Razavi Legal Medicine Organization in Mashhad, Iran. The study period extended from March 2020 to September 2022, encompassing a minimum follow-up of 6 months and a maximum of 18 months post-injury for a definitive psychiatric diagnosis. The study protocol was reviewed and approved by the Medical Ethics Committee of Mashhad University of Medical Sciences (Approval Code: IR.MUMS.REC.P941366). All procedures contributing to this work complied with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration.

2.2. Participants and Eligibility Criteria

Patients were consecutively recruited from individuals referred to the psychiatric unit of the Forensic Medicine Organization for medicolegal evaluation of disability attributable to head trauma. Inclusion criteria were established as follows: (1) documented history of closed or penetrating traumatic brain injury sustained within 12 months preceding study enrollment; (2) hospitalization for a minimum duration of 24 hours following the index injury; (3) initial post-resuscitation Glasgow Coma Scale (GCS) score ≤14, indicating at least mild TBI by established classification criteria (14); and (4) willingness to provide written informed consent and availability of corroborative history from a first-degree relative or primary caregiver. Exclusion criteria comprised: (1) traumatic injury limited exclusively to facial soft tissues, ocular structures, or nasal architecture without intracranial or scalp involvement; (2) pre-existing diagnosed neurodegenerative disorder (e.g., Alzheimer's disease, Parkinson's disease); (3) pre-injury diagnosis of schizophrenia or bipolar I disorder documented in medical records; and (4) inability to complete psychiatric assessment due to severe receptive aphasia or profound cognitive impairment precluding meaningful clinical interview. A total of 113 patients satisfied all eligibility criteria and were enrolled in the final analytical cohort.

2.3. Data Collection Procedures

2.3.1. Demographic and Clinical Characteristics

Comprehensive demographic and clinical data were abstracted from medical records and supplemented by structured patient and caregiver interviews. Variables collected included: age, gender, occupational status, marital status, educational attainment, number of dependents, mechanism of injury, history of opioid or other substance use, and prior psychiatric treatment history. Clinical parameters obtained from acute hospitalization records encompassed: date of injury, initial post-resuscitation GCS score, duration of intensive care unit (ICU) admission, and cranial computed tomography (CT) findings.

2.3.2. Neuroimaging Assessment

All patients underwent non-contrast cranial CT imaging upon initial hospital presentation. CT scans were retrospectively

reviewed by a board-certified radiologist blinded to psychiatric outcome data. Lesions were classified according to: (1) anatomical localization (frontal, temporal, parietal, occipital, or multifocal involvement); and (2) pathological type (contusion, intracerebral hemorrhage, extra-axial hemorrhage (subdural, epidural, or subarachnoid), diffuse axonal injury, or scalp injury without intracranial extension).

2.3.3. Psychiatric Assessment

Psychiatric evaluation was conducted by a trained research clinician under the direct supervision of an experienced attending psychiatrist (M.T.). Diagnostic determinations were rendered using structured clinical interviews that adhered to the diagnostic criteria specified in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (15).

Pre-morbid cognitive functioning was estimated through a clinical interview with first-degree relatives regarding the patient's prior occupational, educational, and daily functioning. We acknowledge that formal pre-injury neuropsychological testing was not available. Post-concussion syndrome (PCS) was diagnosed using the DSM-5 Section III criteria, which require persistent cognitive, somatic, and affective symptoms following TBI. We acknowledge that PCS is not a formal DSM-5 disorder; however, we included it given its clinical relevance and frequent use in TBI literature. Alternative ICD-10 criteria yield comparable prevalence estimates.

For cases presenting with prominent cognitive complaints, definitive diagnostic adjudication was deferred for up to 12 months post-injury to permit resolution of acute posttraumatic confusional states and to ascertain the persistence and functional impact of cognitive deficits. Patients without initially evident cognitive sequelae were followed on an outpatient basis for at least 3 months to confirm diagnostic stability. In diagnostically complex or ambiguous cases, a multidisciplinary psychiatric commission convened formal adjudication to establish consensus diagnoses. The interval between index injury and final psychiatric evaluation was documented for all participants.

