

## THE CLINICAL AND ECONOMIC IMPACTS OF USING SUPPLEMENTAL ENTERAL NUTRITION FORMULAS IN HOSPITALIZED PATIENTS WHO ARE TAKING TOTAL PARENTERAL NUTRITION

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### ABSTRACT

**Objectives:** Most hospitalized ill patients have wasting syndromes, especially kwashiorkor which characterized by hypercatabolic status. Ideally, enteral nutritional formulas (ENFs) nutritional intake should be taken orally or enterally through various feeding tubes at least at trophic feeding (TF) dose (10-20 ml/hr) to maintain the integrity of enterocytes and subsequently to mitigate bacterial translocation. In our study, we evaluated the clinical and economic impacts of using supplemental six ENFs that were available in our institutional at TF dose for at least 1 week in total parenteral nutrition (TPN) dependent patients. **Methods:** Our study was retrospectively conducted in King Hussein Medical Hospital (KMH) and analysis values were compared among the six tested ENFs groups by using ANOVA for continuous variables and Chi square test for nominal data after exclusion all hospitalized patients who were discharged or died before completed at least 1 week of dual enteral nutrition (EN) and TPN after admission. **Results:** The mean overall age was 58.4±9.9 years and 224 participants (68.7%) were male. The percentage changes in albumin level (%ΔALB) and other tested positive clinical and economic impacts were significantly highest in groups who were on ENFs with primarily high protein and caloric density (PD and CD) and were high or enriched with glutamine (GLT). **Conclusion:** In summary, using TF dose of ENFs in TPN dependent wasted hypoalbumenic hospitalized patients may have great positive clinical and economic outcomes especially if the ENF have a unique nutritional characteristic of higher PD, CD, and GLT, prebiotic, and zinc enrichments.

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### INTRODUCTION

Most hospitalized ill patients have wasting syndromes, especially kwashiorkor which characterized by hypercatabolic of endogenously lean body mass (LBM) and ALB protein.<sup>[1-4]</sup>

Ultimately, all hospitalized patients who cannot meet the nutritional requirement enterally need a TPN at least supplemental to fill the gap of caloric and protein deficit.<sup>[5-7]</sup>

Ideally, ENFs nutritional intake should be taken orally or enterally through various feeding tubes at least at TF dose (10-20 ml/hr) to maintain the integrity of enterocytes and subsequently bacterial translocation which have an evidence positive clinical and economic impacts.<sup>[8-12]</sup> In our study, we evaluated the clinical and economic impacts of using supplemental ENFs that were available in our institutional (e.g. Ensure<sup>®</sup>, Resource<sup>®</sup> Optimum, RenaMent<sup>®</sup>, ArgiMent<sup>®</sup>, PROSource<sup>®</sup>, Whey protein (WP)) with PN in wasted hypoalbumenic hospitalized patients for at least 1 week in terms of %ΔALB and c-reactive protein (CRP) to ALB ratio (%ΔCRP:ALB), changes in human albumin consumption (ΔH.ALB), cost effectiveness to increase ALB by 1 g/dl (CER), overall hospital length of stay (LOS), overall 28-day

hospital mortality, incidence of gastrointestinal symptoms (GI Sx), and risk of enteric gram negative bacteria (GNB) translocation among the six tested groups. The tested six groups are fully described in Table 1.

