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RESEARCH ARTICLE
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STUDY TO ASSESS THE EFFICACY AND TOLERABILITY OF HIGH PROTEIN ALBUMIN FORMULA (ALBUWISE) IN INDOOR PATIENTS WITH HYPOALBUMINEMIA: A RETROSPECTIVE ANALYSIS (INDI ALB-PHASE 2)

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Abstract

Background: Hypoalbuminemia is a common problem seen in hospitalized patients. Albumin is a major component of plasma protein and plays an important physiological role in the body. Serum albumin levels are frequently monitored in sick and malnourished individuals. Adequate protein supplementation in acutely sick patients can lower mortality and enhance quality of life. Protein supplementation formula derived from Egg and egg white protein could be an effective for supplementation in patients with hypoalbuminemia. Albuwise (High Protein, Albumin Formula), derived from egg. This study was conducted to assess the safety and efficacy of oral administration of this product in hospitalized patients with hypoalbuminemia.

Materials and Methods: This multicentric, retrospective, prescription event monitoring study included adult hospitalized patients with low serum albumin levels (<3.0 g/dl). Data was collected from data record files. The dosage of high protein Albumin Formula (Albu-wise) supplementation was determined by the dietitian and supplemented by oral route after conventional nutritional counseling. The dosages were divided or increased as per patient's nutritional requirements and dietitian's nutritional intervention. All the enrolled patients were monitored till 45 days for biochemical parameters, dietary intake and nutrition score from baseline and post intervention. Safety parameters were monitored as complaints of feeding intolerance, vomiting and stool consistency.

Results: Total study participants were 15(100%). At baseline mild- moderate malnourishment was in 60 %, food intolerance was absent in 66.7% and nausea & vomiting was present in 26.7%. Statistically significant and consistent improvement seen in all the component of components of serum protein, Calorie and protein intake. While supplementation dose of high protein Albumin Formula was reduced from 30 gm (10.00)/per day at baseline and 28 gm (10.82)/per days on 45th day. Subjective Global Assessment Scoring System was changed to grade A in 6 (40%) patients. Food intolerance was improved in 3 (20%), On the 45th day stool consistency was normal and nausea & vomiting was absent in all patients 15(100%).

Conclusion: High Protein Albumin Formula (Albuwise) is found to be safe and effective in improving serum albumin level among hospitalized patients with low serum albumin levels.

Keywords: High Protein Albumin Formula (Albuwise), Hypoalbuminemia, Malnutrition, SGA score

Background:

Hypoalbuminemia is a frequent problem during hospitalization and commonly associated with morbidity and poor prognosis.[1]

Albumin, a major component of plasma protein, keeps acid-base balance, microvascular permeability, oncotic pressure, and platelet aggregation prevention. Serum albumin levels are frequently monitored in individuals who are extremely sick or undernourished. In hospitalized adult patients, the prevalence of hypoalbuminemia, which is defined as serum albumin levels less than 3.5 g/dL, was 21% at the time of administration.[2]

Acutely sick patients who need nutritional therapy have high protein needs, and research shows that providing them enough protein can lower mortality and enhance quality of life.

However, the existing dearth of concentrated protein solutions poses a serious obstacle to sufficient protein administration. Patients commonly experience difficulties administering fluids, and the protein solutions currently on the market are frequently insufficiently concentrated to meet the patient's protein needs.

As a result, new enteral and parenteral feeding solutions with larger protein contents in lower amounts have been developed. The available data on the benefits of increased protein intakes, particularly in the early stages of nutrition therapy for acute illnesses, the techniques for determining protein requirements, and the high-protein enteral and parenteral nutrition solutions.[3]

Egg whites are recognized as a source of high-quality proteins They exhibit biological activity like antibacterial, antioxidant, metal-chelating, antihypertensive, anticancer, and immunomodulatory ones, egg white and yolk proteins are regarded as functional dietary ingredients.[4,5]

A previous study found that although while the amino acid scores of egg white proteins and whey and soybean proteins are comparable, the net protein utilization (NPU) value for egg white proteins, whether cooked or uncooked, is greater.[6,7]

Previous research has shown that taking egg white proteins increases the body's protein levels. Proteins from egg whites can also increase muscle mass and strength after exercise. Reduced blood LDL cholesterol and visceral fat are two additional benefits of egg white proteins. Protein supplementation formula derived from Egg and egg white protein could be an effective for supplementation in patients with hypoalbuminemia.