2.4. Data Collection Procedures

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA). Cramér's V for categorical comparisons, Cohen's h for proportional differences, and risk ratios (RR) with 95% confidence intervals (CI) for key binary outcomes. For logistic regression, Nagelkerke R^2 is reported. Variance inflation factor (VIF) was checked; all VIFs were <2.5, indicating no significant multicollinearity. Covariates (age, gender, initial GCS, presence of focal lesion, pre-injury psychiatric history) were selected a priori based on published literature. Missing data were minimal (<3% for any variable) and handled by complete-case analysis. No imputation was performed. Given exploratory subgroup analyses, the Bonferroni-corrected threshold would be $p < 0.008$. Uncorrected p-values are reported with explicit caveats. Descriptive statistics are presented as mean ± standard deviation (SD) for normally distributed continuous variables and as frequencies with corresponding percentages for categorical variables. Normality of continuous data distributions was assessed using the Shapiro-Wilk test and visual inspection of Q-Q plots. Between-group comparisons for categorical variables were conducted using Pearson's chi-square (χ^2) test or Fisher's exact test when expected cell frequencies were less than five. Independent-samples t-tests were used to compare continuous variables between two groups. Multivariate binary logistic regression was performed to identify independent predictors of psychiatric outcomes, with covariates

selected based on theoretical relevance and univariate p-values < 0.10. Odds ratios (OR) are reported with corresponding 95% confidence intervals (CI). A two-tailed p-value < 0.05 was considered statistically significant for all analyses.

3. Result

3.1. Demographic and Clinical Characteristics

The study cohort comprised 113 patients with documented traumatic brain injury, of whom 92 (81.4%) were male, and 21 (18.6%) were female, yielding a male-to-female ratio of 4.4:1. The mean age of participants was 36.5 ± 18.4 years (range: 14–78 years). The mean number of children per participant was 2.0 ± 2.5, and the mean duration of ICU hospitalization was 15.2 ± 17.5 days. The mean initial post-resuscitation Glasgow Coma Scale score was 9.3 ± 3.5, consistent with moderate TBI severity across the cohort. The median interval between index injury and final psychiatric evaluation was 13 months (interquartile range: 6–18 months).

Sociodemographic and clinical characteristics of the study population are summarized in Table 1. Briefly, the majority of patients were married (61.9%), self-employed (28.3%), and had sustained their injuries in traffic-related collisions (84.1%). Primary school education was the modal educational attainment (33.6%). The vast majority of participants (85.5%) reported no history of opioid use. Notably, only 36.5% of the cohort had received any formal psychiatric evaluation or treatment prior to their forensic medicine referral. Of the 41 patients with prior psychiatric consultation, 18 (43.9%) met criteria for the same disorder post-injury (exacerbation). In contrast, 23 (56.1%) developed new incident disorders.

Table 1. Demographic and Clinical Characteristics of the Study Cohort (N = 113)

Characteristic		Value
Age (Years), Mean ±SD		36.5±18.4
Gender, n (%)	Male	92(81.4%)
	Female	21(18.6%)
Occupational status, n (%)	Student	11(9.7%)
	Housewife	11 (9.7%)
	Self-Employed	32 (28.3%)
	Manual Worker	20 (17.7%)
	Military Personnel	1(0.9%)
	Retired	8 (7.1%)
	Unemployed	23 (20.4%)
	Employee	6 (5.3%)

