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Identifying Risk Factors for Incidence of Mental Disorders after Traumatic Brain Injury

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Abstract

***Background*:** Organic brain pathology usually may be followed by mental disorders. This research was aimed at constructing a predictive model and investigating the risk factors in the incidence of mental disorders after traumatic brain injury (TBI).

***Materials and Methods*:** Two hundred and thirty eight patients (195 males and 43 females) were entered the study in a descriptive-longitudinal design by non-probable and consecutive sampling method. They were undergone neurosurgical examinations and psychological evaluations. After a 4-month follow-up, 65.1% of the patients (N=155) referred to a psychiatrist in order to determine the nature of mental disorder following TBI, using a structured clinical interview based on DSM-IV diagnostic criteria.

***Results*:** 75.48% (117 cases) of patients had a form of mental disorder secondary to TBI. The Results of binary logistic regression analyses for calculating odds ratio (OR) model with 95% confidence interval (CI) indicating the severity of TBI (OR=3.497, 95% CI =1.259-9.712), presence of subcranial injury (OR=2.834, 95% CI =1.022-7.857) and falling level of general compatibility, as measured by modified version of GHQ-28 (OR=1.072, 95% CI =1.035-1.111) indicated an increasing risk in the incidence of mental disorder.

***Conclusion*:** Findings revealed that in the development of post-TBI mental disorders, first there was a close relationship with organic brain pathology (TBI severity and subcranial injury), although the role of effective psychological factors such as level of general compatibility after trauma should not be neglected. Also in order to predict the people at risk of mental disorders after TBI, the proposed predictive model in this study can be used.

Introduction

TBI (Traumatic Brain Injury) is one of the most important causes of death and long-lasting disabilities in 35-year-olds and younger people. According to recent estimations, about eighty to ninety thousands of people live with prolonged disability following TBI. 5% of those injuries lead patients to death. 14% of them might remain moderate or severe; others are mild injuries [1, 2]. Remarkable advances in head trauma surgeries, medical services plus improvement in caring system of traumatized patients in recent decade in Iran have led to increasing rate in survival and recovery of TBI survivors. However, considerable cognitive and psychological deficits still remain for many patients-particularly for those experiencing moderate to severe trauma. Reviewing previous researches, it was found that individuals with TBI manifest a set of physical, physiological and neurological deficits and mental symptoms of disorders in days and weeks following trauma. Although majority of serious physical and medical problems decrease and stabilize within the first months and rehabilitation period, Hoofien, et al. [3], Fann et al. [4] and Koponen et al. [5, 6] have demonstrated that a remarkable percentage of patients show some signs of mental disorders for years and even decades after TBI. This issue may in its own contribute to being chronically handicapped which is unfortunately not considered and treated appropriately most often, due to its complicated nature of biopsychosocial dimensions. Systematic studies about TBI are commonly difficult, since trauma mechanisms can cause focal or diffuse brain injury and result in incongruent clinical manifestations [7]; therefore, most of researches focused on identifying the nature and effect of cognitive and physical outcomes secondary to TBI. In this regard, surveys about mental disorders following TBI are in primary stages and have a long way to proceed. Although most of the clinicians have obviously realized the implicit effect of behavioral and personality changes following TBI, few studies have comprehensively and objectively surveyed the nature of factors predicting post-TBI mental disorder incidence. With examining the recent related researches [8-18] Table 1 shows methodological points and overall results of the investigation of risk. factors for mental disorders in term of brain injury severity, range of disorders, diagnostic tools and disorder determination criterion in patients with traumatic brain injury. In general, the nature of

psychopathological aspects of TBI, are very complicated and in this study in accordance with previous studies, it is assumed that the interaction of some different variables, e.g demographic and biomedical factors may contribute to those aspects. In current study, it was hypothesized that valuable guidelines may be offered with an integrated and interdisciplinary approach in a biopsychosocial paradigm to both identifying risk factors and enhancing general knowledge in Iran. Constructing a predictive model which could be able to identify individuals at high risk of mental disorders can be thought as another main purpose of recent study

Materials and Methods

This research was a descriptive-longitudinal study, which accomplished after obtaining ethical approval in cooperation with Trauma Research Center in Guilan University of Medical Sciences, in Poursina hospital, Rasht (north of Iran). In this research which lasted since April to February 2010, TBI patients were enrolled in study after obtaining informed written consent forms by non-probable and consecutive sampling method having both inclusion and exclusion criteria. Using binominal logistic regression and odd ratio, according to Hosmer & Lemeshow sample size formula [19], the highest sample size was caculated as 188, with 80% statistical power, and 0.05 significance level. In order to control the drop-out in number of subjects after the follow-up period, a 25% drop-out was added to the sample size and the total number of patients to study reached 238.

Inclusion criteria: Participants were 18 years old or older. The consciousness level score was < 15 based on GCS score; a focal or diffuse injury of brain tissue due to an external mechanical force.

a) Loss of Consciousness for more than 1 minute was witnessed, b) The duration of post-traumatic amnesia was more than 20 minutes, c) Having radiographic or CT findings suggesting TBI (e.g. skull fracture, intracranial hemorrhage or acute brain abnormalities), d) The patients had headache, dizziness or nausea continuously for 3 days despite of GCS=15, e) Exclusion criteria, f) Patients who had spinal cord injury based on clinical or radiological findings, g) Presence of any type of neurological diseases before TBI or brain injury with no traumatic causes such as brain tumors, stroke, aneurismal and other brain vascular incidences, h) Patients had vegetative state or severe LOC so that were unable to answer interviewers, i) Patients who were not able to give consent to enter the study for any reason.