### METHODS AND MATERIALS

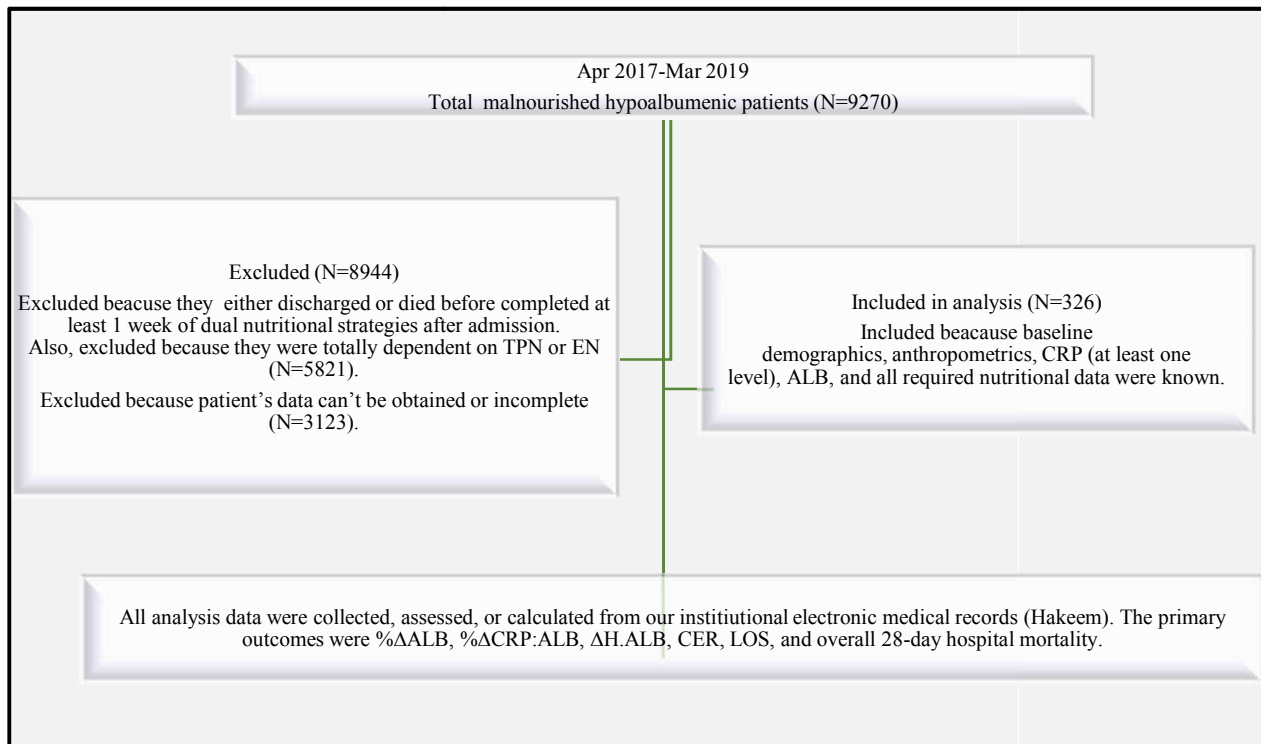
Our study was retrospectively conducted in KMH at Royal Medical Services (RMS) in Jordan between April 2017 to Mar 2019. This study was approved by our Institutional Review Board (IRB) and the requirement for consent was waived owing to its retrospective design. The study included a cohort of wasted hypoalbumenic hospitalized patients with any medical or surgical problem. The flow chart of patient selection and the data collection process is illustrated in Figure 1. Analysis values were compared among the six tested ENFs groups by using ANOVA for continuous variables and Chi square test for nominal data in which the continuous variables of all patients were expressed as Mean±SD and nominal data were expressed as numbers with percentages. All statistical analyses were performed using IBM SPSS ver. 25 (IBM Corp., Armonk, NY, USA); P-values ≤0.05 were considered statistically significant.

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**Table 1** Tested Six Groups Description

Group	Standard ENFs		Specialized MFs		MPFs	
	Group I	Group II	Group III	Group IV	Group V	Group VI
Description	Hospitalized patients on TPN supplemented partially by Ensure®	Hospitalized patients on TPN supplemented partially by Resource® Optimum	Hospitalized patients on TPN supplemented partially by RenaMent®	Hospitalized patients on TPN supplemented partially by ArgiMent®	Hospitalized patients on TPN supplemented partially by PROSource®	Hospitalized patients on TPN supplemented partially by reconstituted WP 100%
	ENFs: Enteral nutritional formulas. MFs: Modular non complete formulas. MPFs: Modular protein formulas.			WP: Whey protein 100% 25 g per scoop reconstituted with 200 ml water to yield final concentration of 11 g/dl.		



**Fig 1.** Flow chart of critically ill patient's selection and data collection process.

**Apr:** April. **CRP:** C-reactive protein. **CRP:ALB:** CRP to ALB ratio.  
**Mar:** March. **LOS:** Length of stay **ALB:** Albumin.  
**N:** Number of studied patients. **CER:** Cost-effectiveness ratio. **H.ALB:** g Human Albumin used.  
**TPN:** Total parenteral nutrition. **EN:** Enteral nutrition. **Δ:** Changes.