Marital status, n (%)	Single	39 (34.5%)
	Married	70 (61.9%)
	Divorced	4 (3.5%)
Educational Attainment, n (%)	Illiterate	13 (11.5%)
	Primary School	38 (33.6%)
	Elementary School	29 (25.7%)
	High School	24 (21.2%)
	Associate/Bachelor's Degree	7 (6.2%)
	Master's Degree or Higher	1 (0.9%)
Mechanism of Injury	Traffic Accident	95 (84.1%)
	Occupational Injury	11 (9.7%)
	Intrapersonal Violence	7 (6.2%)
Opioid Use, n (%)	Yes	12 (10.6%)
	No	97 (85.5%)
	Unknown	4 (3.5%)
Prior Psychiatric Consultation	Yes	41 (36.5%)
	No	72 (63.7%)
ICU Hospitalization (Days), Mean ± SD		15.2±17.5
Initial GCS Score, Mean ± SD		9.3±3.5
Injury-to-Evaluate Interval (Months), Mean ± SD		13.0±8.8
Injury-to-Evaluate Interval (Months) (Median (IQR)		13 (6-8)

Abbreviations: SD, standard deviation; ICU, intensive care unit; GCS, Glasgow Coma Scale.

3.2. Neuroimaging Findings

Cranial computed tomography findings are presented in Table 2 (anatomical localization) and Table 3 (pathological classification). Notably, 47 patients (41.6%) exhibited no radiologically discernible focal parenchymal injury on initial CT imaging. Among those with identifiable intracranial pathology, the temporal lobe was the most frequently affected anatomical region (16.8%), followed by the frontal lobe (15.0%) and frontotemporal regions (7.1%). With respect to pathological subtype, cerebral contusion constituted the most prevalent finding (26.5%), followed by scalp injury without intracranial extension

(23.9%) and combined contusion with extra-axial hemorrhage (17.7%). No statistically significant differences in neuroimaging findings were observed between male and female participants ($p > 0.05$ for all comparisons)(Table 4).

Table 2. Anatomical Localization of Brain Injury on Admission Computed Tomography

Lesion Localization	Male (n= 92)	Female (n= 21)	Total (n=113)
No discernible parenchymal lesion	38 (41.8%)	9 (42.9%)	47 (41.6%)
Frontal lobe	12 (13.2%)	5 (23.8%)	17 (15%)
Temporal lobe	15 (16.5%)	4 (19%)	19 (16.8%)
Parietal lobe	5 (5.5%)	0 (0%)	5 (4.4%)
Occipital lobe	1 (1.1%)	0 (0%)	1(0.9%)
Frontotemporal	7 (7.7%)	1(4.8%)	8 (7.1%)
Tempoparietal	4 (4.4%)	1 (4.8%)	5 (4.4%)
Frontoparietal	5 (5.5%)	1(4.8%)	6 (5.3%)
Frontotemporoparietal	4 (4.4%)	0 (0%)	4 (3.5%)
Overall Comparison	Effect size: Cramér's V = 0.12 p = 0.94		

* Pearson's chi-square test comparing the distribution across all anatomical categories between genders.

Table 3. Pathological Classification of Traumatic Brain Injury on Admission Computed Tomography

Pathological Finding	Male (n=92)	Female (n=21)	Total (n=113)
Contusion	24 (26.4%)	6 (28.6%)	30 (26.5%)
Scalp Injury Only	19 (20.9%)	8 (38.1%)	27 (23.9%)
Contusion + Extra-axial hemorrhage	15 (16.3%)	5 (23.8%)	20 (17.7%)
Extra-axial hemorrhage only (SAH, SDH, and EDH)	14 (15.2%)	0 (0%)	14 (12.4%)
Intracerebral + Extra-axial hemorrhage	8 (8.7%)	0 (0%)	8 (7.1%)
Diffuse Axonal Injury (DAI)	4 (4.3%)	0 (0%)	4 (3.5%)
Intracerebral Hemorrhage (ICH/ IVH)	4 (4.3%)	0 (0%)	4 (3.5%)
Contusion + Intracerebral hemorrhage	2 (2.2%)	2 (9.5%)	4 (3.5%)
Extra-axial hemorrhage + DAI	1(1.1%)	0 (0%)	1 (0.9%)
Overall Comparison	Effect size: Cramér's V = 0.28 p = 0.12		

* Pearson's chi-square test comparing the distribution across all pathological categories between genders.
Abbreviations: SAH, subarachnoid hemorrhage; SDH, subdural hematoma; EDH, epidural hematoma; ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; DAI, diffuse axonal injury.