Fresh chicken egg white is hydrolyzed using enzymes to produce Egg White Peptides (EP-1).

Peptides generated from egg whites have unique properties not seen in amino acids or proteins.

The order, quantity, and length of amino acids all have an effect on peptide activity. It enables quick absorption in the intestines. In an animal study, Matsuoka et al. found that egg white hydrolysates maintain the nutritious content of egg whites while being readily absorbed by the body. 2019 (Matsuoka). Aim of this study is to assess the safety and efficacy of an oral administration of the product Albuwise (High Protein, Albumin Formula) in hospitalized patients with hypoalbuminemia.

Materials and Methods:

Study design: A multicentric, retrospective, observational study that monitors prescription events. The research was carried out in compliance with the accepted practices and guidelines for performing retrospective studies (Motherol et al., 2003). Retrospective data of patients were collected between June 2023 to December 2023

Study objective: The purpose of this study is to assess the safety and effectiveness of High Protein Albumin Formula (Albuwise) in hospitalized Patients in relation to low serum albumin levels (less than 3.0 g/dl).

Subject inclusion Criteria: Data of all the patients from IPD department with age ≥ 18 years, **low serum albumin levels (less than 3.0 g/dl)**, require nutritional support for 1 week or more as per the attending consultants and should not have any Gastrointestinal Obstructions were included in the study.

Study procedure: Patients were enrolled in the study after screening for inclusion criteria through data record file. The baseline data was collected on following parameters such as demographic details, Scoring of nutritional status by SGA score and laboratory parameters: CRP, Serum albumin, Serum Prealbumin, Serum Protein in the first 24-28hrs hours as shown in table 1.
The dosage of high protein Albumin Formula (Albu-wise) supplementation was determined by the dietitian on a case-to-case basis. High protein Albumin Formula supplementation was initiated by oral route after conventional nutritional counseling. The dosages were divided or increased as per patient's nutritional requirements and dietitian's nutritional intervention. The details of nutrition formula as shown in table 2.

Table 1: The composition of test supplementation			
Contents	Per 10 g	Per 30g	per 100 gm
Water	60 ml	180 ml	600 ml
Feed volume	65 ml	200 ml	650 ml
Energy (kcal)	43	129	430
Protein(g)	6.1	18.3	61
Carb(g)	2.4	7.2	24
Fat (g)	1	3	10
Sodium (mg)	45	135	450
Potassium (mg)	39	117	390
Phosphorus(mg)	9	27	90

In the follow up, data was collected on 7th ,14th ,30th and 45th day for analysis of efficacy and safety. Efficacy Assessments: Effectiveness of supplement was assessed by changes in biochemical parameters, improvement in dietary intake and nutrition score at baseline and post intervention. Tolerance assessments: Safety of High Protein Albumin Formula (Albuwise) was assessed by patient complaints and healthcare professionals' opinions of GI intolerance. Gastrointestinal intolerance: GI intolerance was assessed based on patients' complaints of feeding intolerance (abdominal distension/gas), vomiting and stool consistency. These parameters were assessed at baseline, after 7 days, after 1 month, after 2 months. Feeding intolerance and vomiting were assessed as no change, tolerance improved, tolerance worsened. Stool consistency issues were assessed as no change, too hard, too loose.

Statistical analysis:
The statistical analysis was carried out using the statistical software SPSS version 10.0. Data analysis includes descriptive statistics and outcome analysis using paired t-test for numerical data and chi square test for categorical data.