Research tools: 1) A researcher-made questionnaire based on hospital and demographic information which included age, gender, marital status, level of education, urban or rural status, the cause of TBI and history of post-TBI operation, job status after TBI, duration of confinement in different sections of hospital, LOC duration, presence of litigation due to TBI, smoking history before TBI (for more than 6 months), linguistic deficit due to TBI and physical damage accompanying TBI.

2) The researcher-made questionnaire based on neurological evaluation and organic brain pathology, which was made to obtain the following information: patient's consciousness after 3 hours since admission according to GCS, the overall disability level of patient at discharge time according to GOS (Glasgow Outcome Scale), type of skull fracture with respect to skull radiographic images, hemispheric side of lesion, the location of brain injury and type of focal or diffuse brain injury regarding computerized tomography (CT scan) and presence of physical trauma with TBI.

3) In current study, Visual Analog Scale (VAS) was used to assess the pain severity related to head injury.VAS is an acceptable method for clinical researchers to evaluate majority scopes of clinical pains. VAS consists of a 100mm horizontal line with a "no pain" phrase written on one side and "worst possible pain" on the other side. The patient, who has headache most of the times after TBI, marks on the 100 mm continuum of this straight line. Then, by using a scale ruler and estimating the distance between patient's mark and zero point of continuum, the severity of pain is estimated. This scale is widely used in recent researches on pain and its validity and reliability have been already confirmed [20-22]. This scale has also been utilized successfully in Ofek and Defrin's [23] study on TBI patients.

4) Oklahoma Premorbid Intelligence Estimate (OPIE) algorithm: in order to estimate the premorbid intelligence functioning level in TBI patients in present study, the algorithm of intelligence quotient prediction from full scale IQ (FSIQ) was used as follow:

FISQ= 53.80+0.10 (age) + 0.64 (educ) - 1.73 (race) - 0.51 (occup) + 0.57(vocabulary raw score) + 1.33 (picture completion raw score).

Krull et al. [24] demonstrated a high correlation between predicted FSIQ, VIQ (verbal IQ), PIQ (performance IQ) and the cross-validation ones from standardization sample of WAIS-R (Wechsler adult intelligence scale-revised) which were 0.86, 0.87, and 0.79, respectively. Furthermore, the true values of FSIQ belonging to 91.4% of subjects were predicted with a 95% CI. Finally these researchers proposed that their combined approach is applicable for estimating premorbid intelligence functioning in patients with focal, lateral and diffuse brain tissues and also psychiatric patients. A combination of two subtests including vocabulary and picture completion from Wechsler adult intelligence scale, were used to obtain the score.

5) In this research, MMSE was used to estimate cognitive deficit in TBI patients. This examination is a brief instrument for general assessment of cognitive functioning. This test evaluates orientation, memory, calculation, reading and writing ability, visual-spatial and language ability. MMSE is widely used as a simple and quick means for possible cognitive deficit evaluation [25]. Reviewing psychometric characteristics of this instrument, Rosselli [26] mentioned that other researchers have reported 0.69 to 0.95 for inter-rater reliability values and 0.85 to 0.99 for test-retest reliability. MMSE (p 678) . Tateno et al. [12]. Rao et al. [17], also used MMSE

successfully to measure cognitive deficit or functioning of TBI survivors. Here, the rate of internal consistency items of MMSE was also obtained using 0.85 Cronbach's Alpha Coefficient (N=206). Similar to prior studies [5, 27] obtaining 23 or less than the total of 30 scores was used to identify cognitive deficit in TBI patients.

6) In this project, the 28-item modified version for general health questionnaire (GHQ-28) was applied for TBI cases whose psychometric properties were studied by Rezaei et al. [28] to measure the level of general compatibility with TBI outcomes in survivors with symptoms including physical, anxiety and insomnia, social dysfunction and depression. Higher scores in this questionnaire indicate the worsening duration of general compatibility in patients with post-traumatic symptoms. In relevant researches, including Deb et al., [27]; Middelobe et al, [29]; Feinestein et al, [30] GHQ-28 has been used; however, none of them calculated either the validity, reliability, clinical cut-off point in TBI patients or factor structure; thus Rezaei, et al. [28] analyzed the data relevant to modified version of GHQ-28 in 192 TBI individuals using Exploratory Factor Analysis (EFA) and Principal Component Analysis (PCA). The results with an eigenvalue more than 1 using Oblimin Rotation method extracted four factors: these researchers reported a 40 cut-off point, 0.72 sensitivity, and 0.57 specificity by means of Likert Scoring method (0-1-2-3). Furthermore, Cronbach's Alpha Coefficients for four subtests i.e.
physical symptoms, anxiety and insomnia, social dysfunction and depression subscales were 0.81, 0.78, 0.91 and 0.86, respectively. The rate of internal consistency of all test items and reliability coefficient were calculated 0.92 and 0.81, respectively.