3.3. Psychiatric Outcomes

Table 4. Frequency Distribution of DSM-5 Psychiatric Diagnoses

Psychiatric Diagnosis	Male (n= 92)	Female (n= 21)	Total (n=113)
Neurocognitive disorder due to TBI	21(22.8%)	5 (23.8%)	26 (23%)
Major Depressive Disorder	18 (19.6%)	4(19%)	22 (19.5%)
Personality Change due to TBI	13 (14.1%)	2 (9.5%)	15 (13.3%)
Post-Concussion Syndrome (DSM-5, section Ⅲ)	14 (15.2%)	1 (4.8%)	15 (13.3%)
Personality Change + Neurocognitive Disorder (Comorbid)	11(12%)	3 (14.3%)	14 (12.4%)
Adjustment disorder	3 (3.3%)	2 (9.5%)	5 (4.4%)
Anxiety Disorder (GAD/ PTSD)	2 (2.2%)	2 (9.5%)	4 (3.5%)
Malingering	3 (3.3%)	1(4.8%)	4 (3.5%)
Depressive disorder + Neurocognitive Disorder	2 (2.2%)	0 (0%)	2 (1.8%)
Psychotic disorder + Neurocognitive Disorder	2(2.2%)	0(0%)	2(1.8%)
Conversion disorder	1(1.1%)	0(0%)	1 (0.9%)
Major Depression + Conversion Disorder	0 (0%)	1(4.8%)	1 (0.9%)
Anxiety Disorder + Neurocognitive Disorder	1(1.1%)	0 (0%)	1 (0.9%)
Delirium	1(1.1%)	0 (0%)	1(0.9%)
Overall Comparison	Effect size: Cramér's V = 0.23 p = 0.53		

* Pearson's chi-square test comparing the distribution of psychiatric diagnoses between genders.
Abbreviations: TBI, traumatic brain injury; GAD, generalized anxiety disorder; PTSD, posttraumatic stress disorder.

3.4. Exploratory Analysis: Lesion Localization and Psychiatric Phenotype

An exploratory subgroup analysis was conducted to examine potential associations between specific neuroanatomical lesion localizations and particular psychiatric outcomes (Table 5). Although limited subgroup sample sizes constrained formal statistical comparisons, several clinically informative trends emerged. Patients with frontal lobe involvement demonstrated a numerically higher frequency of trauma-induced personality change relative to those without frontal injury (29.4% vs. 10.5%, Fisher's exact p = 0.078). Temporal lobe pathology was associated with a modest, non-significant elevation in the frequency of neurocognitive disorder (31.6% vs. 21.3%, p = 0.37). Notably, among the 47 patients with normal CT findings, 44.7% received a diagnosis of either neurocognitive disorder or major depressive disorder, underscoring the substantial psychiatric morbidity that occurs independent of radiologically apparent structural brain injury.

Table 5. Association Between Lesion Localization and Selected Psychiatric Outcomes.

Lesion Localization	Personality Change (n= 92)	Neurocognitive Disorder (n= 42)	Major Depression Disorder (n=22)
Frontal Lobe Involved (n = 17)	5 (29.4%)	5 (29.4%)	3 (17.6%)
Frontal Lobe Not Involved (n = 96)	10 (10.5%)	21 (21.9%)	19 (19.8%)
ARD	18.9%	7.5%	- 2.2%
RR (95% CI)	2.80 (0.98-7.99)	1.34 (0.58-3.12)	0.89 (0.29-2.70)
Cramér's V	0.21	0.07	0.02
P-value (Fisher's exact)	0.078	0.53	1.00
Temporal Lobe Involved (n = 19)	2 (10.5%)	6 (31.6%)	3 (15.8%)
Temporal Lobe Not Involved (n = 94)	13 (13.8%)	20 (21.3%)	19 (20.2%)
P-value (Fisher's exact)	1.00	0.37	1.00
No Parenchymal Lesion (n = 47)	7 (14.9%)	10 (21.3%)	11 (23.4%)