Results:

Table 2: Baseline profile of participants	
Age group	N (%)
<65 years	7 (46.7)
>=65 years.	8(53.3)
Gender	
Male	8(53.3)
Female	7 (46.7)
BMI Category	
Underweight	2(13.3)
Normal weight	12(80.0)
Overweight	1(6.7)
SGA Score	
Mild-Moderately malnourished(B)	9(60.0)

Severely malnourished (C)	6(40.0)
Food intolerance	
Absent	10(66.7%)
Present	5(33.3%)
Vomiting	
No Nausea/Vomiting	5(33.3%)
Mild Nausea	4(26.7%)
Moderate Nausea	2(13.3%)
Vomiting	4(26.7%)
Stool consistency	
Normal	2(13.3%)
Constipation	9(60.0%)
Diarrhoea	4(26.75)

As shown in table 2, total study participants were 15 (100%),53.3% 0f patients were from elderly group,53.3% were male, 80 % were with normal weight, 60 % of patients were with mild- moderate malnourishment, food intolerance is absent in 66.7%. 33.3 % were not having nausea and vomiting, but nausea & vomiting is present in 26.7%.

Efficacy Assessments

1. Biochemical parameters

Table 3: Biochemical parameters Mean (SD)

Parameters (gm/dl)	Baseline	Day 7th	Day 14th	Day 30th	Day 45th	
Ser. Albumin	2.35(0.49)	2.59(0.46)	2.93(0.34)	3.29(0.23)	3.63(0.21)	P <0.001
Sr. Pre- Albumin	9.67 (2.53)	11.87(3.09)	15.47(2.29)	19(2.56)	22.53(2.59)	
Ser. Protein	4.87 (0.83)	5.27serum protein (0.6)	5.79 (0.49)	6.15(0.35)	6.62(0.34)	
CRP	161.67 (74.38)	117.77 (78.65)	61.07 (41.2)	18.8 (10.73)	10.47 (3.02)	
Paired t test and highly significant difference						

As shown in table 3, there was constant increase in all components of serum protein such as Ser. Albumin, Sr. Pre-Albumin, Serum Protein from baseline 2.35(0.49), 9.67 (2.53), 4.87 (0.83) to 3.63(0.21), 22.53(2.59), 6.62(0.34) at 45th day respectively. While in CRP levels there was a fall from baseline level 161.67 (74.38) to 10.47 (3.02) on the 45th day. These changes were statistically significant with the Paired t test. This was statistically significant change with P <0.001 as per paired t test.