7) Checklist of clinical structured interview based on DSM-IV diagnostic criteria: in current study, we used this checklist which was prepared and developed by Noorbala et al. [31] to determine the nature of different types of axis I mental disorders post-TBI. This checklist includes 149 mental disorder symptoms consisting of mood, anxiety, psychotic, psychosomatic disorder symptoms, seizure, mental retardation and organic brain disorders. This symptoms are as "yes, no" and at the beginning of questioning symptoms of each part, the duration and severity of disorders were asked. Severity scoring of symptoms according to a 3-graded scale i.e. mild, moderate, and severe which is identified by interviewer based on the effect of disease on personal, vocational, educational, family and social functions. After interview and checking all symptoms and signs of cited disorders in checklist, regarding diagnosis are recorded considering severity and history of symptoms in patient. Noorbala et al. [31] interviewed 30 patients, who referred to psychiatry clinic of Rouzbeh Hospital, Separately by two psychiatrists, in order to measure the reliability of diagnoses between psychiatrists using this checklist. These researchers used Kappa coefficient to measure the rate of agreement between the two psychiatrists and reported K=0.87. They finally concluded that the information of this checklist displays the high reliability of this instrument which can be successfully applied in diagnostic assessment of mental disorders.

The patients have been referred from emergency, trauma and neurology wards of Poursina Hospital and medico-legal Department of Guilan Province or physicians of local clinics, and TBI diagnosis of all them was finally confirmed by a neurosurgeon at Imam Reza special Clinic in Rasht. After examining and identifying TBI patients according to inclusion criteria by a neurosurgeon, they were then given hospital information record and psychological tests to fill by a clinical psychologist. Due to the illiteracy of some subjects, all of the questions had been read for them and their oral answers had been registered in the test record sheets. Administration of the tests was usually lasting between 20 to 30 minutes in average. In order to measure the severity of amnesia, Lezak classification criteria [32] was used, which is consisted of 6 categories (very mild, mild, moderate, severe, very severe, and extremely severe). Moreover, for the assessment of amnesia's duration, the method, of Snyder et al. [33] was used, in which they recommend that the duration of post-traumatic amnesia (PTA) have to be measured only based on the patients' real memory of events occurred, not of what being told by caregivers. Therefore, it was clarified for the patients that their own memories which they recall from the past (before and after TBI) is the criterion of accuracy of their response, and not the things that might be told by others about the quality, cause and the duration of their TBI. Then, the patients were asked to refer to a psychiatrist at least 3 months after TBI for further examinations of head trauma. Although this psychiatrist was one of authors, the information of neurological and pathological organic evaluation and psychological assessments were blind for him. Research authorities believed that keeping the neurosurgical and psychological information away, can eliminate or reduce non-blinded outcome, assessment bias or diagnostic suspicion bias. Types of mental disorders were determined using clinical structured interview of a psychiatrist based on DSM-IV diagnostic criteria and if a subject with TBI was also diagnosed to also have mental disorder, then clinical file was recorded and kept for him. To describe the data, the authors have used descriptive statistic indices such as percentage, frequency, mean, standard deviation (Mean±SD) and range. Binary (binominal) Logistic Regression (BLR) was used to predict the incidence of mental disorders, because this dependant variable was recorded in form of presence and absence (0 to 1) and was predicted based on a set of independent variables (in qualitative and quantitative levels). The variable selection in logistic regression was carried out by Forward Likelihood Ratio (Forward LR) method. In this research, in order to find the significance of the effect of other variables on dependant variable, we have used Wald Statistics. Besides, OR statistic (odds ratio) with a 95% confidence interval (CI) was used to find the amount of each variable's effect on dependent variable. Omnibus test which includes χ^2 statistics was also employed to represent the ability and efficiency of

the model, in the other words the rate of goodness-of-fit of logistic regression full model. Hosmer-Lemeshow goodness-of-fit was used to fit the data, and to predict dependent variable changes in an error level smaller than 0.01. As Brace et al. [34] have described, this index is a test for null hypothesis and shows the fitness of model; albeit a good model has a high *p*-value. If it would be less than 0.05, the model does not fit the data [35]. In this research all statistical analyses were performed by SPSS-16.

Results

In the first 9 months of 2010, totally 238 TBI patients (195 male, 43 female) with inclusion criteria underwent neurological and pathological examinations. After referring from neurosurgeon, their demographic characteristics and hospital information were recorded and they were evaluated psychologically. Table 2 shows demographic characteristics of the patients. Mean age of the patients was 36.7±1.7 years with age range of 18-85 at the time of TBI occurrence. Thirty one patients (13%) were illiterate and their information forms were filled by the help of the interviewer and family members, 21 (8.8%) patients had academic education. Nevertheless, the average education level was 7.8±4.25 and range of training years varied from 0 to 18. Figure 1 illustrates the percentage and frequency of causes of TBI. As shown in this graph, car and motorcycle accidents had the highest rate in the figure. Furthermore, 68 (28.57 %) patients had a history of surgery following their TBI. Table 3 displays the mean, SD and length of hospitalization in different wards of hospital and duration of being unconscious or LOC. The data indicates that a TBI patient spends 16.6±45.9 days in average to be recovered. However, some patients were not hospitalized at all, or they might be discharged from hospital after a brief outpatient examination or a simple radiography of skull, while some others might be hospitalized for more than 6 months in different wards (such as ICU, trauma, emergency, internal neurology ward). The mean time of being unconscious or LOC was 1.52±4.04 hrs. On one hand, some patients have had not LOC at all but headaches, dizziness and nausea; on the other hand, some might have a period of being unconscious for 4 to 6 months (180 days) (Table 3). Results also have shown that 146 patients (61.34%) have provided with a letter from forensic medicine department, enabling them to compensate for their casualties following TBI. Twenty one of the patients (8.82%) have complained of post-TBI lingual deficits and 64 (26.89%) patients reported a history of smoking for more than 6 months before TBI.