**RESULTS**

The mean overall age was 58.4±9.9 years and 224 participants(68.7%) were male. There were insignificant differences regarding non-critical versus critical admission wards and medical versus surgical admission diagnostics. Although the ALB<sub>1</sub>, CRP<sub>1</sub>, H.ALB<sub>1</sub>, and CRP:ALB<sub>1</sub>, total calories requirement (TCR), %Goal Cal, and overall dual TPN and EN administration days were insignificantly different among the tested groups, the %ΔALB was significantly highest in Group IV followed by Group V, Group VI, Group III, Group II, and lastly Group I (114%±19%, 91%±12%, 46%±7%, 33%±4%, 16.3%±1.8%, and 14%±1.7%, respectively) in kwashiorkoricpatients who were on dual TPN and ENFs of (ArgiMent®, PRO Source®, WP100%, Rena Ment®, Resource® Optimum, and Ensure®, respectively) for at least 1 week. This significant higher %ΔALB was also accompanied by significant lower of ΔH.ALB and %ΔCRP:ALB

(-24.81±7.95 g/day, -24.07±5.67 g/day, -15.6±5.02 g/day, -11.85±3.92 g/day, -5.93±4.96 g/day, and -5.36±5.03 g/day, respectively) and (-45%±22%, -23%±33%, -3%±42%, 16%±39%, 16.3%±50.6%, and 5.6%±55%, respectively).The overall hospital LOS and overall 28-day hospital mortality were also significantly lowestin Group IV followed by Group V, Group VI, Group III, Group II, and lastly Group I(12.56±1.49 days, 13.44±1.51 days, 14.74±0.65 days, 14.89±2.57 days, 16.59±1.46 days, 17.82±1.27 days and 7 (12.96%), 10 (18.52%), 12 (22.22%), 14 (25.93%), 16 (29.63%), 21 (37.5%), respectively).Economically, the cost expenditure to increase ALB by 1 g/dl was significantly lowest in Group IV followed by Group V, Group VI, Group III, Group II, and lastly Group I(20.6±6.7 USD, 25.8±8.5 USD, 77.2±23.7 USD, 116.8±29.2 USD, 271.9±40.9 USD, and 364.7±86.3 USD, respectively) although there were insignificant differences in TPN cost among the tested six groups.