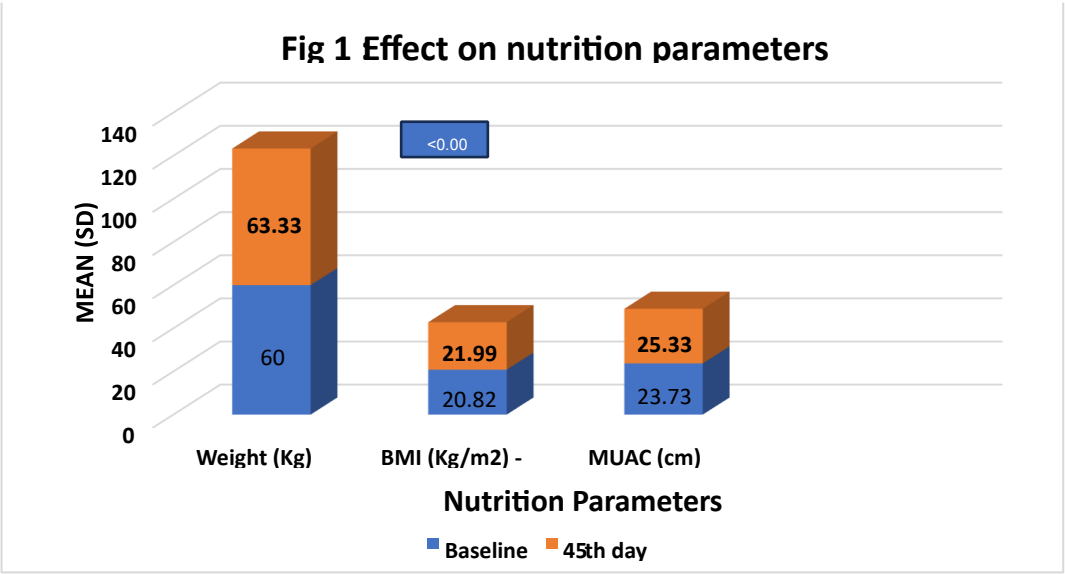
2. Dietary Intake

Table 4: Improvement in Dietary intake Mean (SD)

Dietary parameters	Baseline	Day 7th	Day 14th	Day 30th	Day 45th	P <0.001
Calorie Intake (kcal)	1040 (256.99)	1250.67 (273.25)	1435 (292.88)	1607.87 (154.38)	1674 (113.9)	
Protein Intake (gm)	26.87(13.27)	38.8(14.22)	46.4 (13.63)	55.8 (8.08)	58.27 (6.16)	
Supplementation dose(gm)	30(10.00)	40 (9.26)	42.67(11.63)	41.33(12.46)	28 (10.82)	
Paired t test and highly significant difference						

As shown in table 4, there was constant increase in the dietary intake components such as calorie and protein intake from baseline1040 (256.99), 26.87 to 1674 (113.9),58.27 (6.16) at 45th day respectively. While Supplementation dose was increased up to 14th day and reduced onwards.
The baseline dose was 30 gm (10.00)/per day and reduced to 28 gm (10.82)/per days. These changes were statistically significant as per paired t test with P <0.001.

3. Nutrition Score



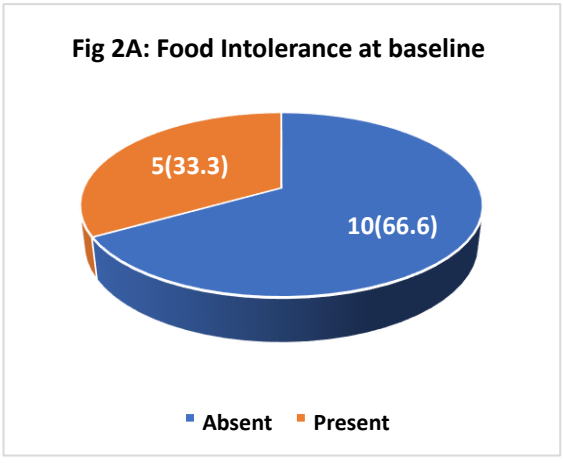
As shown in fig 1, there was increase in weight, BMI and MUAC from baseline 60kg,20.82(kg/m2) and 23.73 cm at baseline to 63.33 kg, 21.99 (kg/m2) and 25.33 cm on 45th day. This was statistically significant change (paired t test).

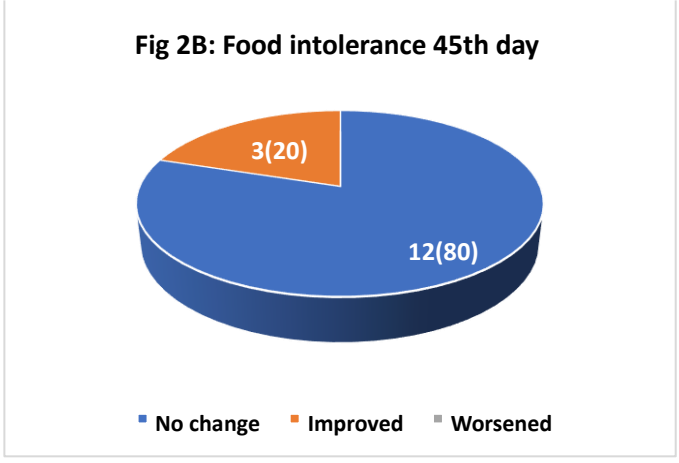
Table 5: Effect on Subjective Global Assessment (SGA) score			
	Grade -A N (%)	Grade - B N (%)	Grade - C N (%)
Baseline	**NIL**	**9(60.0)**	**6(40.0)**
45th Day	**6(40.0)**	**9(60.0)**	**NIL**

As shown in table 5, Subjective Global Assessment Scoring System shows statistically significant change (paired t test) from baseline as 6 (40%) patients changed to grade A and no patients in Grade C.