Moreover, 40 (19%) patients had substance abuse history based on diagnostic DSM-IV-TR criteria of which 36 (90%) patients had abused opium, 3 (0.75%) patients abused hashish and 1 patient (0.25%) abused methamphetamine which is called glass in Persian slang language. Table 4 shows the results of neurosurgical examinations, and findings of neuroimaging techniques including CT scan, and in some cases MRI and skull radiography. According to the data in table 4, most patients (67.2%) had mild TBI and 33 (13.9%) of them had severe TBI while the mean of consciousness level variable was 12.61±3.30 based on GCS and its range was fluctuating between 5 to 15. One hundred and ninety nine patients (83.6%) patients have recovered, yet 9 (3.8%) patients had severe disability at the time of discharge based on GOS. Visible fractures in skull graphs appeared in diverse types with different lesion locations in brain according to CT scans. Meanwhile, frontal lobe injuries (left, right and bilateral) were more than others. It is noteworthy to mention that there was a high rate of multiple or combined lesions in different brain locations or in focal ones, each of which had 11.8% and 12.8% of injuries, respectively. Moreover, 61 (25.63%) patients had also physical trauma accompanying TBI (e.g. orthopedic lesions or related damages following surgery). Psychological interviews indicated that 171 (71.8%) patients developed severe amnesia following TBI, and only 48 patients (20.2 %) have not faced such a problem. Further, it was impracticable to survey the amnesia incidence in 19 (8%) patients due to their high irritability regarding the cause of trauma. In this research, due to a high variation in results of patients' evaluations for the duration of amnesia following trauma, this variable was estimated and recorded in hours and minutes. Therefore, the mean amnesic period was 238.70±639.92 hrs (about 10 days) for 209 patients and between 0-53 days. Also 17 (8.31%) patients still had amnesia during psychological interviews and were not able to recall their family members or relatives. But since they were aware of time and place and could answer the questions consciously, they also took the psychological tests. Four patients did not give their consent for psychological assessment. Table-5 represented the percent and frequency of amnesia severity variable based on Lezak categorization criteria [32] for 209 patients. According to this table, 139 (51.66%) patients out of 209 experienced different degrees of amnesia severity, most of them were severe amnesic, lasting between 1-7 days (22.01%). More than that, based on VAS scale, the mean of pain severity variable related to head injury was estimated 36.54±3.11 mm. Some patients had no headache (0 mm); however, some others reported the severe headache following injury. Figure 2 depicted the variation of estimation rate of pain severity in TBI survivors. Table 5 sums up results of psychological assessments of TBI patients. Conducting MMSE on 206 patients and asserting 23 cut-off point, 96 patients (46.60%) appeared to have cognitive deficit following TBI. After the administration of vocabulary and picture completion subtests form Wechsler's Adult Intelligence Scale-Revised (WAIS-R), its rates with age, education level, race and job variables (as shown in FSIQ) were combined, then intellectual functioning level before TBI was calculated. The mean of GHQ-28 also has shown that most patients compromised with post-trauma symptoms based on Likert scale (46.86 ±15.71). After a 3-month follow-up of 238 patients it was found that only 107 of them have been referred for psychiatric examinations. So, the patients were telephoned twice

during two weeks to be reminded for psychiatric examination. After telephone calls and a month follow-up, 48 other patients also referred for psychiatric examinations. Generally, after an average of 145 ± 53 days (nearly 4 months), 155 (65.1%) of 238 evaluated patients were investigated by structured clinical interview based on DSM-IV diagnostic criteria to determine post-TBI mental disorders. In other words, 99 males and 18 females (63.87% and 11.61% respectively) 4 months following injury have been diagnosed as having a type of mental disorders secondary to TBI, which was not present before the trauma. (For detailed review of axis I psychopathology in first 4 months after TBI, refer to Rezaei et al, [36]. However, the most prevalent mental disorders following TBI were personality change disorder (58.59%), mood disorders (32.26%), anxiety disorders (20%), and sleep disorders (19.34%), chronic amnesic disorder (12.9%) and somatoform disorder (1.29%). Delirium, eating disorder and psychotic disorders due to TBI were also diagnosed to a 0.64% rate. One hundred and fourteen (74%) of 155 patients completed a 4-month follow-up after trauma and underwent psychiatric examination. Their files were analyzed and the files of 41 cases were excluded from regression analysis due to missing values. Results of Omnibus test elucidated that fitting of full model in fourth step is acceptable and significantly reliable (χ^2=31.310, df=4, p<0.001). Considering the result of Hosmer & Lemeshow test in fourth step (χ^2=10.7), goodness-of-fit of predicting dependent variable changes was acceptable in a significant level more than 0.05. This has shown that the fitted model was efficient to predict incidence of mental disorders. As seen in table 6, only 4 of the variables in regression analysis remained in the fourth step, among which only 3 variables: brain injury severity, subcranial injury and the general compatibility level after TBI can predict mental disorder which are able to predict dependent variable after TBI in a level smaller than 0.05.

