Clinical malnutrition in severe traumatic brain injury: Factors associated and outcome at 6 months

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Abstract: Traumatic brain injury increases the metabolic response of body, and therefore nutritional demands. This study was undertaken to evaluate various clinical features of malnutrition in TBI and their influence on neurological outcome. Eighty eight adult patients within 24 hours of TBI admitted with GCS 4 to 8 without serious systemic disorder were enrolled for the study. They were monitored serially for various clinical features of malnutrition till 3 weeks and outcome assessed at 6 months. Every week there was a significant increase in number of patients with various clinical features of malnutrition. Pedal edema was the most frequent sign present in 70% of patients at three weeks, followed by skeletal prominence (19%) and cheilosis (12%). Clinical malnutrition showed significant association with poorer GCS (p=0.03), admission hypoproteinemia (p=0.03), and delayed full enteral feeding (p<0.001). Unfavorable outcome at 6 months was noted in 30 out of 37 patients who had clinical malnutrition as compared to 3 out of 15 patients who had no clinical features of malnutrition (odds ratio 17.2, p<0.001). In multivariate analysis, clinical malnutrition was significantly associated with unfavorable outcome independent of GCS (p=0.002). Analysis of individual clinical markers revealed pedal edema as the only single clinical marker with significant influence on unfavorable outcome at 6 months (p=0.01). Clinical malnutrition developed more among patients with poorer GCS, admission hypoproteinemia, delayed full enteral feeding, and was associated with unfavorable outcome at 6 months. Among the various clinical markers, only pedal edema showed independent association with unfavorable outcome.

Keywords: Brain injury, clinical features, malnutrition, outcome

INTRODUCTION

Traumatic brain injury (TBI) is a major cause of disability, death and economic cost to our society[1,2]. The increased energy expenditure and nitrogen excretion following severe TBI mandates adequate nutritional support to provide the optimal milieu for neurological and systemic recovery[3,4,5]. Despite the growing importance of nutritional support in patients with severe TBI, the clinical features suggestive of malnutrition has not been adequately studied in relation to other factors and neurological outcome. This was a prospective study to evaluate various clinical markers of malnutrition in patients with severe TBI, factors associated and their influence on outcome at 6 months.

MATERIALS AND METHODS

Adult patients within 24 hours of TBI admitted with Glasgow coma scale (GCS)[6] 4 to 8, hospitalized at least for 1 week, under the Department of Neurosurgery, AIIMS, New Delhi, from June to December 2005, were enrolled for the study. Patients with age more than 60 years, GCS 3, those with any significant systemic disorder or patients who expired within 1 week had been excluded.

Standard care given to study patients consisted of ventilation, seizure prophylaxis with phenytoin, antibitiotic prophylaxis with cefotaxime or ceftriaxone and netilmycin, and gastric ulcer prophylaxis with ranitidine. Mannitol was given to patients with computed tomography (CT) having evidence of mass effect. Frusemide was added to patients with midline shift. Fluid and electrolyte homeostasis was maintained. Decision regarding surgical decompression was taken according to the mass effect noted in CT and was individualized to each patient. Enteral feeding was initiated either through nasogastric tube or orally as early as possible and the volume of feed increased gradually according to the gastric tolerance. Patient characteristics, post-resuscitation admission GCS, biochemical parameters at admission and serial monitoring for various clinical features of malnutrition till 21 days were noted down in a pre-planned prospective database and were followed up.

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Serum albumin and total protein levels at admission were tested by Bromcresol green dye binding method and Biuret method respectively using Beckman Synchron CX5 Delta Clinical System (GMI Inc, Minnesota)[7]. An observational check list to assess the clinical features of malnutrition[8,9,10] was developed with the following five clinical markers: pedal edema, cheilosis, skeletal prominence, xerosis and gingival bleeding. The inter rater reliability of observational check list on trial 10 patients, obtained between two investigators was more than 90% (100% among four parameters).

Outcome

The primary outcome was Glasgow outcome scale (GOS)[11] assessed at 3 and 6 months following injury either directly or over telephone. Good recovery or moderate disability was considered as favorable outcome and severe disability, persistent vegetative state or death was considered as unfavorable outcome.

Statistical analysis

SPSS software (version 10, SPSS Inc, Chicago) was used for the statistical analyses. Continuous variables in two groups were compared by using independent-samples T test. Proportions were compared by using chi-square tests or Fisher's exact test, wherever appropriate. Multivariate analysis was conducted with logistic regression adjusting for age, admission GCS, systemic injury, surgical intervention, and presence of clinical features of malnutrition. Two sided significance tests were used throughout, and the significance level was kept at $P \leq 0.05$.

RESULTS

From June to December 2005, 88 patients in the age group 18-60, that fulfilled the eligibility criteria were enrolled for the study. The mean age of study sample was 35.4. There were 81 males and 7 females. Every week there was a significant increase in number of patients with various clinical features of malnutrition (Fig 1). 76% of patients presented with clinical features of malnutrition at three weeks.