4. Safety parameters

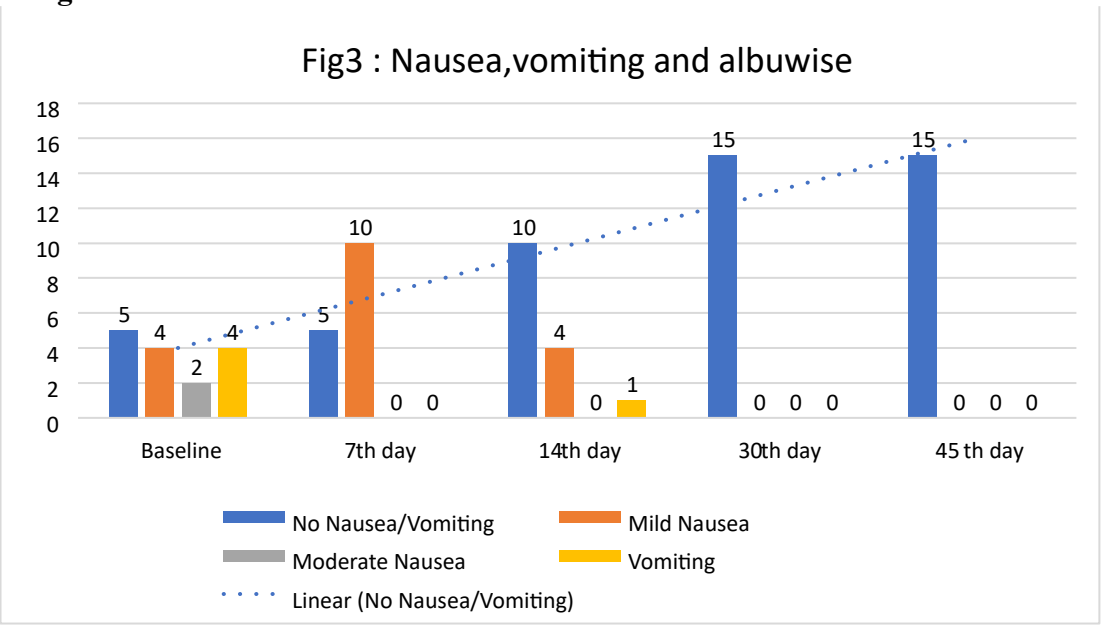
1. Food intolerance





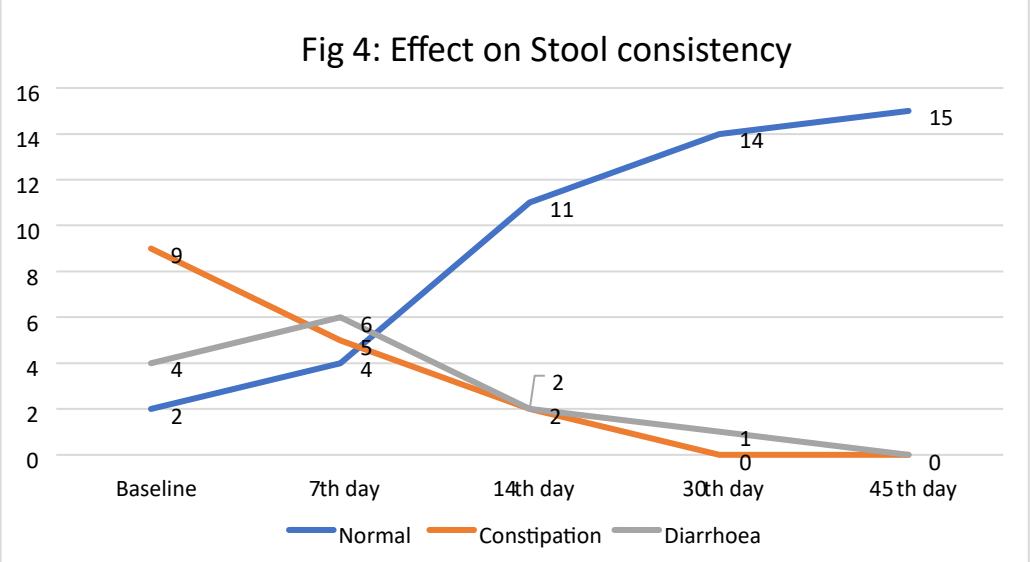
As shown in fig 2A food intolerance was present in 20(66.6) patients at baseline. On 45thday, food intolerance was seen in no change 12 (80%) & improved 3 (20%) category was seen.

2. Vomiting



As shown in fig 3 there was significant improvement in the nausea and vomiting over a study period. At baseline no nausea, mild nausea, moderate nausea, and vomiting were seen in 5,4,2, & 4 patients. On the 45th day nausea & vomiting was not seen in all patients 15 (100%). P value <0.001 with Friedman test.

3. Stool consistency.



As shown in fig 4 there was marked improvement in stool consistency from baseline. At baseline constipation and diarrhea were seen in 9(%) and 4(%) patients respectively. A minimum increase in diarrhea on the 7th day followed by a consistent fall in the number of patients with diarrhea. There was a consistent fall in the number of patients with constipation. On 45thday all the patients were having normal stool consistency. P value <0.001 with Friedman test.

Discussion

In the current study, we analyzed the effectiveness and safety of High Protein Albumin Formula (Albuwise) supplementations in hospitalized patients with low serum albumin levels. Demographically, most patients had mild to moderate malnutrition, which is consistent with the findings of Bellanti et al. [8]

In hospitals, malnutrition is often underdiagnosed and undertreated. The development of customized nutritional intervention depends on a precise screening process to identify individuals who are at risk of malnutrition or undernourishment. Compared to healthy people, older hospitalized patients have poorer nutritional status. Hospitalization is, in fact, linked to significant modifications in the usual intake of nutrients due to many reasons, including limited food availability, reduced appetite, negative drug reactions, and recommended fasting times. Weijen et al.[9]