Table 1. Results summation of risk factors studies of mental disorders in TBI patients

Researchers & year of publication	Sample Size	Sampling source	Brain injury severity	Range of disorders	Diagnostic tools	Disorder determination criterion	Risk factors
Van Reekum et al. [8]	18	Outpatients & patients of rehabilitation center	mild, moderate, severe	Axis 1 & 2	SADS-L	DSM-III	Age and primary severity of TBI
Fujii & Ahmed [9].	25	Hospitalized patients	mild, moderate - severe	Psychosis secondary to TBI	Neuropsychological tests	DSM-IV	Congenital neurological disorders and history of TBI before adolescence
Sachdev et al. [10]	90	Hospitalized patients & outpatients	mild, moderate, severe	Psychosis secondary to TBI	_	DSM-IV	Family history of psychosis and duration LOC
Seel et al.[11]	666	Outpatients	severe	depression	NFI	DSM-IV-R	Unemployment & poverty
Tateno A. et al .[12]	89	Hospitalized patients & outpatients	mild, moderate, severe	Aggression + disorders of axis 1	SCID OAS	DSM-III-R	Major depression, frontal lobe injuries, poor pre-morbid social function, history of alcohol & substance abuse
Golden & Golden, [13].	320	outpatients	mild, moderate, severe	Personality change	MMPI-2 The Haleasted-Retain Test Battery	_	LOC & cognitive impairment
Max et al. [14]	177	Patients of trauma center	mild, moderate, severe	Personality change	DIS	DSM-IV	severity TBI
Bombardier et al. [15]	124	Hospitalized patients & patients of trauma center	mild, moderate, severe	PTSD	PCL-C	DSM-IV	Not completed high school, presence of brain injury, recalling panic feeling or distress & positive drug test
Mainio et al. [16]	103	Records of hospital information	brain lesion or concussion.	Axis 1	According to hospital reports	ICD-8,9,10	TBI Severity, male gender, older age, being unemployed, psychiatric disorders and alcohol
Rao et al. [17]	54	Hospitalized patients & outpatients	mild, moderate, severe	Axis 1& 2	DIS MMSE	DSM-IV	Being non-white, lower scores in MMSE, more severe TBI, more likely to be unemployed after TBI, drug therapy failure
Brenner et al. [18]	96	Hospital information file & medical records	mild, moderate, severe	Substance & alcohol abuse & other symptoms	According to hospital reports	_	History of substance & alcohol abuse

DIS=Diagnostic Interview Schedule, MMPI=Minnesota Multiphasic Personality Inventory, MMSE=Mini-Mental State Examination, NFI=Neurobehavioral Function Inventory, OAS=Overt Aggression Scale, PCL-C=PTSD Checklist–Civilian Version, SADS-L=Schedule for Affective Disorders and Schizophrenia–Lifetime Version, SCID=Structured Clinical Interview for DSM

Table 2. Demographic characteristics of TBI patients (N=238)

Variables	N(%)
Age (yrs)	
18-25	72(30.8)
26-35	52(21.8)
36-45	29(12.2)
46-65	41(17.2)
66-85	17(7.1)
Not clear	27(11.3)
Gender	
Male	195(81.9)
Female	43(18.1)
Marital status	
Single	78(37)
Married	157(61.8)
Divorced	1(0.4)
Widow/widower	2(0.8)
Education level	
Illiterate	31(13)
Elementary school	40(16.8)
Guidance school	59(24.8)
High school	59(24.8)
University	21(8.8)
Not clear	28(11.8)
Habitancy status	
City	102(42.9)
Country	108(4.4)
Not clear	28(11.8)
Job status before TBI	
Professional-specialist	2(0.85)
Middle Manager/clerk/employee/seller	22(9.2)
Craftsman/ repairman/headworker(university student)	51(21.4)
Machine/operator/serviceman/housekeeper/-	91(38.2)
Farmer (student)	31(13)
Simple worker (nonprofessional)	4(1.7)
Unemployed	37(23.87)
Not clear	

Table 3. Mean and SD of length of stay in different wards of hospital and LOC

Variables	Mean± SD	Range
Length of stay (day)		
Intensive care unit	8.21±38.2	0-60
General ward	8.8±16.9	0-150
Overall length of stay	16.6±45.9	0-195
Loss of consciousness (hour)	1.52±4.04	0-180 days