***Note:** The "Personality Change" group includes patients with isolated personality change (n = 15) and personality change with comorbid neurocognitive disorder (n = 14). The "Neurocognitive Disorder" group includes isolated neurocognitive disorder (n = 26), neurocognitive disorder with personality change (n = 14), and neurocognitive disorder with other comorbidities (n = 2). Six exploratory comparisons were conducted. Using Bonferroni correction, the threshold for statistical significance would be $p < 0.008$. None of the reported p-values meet this threshold.

3.5. Multivariate Analysis

Multivariate binary logistic regression analysis was performed to identify independent predictors of any psychiatric diagnosis (given that 100% of the cohort received at least one diagnosis, this analysis focused on predictors of neurocognitive Disorder and major depressive Disorder as the primary outcomes of interest). After adjusting for age, gender, initial GCS score, and presence of focal parenchymal lesion on CT, and pre-injury psychiatric history, gender was not identified as a significant independent predictor of either neurocognitive disorder (adjusted OR = 1.24, 95% CI: 0.48–3.21, p = 0.66) or major depressive disorder (adjusted OR = 0.91, 95% CI: 0.31–2.68, p = 0.86). Nagelkerke $R^2 = 0.09$ for the neurocognitive model and 0.07 for the depression model.

Similarly, the initial GCS score demonstrated no independent association with the development of neurocognitive disorder (adjusted OR = 0.97 per 1-point increase, 95% CI: 0.86–1.09, p = 0.61) or major depression (adjusted OR = 1.02, 95% CI: 0.90–1.15, p = 0.75) in this forensic cohort.

4. Discussion

The present investigation characterized the frequency and typology of DSM-5 psychiatric diagnoses in a longitudinal forensic cohort of 113 Iranian TBI survivors, with a particular focus on elucidating potential associations between neuroanatomical lesion localization and specific psychopathological outcomes. Several salient findings warrant detailed consideration.

4.1. Prevalence and Pattern of Psychiatric Morbidity

The observation that 100% of participants received at least one psychiatric diagnosis approximately 13 months post-injury is striking but must be interpreted within the medicolegal context. This figure substantially exceeds general TBI cohort estimates (45–

65%) and likely reflects referral bias, incentive effects, and the absence of performance validity testing, rather than true population prevalence (16-17). The discrepancy between our findings and these prior estimates likely reflects the unique characteristics of our forensic cohort—individuals specifically referred for medicolegal disability evaluation. Such patients may differ systematically from the broader TBI population with respect to injury severity, motivation for symptom reporting, and access to mental health services (13). Moreover, the structured DSM-5 clinical interview methodology employed in our study, which systematically assesses a comprehensive range of psychopathology, may enhance diagnostic sensitivity relative to screening instruments or medical record review alone.

Consistent with prior investigations, neurocognitive Disorder and major depressive Disorder emerged as the predominant psychiatric sequelae in our cohort. The 23.0% prevalence of neurocognitive disorder aligns reasonably with meta-analytic estimates, suggesting that approximately 20–30% of moderate-to-severe TBI survivors experience persistent cognitive impairment sufficient to warrant a formal DSM-5 diagnosis (18). The 19.5% prevalence of major depressive disorder is similarly congruent with a systematic review by Scholten et al., which documented pooled depression prevalence estimates of 17% in the first year post-TBI and 43% in long-term follow-up (19).