We have observed that all of the serum protein components, including serum albumin, serum prealbumin, and serum protein, have consistently increased since the baseline and have continued to do so at every follow-up and 45-day interval. While in CRP levels there was a consistent fall from and in each follow-up and 45th day. These changes were statistically significant with the Paired t test. This is in line with the study conducted by Fei Tian et al.[10]

For many years, cow's milk protein or casein protein was the usual protein supplement in many hospitals, but availability is restricted, and the cost is exorbitant. As a result, because it is readily available and less expensive than other types of protein supplements, egg white protein powder, which is often used in the food sector, could be adopted as the standard supplementary protein supplementation in hospitalized patients. As per Bhurayanontachai, Rungsun et al because the biological value (BV) and protein efficiency ratio (PER) of egg white protein are comparable to those of casein protein, the benefits of egg white protein may be comparable to those of casein protein additive.[11]

The consistent and slow rise of all serum protein parameters indicate the efficacy of albuwise because of directly or indirectly affect the production, absorption and decomposition of serum albumin by regulating intestinal absorption capacity, alleviating stress reaction, inhibiting inflammatory reaction.[12]

A steady decline in the level of the sensitive inflammatory marker C-reactive protein (CRP) suggests that the inflammatory response is being inhibited. Our results are in line with the metaanalysis carried out by Ling-Mei Zhou et al.[13]