More details about the effect and role of the significant variables in the fourth step are stated hereunder in order to maintain the highest rate of capability in predicting the status of mental disorder incidence. According to table 6, the severity of brain injury was the first variable which had the most significant impact on possibility of post-TBI mental disorder (95% CI: 1.259-9.712, OR=3.497), indicating that 1 unit change (or increase) in this variable, promotes the incidence possibility of mental disorder to 3.497 or nearly to 3.5 (3 and a half) times. After that, as before, the presence of subcranial injury variable (OR: 2.834, 95% CI: 1.022-7.857) obtained from combining values of local and diffuse injuries, had the highest significant effect on incidence of post-TBI mental disorder, i.e. by every 1-unit increase in this variable compared to the individuals who lack any subcranial injury, the incidence of post-TBI mental disorder raises to 2.834 or nearly to 2.5 times. finally, based on table 6, general compatibility level after TBI (OR: 1.072, CI 95%: 1.035-1.111) also significantly affect the possibility of post-TBI mental disorder incidence so, by each 1-unit increase in the rate of scores of the modified version for GHQ-28 (i.e. fall of compatibility) the possibility of mental disorder following TBI grows to 0.61 or more than a half time. Meanwhile, although litigation or compensation claim variable remained in the fourth step, its effect appeared to be a borderline and insignificantly negative. Overall, based on results of the fourth step, in predicting post-TBI mental disorders, the logistic regression model can be inscribed as:

$$Ln\left(\frac{\pi}{1-\pi}\right) = a + \beta_1 X_1 + \beta_1 X_1 + \cdots + \beta_k X_k$$

Logistic regression model = - 3.542 (constant) + 1.252 (brain injury severity)+0.070 (general compatibility level after trauma)+1.042 (presence of subcranial injury). For instance, to predict the chance of mental disorder incidence in a TBI patient according to above model, if a victim with subcranial injury exhibits fall of general compatibility level to 10 and 1 rank increase in brain injury severity, the incidence possibility of mental disorder for him, goes up to 19.96 compared to a person without subcranial injury.

Table 4. Results of neurosurgery examinations and neuroimaging findings of TBI patients

Variables	Frequency N(%)
TBI severity:	
Mild GCS (between 13-15)	160(67.2)
Moderate GCS (between 9-12)	45(18.9)
Severe GCS (8 and lower)	33(13.9)
Level of post-TBI disability	
Good recovery (5 in GOS)	199(83.6)
Moderate disability (4 in GOS)	30(12.6)
Severe disability (3 in GOS)	9(3.8)
Skull fractures	
Linear(simple)	50(21)
Depressed	24(10.1)
Basilar fracture	5 (2.1)
Side of hemisphere injury	
Left	52(21.8)
Right	37(15.5)
Bilateral	52(21.8)
Brain injury site (side of hemisphere)	
Frontal lobe (right)	21(8.8)
Frontal lobe (left)	23(9.7)
Frontal lobe (bilateral)	11(4.6)
Parietal lobe (right)	12(5)
Parietal lobe (left)	15(6.3)
Parietal lobe (bilateral)	0(0)
Temporal lobe (right)	2(0.8)
Temporal lobe (left)	5(2.1)
Temporal lobe (bilateral)	0(0)
Occipital lobes	2(0.8)
Cerebellum	1(0.4)
Brainstem	1(0.4)
Several damaged places	28(11.8)
Focal injury:	
Brain Contusion	30(12.6)
EDH(epidural hematoma)	31(13)
SDH sub dural hematoma)	14(5.9)
SAH(subarachnoid hemmorrage)	3(1.3)
IVH(Intraventricular hemmorrage)	1(0.6)
ICH(Intracerebral hemmorrage)	6(2.5)
Several focal damages	29(12.8)
Diffused injury:	
Edema	14(5.9)
Diffused axonal injury	166.7 ()
DAI+Edema	7(2.9)

Table 5. Findings of psychological evaluations in TBI patients

Variables	Mean±SD	Range
Pain severity related to head injury (VAS)	36.54±3.11	0-100
Mini-mental State Examination (MMSE)	22.74±5.52	0-30
Vocabulary (VOC)	22.04±13.28	2-70
Picture completion (PC)	5.74±3.83	1-19
Oklahoma Pre-morbid Intelligence Estimate (OPIE)	75.85±11.63	58.13-116.09
Post-TBI adjustment level:		
Physical symptoms subscale	12.89±4.54	0-21
Anxiety and insomnia subscale	12.35±4.77	0-21
Social dysfunction subscale	14.25±4.61	2-21
Depression symptoms subscale	7.24±4.54	0-21
The whole questionnaire (GHQ-28)	46.86±15.71	9-84

Table 6. Results of fourth step in binary logistic regression analysis related to risk factors of mental disorders' development after TBI

Variables	B	Wald	Sig	odds ratio (OR)	95% (CI) for odds ratio	
					High	Low
Brain injury severity	1.252	5.768	0.016	3.497	9.712	1.259
Litigation/financial compensation claim	-1.103	3.803	0.051	0.332	1.006	0.110
General compatibility level	0.070	15.036	0.0001	1.072	1.111	1.035
Any subcranial damage	1.042	4.006	0.045	2.834	7.857	1.022