4.2. The "Normal CT" Paradox: Psychiatric Morbidity Without Structural Injury

A particularly noteworthy finding is the substantial psychiatric morbidity among patients with normal admission CT scans. Over 40% of our cohort had no radiologically discernible focal parenchymal injury, yet 44.7% of these patients received diagnoses of neurocognitive Disorder or major depressive Disorder. This observation underscores a critical clinical imperative: the absence of macroscopic structural injury on conventional neuroimaging does not preclude significant psychopathology. Mechanisms may include occult diffuse axonal injury, neuroinflammation, and psychological factors (20-23).

4.3. Lesion Localization and Psychiatric Phenotype: Emerging Trends

Our exploratory analysis of lesion-symptom relationships revealed a trend-level association between frontal lobe involvement and trauma-induced personality change (29.4% vs. 10.5%, $p = 0.078$, RR=2.80). However, the effect size (Cohen's $h = 0.48$) suggests a moderate association that warrants investigation in larger, adequately powered samples. This observation is biologically plausible and consistent with established neuroanatomical models implicating prefrontal cortical circuits in executive function, impulse control, and social comportment (24). The ventromedial prefrontal cortex and orbitofrontal cortex, in particular, have been consistently implicated in the pathogenesis of acquired sociopathy and disinhibited behavior following TBI (25). Although our subgroup sample sizes precluded definitive statistical inference, the magnitude of the observed difference suggests that frontal lobe pathology may nearly triple the risk of post-TBI personality change.

The absence of a robust statistical association between temporal lobe pathology and neurocognitive disorder (31.6% vs. 21.3%, $p = 0.37$) was somewhat unexpected, given the well-established role of medial temporal lobe structures—particularly the hippocampus and entorhinal cortex—in declarative memory function (26). Several factors may account for this null finding. First, the heterogeneity of temporal lobe pathology within our cohort (encompassing both lateral and medial

structures) may have obscured region-specific effects. Second, the retrospective classification of lesion localization based on admission CT scans lacks the anatomical precision of research-grade MRI with volumetric analysis. Third, neurocognitive Disorder following TBI is typically multifactorial in etiology, reflecting the cumulative impact of diffuse axonal injury, secondary ischemic injury, and neuroinflammatory processes in addition to focal parenchymal damage (27).

4.4. Gender as a Non-Predictor of Psychiatric Outcome

Consistent with our multivariate analysis, gender was not identified as an independent predictor of psychiatric morbidity in this cohort. However, post hoc power analysis revealed only 32% power to detect a small-to-medium effect; thus, the null finding may reflect a Type II error rather than true equivalence. This finding diverges from some prior investigations that have documented female gender as a risk factor for post-TBI depression and anxiety (28), while aligning with others that have failed to detect significant gender differences (29). Several potential explanations for this discrepancy warrant consideration. First, the substantial male predominance in our cohort (81.4%) may have limited statistical power to detect gender-specific effects of modest magnitude. Second, the forensic context of our study may have introduced selection biases that differentially influence referral patterns for male versus female TBI survivors. Third, sociocultural factors specific to the Iranian context—including gender differences in social support availability, illness attribution, and healthcare-seeking behavior—may modulate the relationship between gender and post-TBI psychiatric outcomes in ways that differ from Western populations (30).

4.5. Clinical and Public Health Implications

Our findings carry several implications for clinical practice and health policy. First, the preponderance of traffic-related injuries (84.1%) underscores the urgent public health imperative for enhanced road safety interventions in Iran, including stricter enforcement of traffic regulations, improved vehicle safety standards, and sustained public education campaigns promoting safe driving practices. Second, the substantial burden of undiagnosed psychiatric morbidity in our cohort—evidenced by the fact that fewer than 40% of patients had received prior psychiatric consultation despite uniformly meeting diagnostic criteria—highlights critical gaps in the post-TBI care continuum. We advocate for the integration of systematic mental health screening and referral pathways into routine follow-up protocols for all TBI survivors, regardless of injury severity or neuroimaging findings. Third, the complex interplay between cognitive, affective, and personality disturbances documented in our cohort suggests that optimal post-TBI psychiatric care necessitates a multidisciplinary approach incorporating psychiatry, neuropsychology, occupational therapy, and social work services.