There was a homogeneous increase in the dietary intake components such as calorie and protein intake from and in each follow-up. This is in line with the study conducted by Robert s.[14]

Mehnoosh Samadi and Wischmeyer, Paul E. et al. found that dietary supplements dramatically enhanced calorie, carbohydrate, and protein intake, decreased the severity of malnutrition, and enhanced nutritional status as well as laboratory values, such as albumin, prealbumin, and TLC, in patients admitted to intensive care unit. Higher calorie and protein intake improved clinical outcomes, decreased the 60-day mortality rate, and extended the period patients could go without a ventilator.[15–17]

While high protein formula supplementation dose was increased up to 14th day and reduced onwards. These changes were statistically significant as per paired t test with $P < 0.001$. The nutritional requirements of critically ill elderly people are not well understood and change depending on the stage of illness and recovery, according to Rachel R. Deer et al. Early on in their hospital stay, patients' nutritional needs should be evaluated, and they should continue to do so throughout.[18]

There was an increase in weight, BMI and MUAC from baseline to 45th day. This has proved the effectiveness of formulas. Malnutrition is more common in older people groups and deterioration of nutritional status can occur during illness. Body mass index (BMI) (weight in kg / height in m2), anthropometry (such as arm muscle circumference and triceps skin fold thickness), and history of recent weight loss are often used techniques to assess nutritional health. Because malnutrition slows down the rate at which albumin is synthesized, serum albumin has also been employed as a gauge of nutritional status.[19]

As per Modified Subjective Global Assessment Scoring System (SGA), categories are A - well nourished, B- moderately malnourished and C- severely malnourished.[20]We have observed a change of SGA in 6 (40%) of patients and it was changed as grade C (Mild – Moderate malnutrition) to Grade A (Normal) from baseline to 45th day of study respectively.

We have observed in safety parameters, there was improvement in food intolerance, nausea and vomiting and stool consistency over a study period. As its being the enteral nutrition, complications such as gastric retention, vomiting, diarrhea, abdominal distension, constipation need to be observed Fei Tian.[10]

We have observed that there is improvement in gastrointestinal tolerance post supplementations of High Protein Albumin Formula (Albu-wise) additionally we noticed, this can be attributed to the semi-elemental nature of the formulations.

Limitations of the study

Although it's a multicentric study, less sample size is a main limitation.

Conclusion

For hospitalized patients with hypoalbuminemia, oral high protein supplements obtained from egg white can be a useful alternative. Other methods of protein supplementation have their own set of drawbacks, such as parenteral albumin administration and allergic responses. Supplements made from cow's milk protein or casein protein are not widely available and are expensive.

As per our study, administration of High Protein Albumin Formula (Albuwise) is found to be safe and effective in improving serum albumin level among hospitalized patient with low serum albumin levels. However, it's required to pay more attention for persistent inflammatory responses and subsequent infections in hospitalized patients with hypoalbuminemia. More studies on larger sample size at various levels are required to find more data to help better management of these patients.

Disclaimers:

- **Ethics committee approval:** Ethics approval was not obtained for present PMS for as case series were reported
- **Consent:** Consent was obtained or waived by all participants in this study
- **Other consents:** Nil
- **Funding: Nil**
- **Support:** None
- **Acknowledgments:** Authors, thank all the participants for their enormous support in the study.
- **Conflict of interest:** Author(s) declare(s) that there is no conflict of interest.

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Date: 05/02/2024

To,

The Editor in Chief

Sub: Submission of article for publication
Respected Sir,

We wish to submit the article titled “Study To Assess The Efficacy And Tolerability Of High Protein Albumin Formula (Albuwise) In Indoor Patients With Hypoalbuminemia: A Retrospective Analysis (Indi Alb-Phase 2)” for publication as an “Original article.”
This article is not published or under consideration for publication in any other journal. Other information about the article including author details is provided in the title page.
We request you to please process the article for review and publication.

Thank you.

Regards,
Nidhi Singh