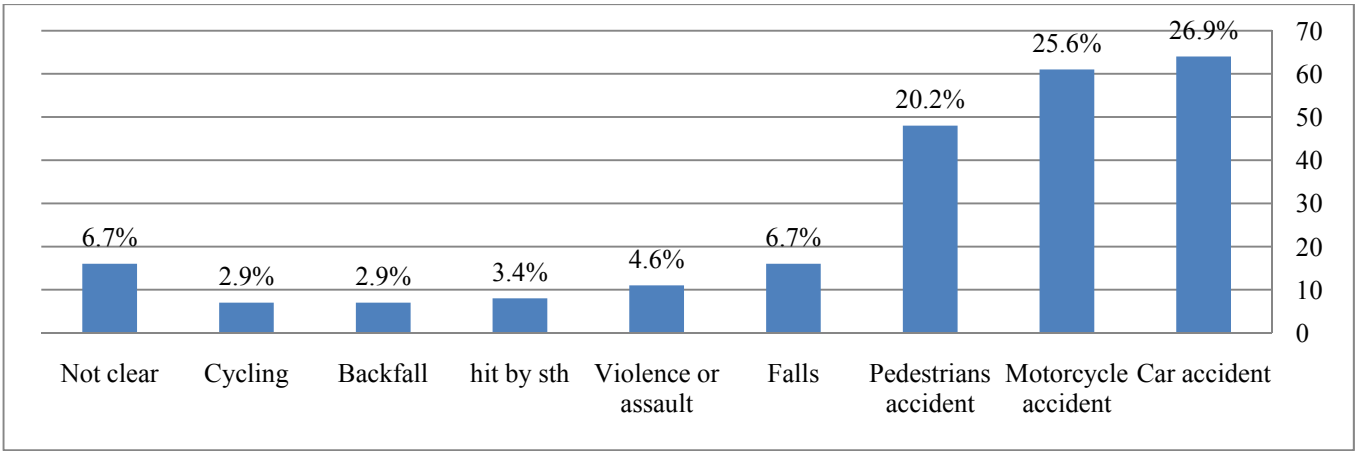

Figure 1. Percentage and frequency of TBI causes

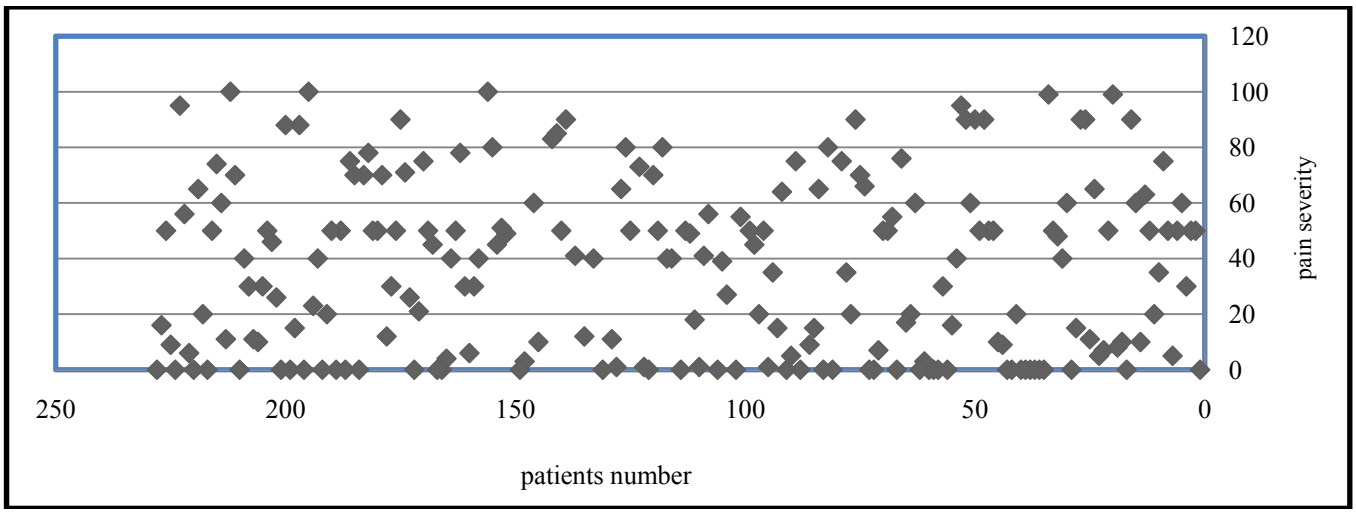

Figure 2. Frequency of pain severity related to head injury in TBI patients

Discussion

The purpose of this research was to detect the effective risk factors in the incidence of mental disorder after TBI; as well as constructing a predictive model by which mental disorder incidence can reliably be predicted after 4- month following brain injury. Since world war II, an increasingly body of knowledge has been gathered in the