Pedal edema was the most frequent sign present in 70% of patients at three weeks, followed by skeletal prominence (19%) and cheilosis (12%). The distribution based on clinical features at weekly intervals is as shown (Fig 2).

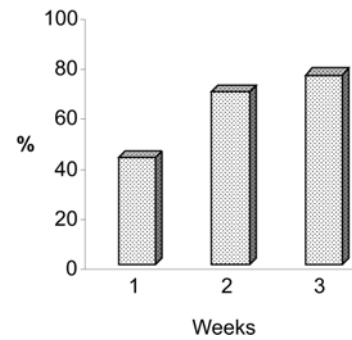The mean age of patients with or without clinical

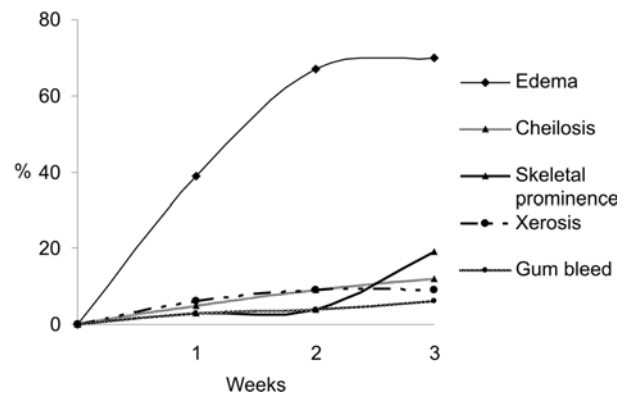**Fig 1:** Prevalence of clinical malnutrition

Fig 2: Clinical markers of malnutrition

features of malnutrition (37 Vs 32 years) did not show significant difference (P=0.07). Also there was no significant gender difference (P=0.09). However the clinical features showed significant association with poorer admission GCS (P=0.03), as shown (Fig 3).
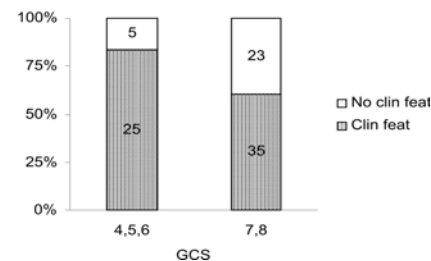

Fig 3: GCS Vs Clinical features

Hypoproteinemia (serum total protein < 5.5 g/dL) at admission showed significant association with development of clinical features of malnutrition with odds ratio (OR) 7.5 (95% CI 0.9- 58.8) and P value 0.03 (Fig 4). The mean admission serum albumin level in patients who developed clinical features of malnutrition was 3.16 (±SD 0.5) g/dL, as compared to 3.39 (±SD 0.4) g/dL
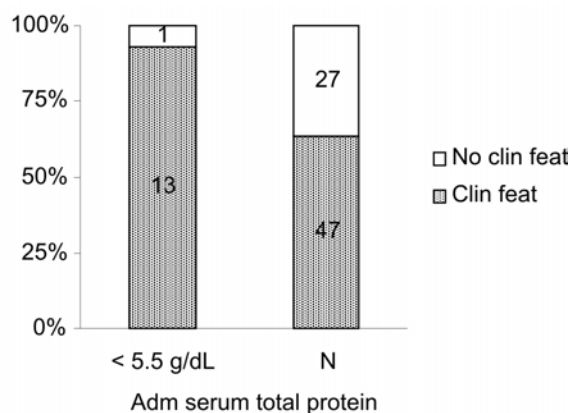
Fig 4: Serum total protein Vs Clinical features

among those who did not develop clinical features. The difference was statistically significant (P=0.046).

Full enteral feeding later than 7 days after admission showed significant association with development of clinical malnutrition (94%) as compared to early enteral feeding (54%) with OR 13 (95% CI 2.8-59.7) and P < 0.001 (Fig 5). Associated systemic injury, computed tomography findings, surgical intervention and prolonged ventilation showed insignificant association with development of clinical malnutrition.
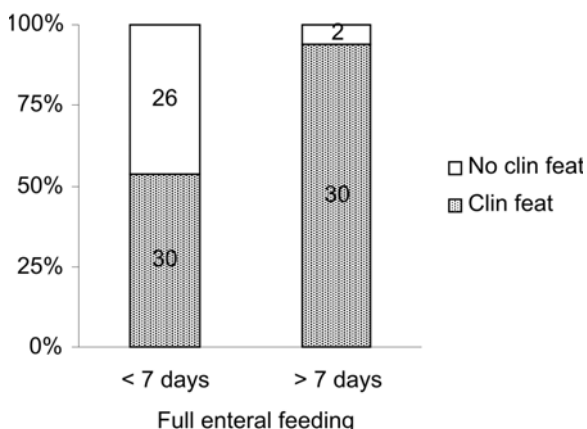

Fig 5: Timing of full enteral feeding Vs Clinical features

Neurological outcome and mortality

Neurological outcome at 3 and 6 months was assessed in 68 and 52 patients respectively. Unfavorable outcome at 6 months was noted in 30 out of 37 patients who had clinical malnutrition as compared to 3 out of 15 patients who had no clinical features of malnutrition. The OR was 17.2 (95% CI 3.8-76.9) and P < 0.001 (Fig 6).