4.6. Limitations and Future Research Directions

Several methodological limitations of the present investigation must be explicitly acknowledged. First, the retrospective cohort design precludes definitive causal inference; unmeasured factors, including pre-injury psychiatric history, genetic vulnerability, and post-injury psychosocial stressors, may confound the observed associations. Second, recruiting participants exclusively from a forensic medicolegal setting introduces substantial selection bias. Patients seeking disability compensation may differ systematically from the general TBI population with respect to symptom reporting behavior, motivation, and illness attribution. Consequently, our prevalence estimates may not generalize to non-forensic

TBI cohorts. Third, the temporal gap between data collection (2020–2022) and the present analysis introduces potential historical bias; advances in neuroimaging technology, acute TBI management, and psychiatric diagnostic practices over the intervening period may limit the contemporary applicability of our findings. Fourth, the reliance on admission CT imaging rather than research-dedicated MRI with advanced sequences (e.g., diffusion tensor imaging, susceptibility-weighted imaging) likely underestimates the true burden of structural brain injury, particularly microstructural white matter pathology and microhemorrhages. Fifth, the modest sample size (N = 113) constrained statistical power for subgroup analyses, particularly for less prevalent psychiatric diagnoses and for multivariate modeling. Sixth, the absence of pre-injury psychiatric data precludes the distinction between incident post-TBI disorders and exacerbations of pre-existing conditions. Seventh, the single-center design may limit the generalizability of our findings to other geographic regions and healthcare systems. Last but not least, no performance validity tests (PVTs) or symptom validity tests (SVTs) were administered. In forensic samples, symptom exaggeration rates typically range from 30–50%, and our observed malingering diagnosis rate of 3.5% likely underestimates this phenomenon. Consequently, prevalence estimates for certain disorders (particularly neurocognitive and depressive disorders) may be inflated by incentive effects associated with disability seeking. Future forensic TBI studies should routinely incorporate PVTs/SVTs.

Future investigations should endeavor to address the limitations enumerated above. Prospective, multi-center cohort studies incorporating comprehensive pre-injury psychiatric phenotyping, advanced multimodal neuroimaging, and extended longitudinal follow-up are urgently needed to delineate the trajectory of post-TBI psychopathology and to identify modifiable risk and resilience factors. The integration of fluid biomarkers (e.g., neurofilament light chain and glial fibrillary acidic protein) and genetic markers into predictive models may enhance risk stratification and facilitate personalized treatment. Finally, intervention studies evaluating the efficacy of integrated, multidisciplinary care models for post-TBI psychiatric sequelae represent a high-priority research domain.

5. *Conclusion*

In this longitudinal analysis of 113 Iranian TBI survivors undergoing forensic psychiatric evaluation, neurocognitive Disorder and major depressive Disorder were the predominant psychiatric sequelae. Notably, a substantial proportion of psychiatric morbidity occurred in the absence of radiologically evident structural brain injury—the "normal CT paradox"—underscoring the importance of psychiatric surveillance following TBI irrespective of neuroimaging findings. These findings are limited to a forensic medicolegal cohort and do not generalize to the general TBI population. Frontal lobe involvement showed a moderate but non-significant association with personality change (RR = 2.80, p = 0.078), requiring replication in larger samples. Gender was not an independent predictor, although power was limited. Systematic mental health screening should be integrated into post-TBI care pathways for forensic referrals, regardless of CT findings.

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Data Availability Statement: The data supporting the findings of this study are available from the Legal Medicine Organization of Khorasan Razavi. However,

access is restricted and used under ethical approval for the current study. De-identified data are available from the corresponding author upon reasonable request and with permission of the Legal Medicine Organization.

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Ethical Approval: This study was approved by the Medical Ethics Committee of Mashhad University of Medical Sciences (Approval Code: IR.MUMS.REC.P941366). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments, or with comparable ethical standards. Written informed consent was obtained from all individual participants included in the study.

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