area of TBI [37]. As elucidated in present study, the injuries in frontal and temporal lobes are so common in TBI survivors (Table 4). As Granacher [38] have claimed, there are systems, mechanisms and circuits in brain structures which regulate mood and affection; therefore, it is not beyond expectations that traumatic brain-injured victims develop mental disorders. Apparently, this is not a novel issue and it even has been pointed in classic researches in the early 20th century e.g. Kraepelin proposed that focal brain injuries could be the straight reason of depression disorder. Precedingly, Meyer had also declared that injuries to specific regions of brain can be accompanied by special psychopathology [39]. Among all of our variables, founded that TBI severity with the most significant effect on possibility of mental disorder incidence (Table 6). This finding is in accordance with Smith [40] idea who previously suggested that mental disorder incidence and other neuropsychological complications enhance with brain injury severity. Along with this, Van Reekum et al., [8] reached the same result in their effort. In addition, Max et al, [14] also concluded that TBI severity is the mere variable which predicts post-TBI personality change. Mainio et al. [16] discovered a relationship between TBI severity and possibility of suicide. Ultimately, Rao et al. [17] found the post-TBI personality changes correlated with TBI severity. To explain this significant relationship, it can be cited that a more severe TBI inducing more physical, neurological and cognitive disability due to which more extended social limitations may prepare circumstance leading to mental disorders for individuals. In the present research, subcranial injury presence variable as indicated in analysis of risk factors exposed a significant impact on incidence of post-TBI mental disorders. With regard to the finding, is inferred that the group of patients with any sort of subcranial injury (including focal or diffuse) compared to patients without, are predisposed to more mental disorders. It is essentially notable that no research has scrutinized TBI victims with such a method so far, the results of which could be used to compare with those of present project. Results also highlighted that level of general compatibility (GHQ-28) significantly influences the incidence of mental disorders (Table 6). This meaningful link explains that patients with stronger level of general compatibility develop less mental disorders, considering the physical, anxiety and insomnia, social dysfunction and depression averagely 4 months after trauma. The reason of this can more substantially originate from using more adjustment coping styles of some patients after trauma which deems to require further researches from psychological aspect in future. In elucidating this significance it can hint the overlap of mental disorder symptoms and what measured that items of GHQ-28. Nevertheless, by comparing these findings with other analogues reviewed studies, it was noticed that effective risk factors in incidence of post-TBI mental disorders are in variable amplitude (Table 1). The reasons can be clarified by hereunder factors:

A) Differences between definition of symptoms or using diverse criteria for mental disorder diagnosis: for instance, using DSM and ICD criteria and its different revisions.

B) Using self-evaluation questionnaire or different diagnosis instruments and methods to determine the disorder: Focus of some researches on different scales or questionnaires and also using semi-structured clinical methods can increase dispersion in results of mental disorders frequency. Additionally, as shown in table 1, some studies have used diagnosis and measuring instruments such as SCID, SADS-K, PCL-C, OAS, NFL, MMPI, DIS in order to determine the disorders which can result in different outcomes. However, all these researches, though fluctuant, have evaluated the rate of mental disorders, but have also found a fact in common i.e. post-TBI symptom development is problematic.

C) Differences in TBI severity among evaluated patients: Different TBI severities (mild, moderate and severe) can be effective in frequency, severity and scope of psychoneurological symptoms after TBI. Regarding this, table 1 has shown the dispersion of different researches.

D) Differences in plan or methodology of researches: Reviewed studies in present research had very different ranges of various research design such as cross-sectional, retrospective, prospective, case-control, cohort, comparison of different groups and so forth. Difference between methodology of researches, selection and pursuing various aims is considered as an outstanding factor in different results.

E) Differences in patient selection or sampling resources: Utilization of different types of inclusion and exclusion criteria for TBI patients and also sampling of different populations including outpatients, rehabilitation centers, acute trauma centers, psychiatric clinics and hospital information record office were effective in creating varied results (Table 1).

F) Focus on different ranges of mental disorders can be another effective factor (Table 1).

In summary, the possibility of mental disorder incidence after TBI is more when: The rate of severity of TBI is more and the rate of subcranial injury incidence is more.

The rate of 28-item modified version from general health questionnaire (GHQ-28) after TBI in aspects of physical symptoms, anxiety and insomnia, social dysfunction and depression is more (Table 6).

Thoroughly, the findings of this research accentuates that developing post-TBI mental disorders, first has a close relationship with organic brain pathology (TBI severity and subcranial injury), meanwhile the role of effective psychological factors after TBI should not be neglected. Today, it is accepted that incidence of mental disorders after TBI depends upon the complicated interaction of biopsychosocial factors and it seems that findings of current research widely supports this point of view. Moreover, in order to predict exposed individuals to post-TBI mental disorder, the constructed efficient predictive model of this research can be exercised (Table 7). Although, causality is not implied of this model, educational, psychological and psychotherapy interventions for prediction and a better management of

mental disorder syndrome can be designed based on its information. In current research, we could not monitor drug interventions, care level and rate of hospital emprise, quality of in-family caring after trauma and the rate of social supports. Furthermore, leaning on some of self-reported data such as PTA and LOC and 34.9 % loss of TBI patients at the end of follow-up are among limitations of this study. In a low sample size, there exists the possibility of error type II. Thus, it is proposed that in future studies, along with resolving such limitations, effective intervention protocols be regarded in post-TBI neuropsychological rehabilitation programs for selected variables in regression model as mental disorder predictors to reduce the rate of risk and the consequences due to it. Finally, according to Schwarzbold et al. [41], it can be said that conducting prospective studies by multivariate analyses and constructing predictive models for mental disorders are mandatory challenges in this scientific field. Such models should ideally include clinical, demographic, biochemical, hormonal, neurochemical, neurosurgical, neuroimaging and immunology variables. This approach will be successful only through an interdisciplinary work among researchers from the basic and clinical area.

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Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

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