Among the individual clinical markers, pedal edema and cheilosis were significantly associated with unfavorable outcome at 6 months (OR P < 0.001 and P = 0.02, respectively). The presence of skeletal prominence showed significant association with unfavorable outcome at 3 months (P=0.002), but insignificant at 6 months (P=0.07).
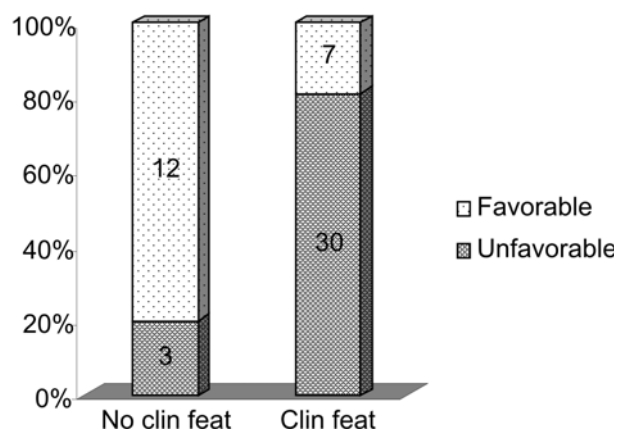

Fig 6: Clinical malnutrition Vs Outcome at 6 months

There was significant association of clinical malnutrition with mortality (40%) as compared to patients who had no clinical features of malnutrition (11%). The OR was 5.6 (95% CI 1.5-20.4) and P value 0.006 (Fig 7).
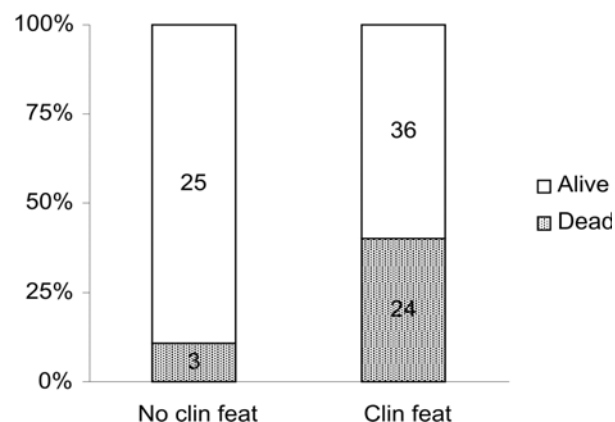

Fig 7: Clinical malnutrition Vs Mortality

Multivariate analysis

Logistic regression analysis was performed on neurological outcome adjusting for the influence of age, GCS, associated systemic injury and surgical intervention. The presence of clinical malnutrition was

significantly associated with unfavorable outcome at 6 months with adjusted OR 12.5 (95% CI 2.6-61) and P value 0.002. Among the individual clinical markers, only pedal edema emerged in multivariate analysis to be significantly associated with unfavorable outcome at 6 months (adj. OR 8.4, P=0.01).

DISCUSSION

Traumatic brain injury (TBI) is the most common cause of death and disability in young people[1]. Nutritional demand in patients with severe TBI is increased due to hypermetabolism and increased protein catabolism[3,4,5,12]. This hypermetabolic response in TBI has been found to be due to increased release of catecholamines and cortisol[12,13]. Monitoring of nutritional status in patients of TBI is vital, as it can guide us towards better nutritional management. Numerous studies have reported the changes in biochemical measures like Resting Metabolic Expenditure, Nitrogen excretion, blood glucose, and serum albumin in patients of TBI[3,14,15,16]. But no study has been done so far on clinical assessment of malnutrition in patients of TBI.

This study shows progressive increase in prevalence of clinical malnutrition in patients admitted with severe TBI, with three fourth having clinical markers of malnutrition at 3 weeks. Pedal edema, the most prevalent and significant clinical marker of malnutrition in our study, is an indicator of visceral protein or vitamin B1 functional status essential for neuronal function and recovery[8-10]. Cheilosis indicates riboflavin, vitamin B6 or niacin deficiency[8-10]. Skeletal prominence indicates somatic protein depletion[8-10]. Xerosis indicates vitamin A or B complex deficiency[8-10]. Gum bleeding indicates vitamin C or K deficiency[8-10].

Poorer GCS, admission total protein and albumin levels had significant influence on the development of clinical features of malnutrition possibly due to increased nutritional demand and limited amino acid reserve respectively. Delayed nutritional replacement by full enteral feeding had significant impact on clinical malnutrition similar to the differential response noted in relation to the timing of feeding in previous studies[17,18,19].

The presence of clinical features of malnutrition was significantly associated with unfavorable outcome at 6 months, probably due to vital organ dysfunction and inadequate neuronal recovery[12,20]. Pedal edema emerged as more significant with respect to neurological outcome,

followed by cheilosis. These may act as valuable markers of the adequacy of nutritional replacement in future studies. In conclusion, clinical assessment is efficient in identifying patients with malnutrition with significant impact on outcome at 6 months.

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