**Table 2** Comparison data among the six tested groups

Variables	Total (N=326)	Standard ENFs (N=110)		Specialized ENFs (N=108)		MPF (N=108)		P-Value	
		Group I Ensure® (N=56)	Group II Resource® Opt (N=54)	Group III RenaMent® (N=54)	Group IV ArgiMent® (N=54)	Group V PROSource® (N=54)	Group VI WP100% (N=54)		
Age (Yrs)	58.4±9.9	61.3±8.7	58.8±10.4	53.9±9.1	58.9±8.9	59.6±10.2	57.7±11.1	0.004(S)	
Sex	Male	224(68.7%)	42 (75.0%)	36 (66.7%)	42(77.8%)	28(51.9%)	42(77.8%)	34(63.0%)	0.021(S)
	Female	102 (31.3%)	14 (25.0%)	18 (33.3%)	12(22.2%)	26(48.1%)	12(22.2%)	20 (37.0%)	
Ward	Non Critical	160 (49.08%)	29 (51.79%)	27 (50%)	28 (51.85%)	31 (57.41%)	22 (40.74%)	23 (42.59%)	0.081 (NS)
	Critical	166 (50.92%)	27 (48.21%)	27 (50%)	26 (48.15%)	23 (42.59%)	32 (59.26%)	31 (57.41%)	
Medical Dx	Medical	153 (46.93%)	28 (50%)	25 (46.29%)	23 (42.59%)	24 (44.44%)	26 (48.15%)	27 (50%)	0.106 (NS)
	Surgical	173 (53.07%)	28 (50%)	29 (53.70%)	31 (57.41%)	30 (55.56%)	28 (51.85%)	27 (50%)	
BW <sub>1</sub> (Kg)	74.9±10.3	73.49±8.51	74.07±11.87	77.73±8.49	73.44±11.24	73.67±11.58	77.22±9.34	0.074 (NS)	
CRP <sub>1</sub> (mg/dl)	6.83±3.58	7.86±4.11	2.11%±0.76%	5.92±3.02	7.75±3.72	6.00±3.02	6.85±4.15	0.05 (NS)	
ALB <sub>1</sub> (g/dl)	2.25±0.32	2.25±0.28	2.28±0.30	2.26±0.27	2.20±0.23	2.26±0.44	2.25±0.37	0.9 (NS)	
H.ALB <sub>1</sub> (g/day)	24.11±6.44	24.64±6.31	22.96±5.37	23.33±6.14	24.81±7.95	24.07±5.67	24.8±6.93	0.5 (NS)	
CRP <sub>1</sub> : ALB <sub>1</sub>	3.18±1.94	3.63±2.14	2.98±1.49	2.81±1.75	3.66±2.11	2.72±1.56	3.26±2.32	0.064 (NS)	
CRP <sub>2</sub> (mg/dl)	7.94±3.11	7.78±2.91	7.62±2.42	8.13±2.94	8.40±3.83	7.60±3.06	8.13±3.37	0.7 (NS)	
ALB <sub>2</sub> (g/dl)	3.40±0.90	2.56±0.28	2.62±0.27	2.93±0.23	4.76±0.44	4.32±0.31	3.25±0.37	0.000 (S)	
H.ALB <sub>2</sub> (g/day)	9.57±8.47	19.29±4.62	17.04±5.36	11.48±4.52	0.00±0.00	0.00±0.00	9.26±4.69	0.000 (S)	
CRP <sub>2</sub> : ALB <sub>2</sub>	2.57±1.33	3.19±1.55	3.02±1.22	2.87±1.32	1.84±0.94	1.82±0.85	2.63±1.29	0.00 (S)	
ΔALB (g/dl)	1.15±0.83	0.31±0.00	0.36±0.00	0.72±0.00	2.50±0.00	2.04±0.00	1.00±0.00	0.000 (S)	
ΔH.ALB (g/day)	-14.54±9.56	-5.36±5.03	-5.93±4.96	-11.85±3.92	-24.81±7.95	-24.07±5.67	-15.6±5.02	0.000 (S)	
%Δ ALB	52%±39%	14%±1.7%	16.3%±1.8%	33%±4%	114%±19%	91%±12%	46%±7%	0.00 (S)	
%Δ CRP	36%±60%	20%±63%	36%±59%	54%±53%	19%±48%	48%±65%	42%±63%	0.007 (S)	
%Δ CRP:ALB ratio	-5.5%±47%	5.6%±55%	16.3%±50.6%	16%±39%	-45%±22%	-23%±33%	-3%±42%	0.00 (S)	

Data are presented as Mean±Standard deviation and are analyzed by using ANOVA test (at p-value< 0.05).

Yrs: Years.  
 BW: Actual body weight.  
 N: Number of study's hospitalized patients.  
 Group I: Hospitalized patients on TPN supplemented partially by Ensure®.  
 Group II: Hospitalized patients on TPN supplemented partially by Resource® Optimum.  
 Group III: Hospitalized patients on TPN supplemented partially by RenaMent®.  
 Group IV: Hospitalized patients on TPN supplemented partially by ArgiMent®.  
 Group V: Hospitalized patients on TPN supplemented partially by PROSource®.  
 Group VI: Hospitalized patients on TPN supplemented partially by reconstituted WP 100%.

1: baseline at admission.  
 2: 2 weeks after admission.  
 Δ: Changes.  
 S: Significant (P-Value <0.05).  
 NS: Non-significant (P-Value >0.05).  
 Dx: Diagnosis.  
 ALB: Albumin level.  
 CRP: C-reactive protein.  
 CRP: ALB: C-reactive protein to albumin ratio.  
 H.ALB: Human albumin.

**Table 3** Comparison data among the six tested groups

Variables	Total (N=326)	Standard ENFs (N=110)		Specialized ENFs (N=108)		MPF (N=108)		P-Value	
		Group I Ensure® (N=56)	Group II Resource® Opt (N=54)	Group III RenaMent® (N=54)	Group IV ArgiMent® (N=54)	Group V PROSource® (N=54)	Group VI WP100% (N=54)		
Enteric	271 (83.1%)	41 (73.2%)	42 (77.8%)	44(81.1%)	50 (92.6%)	48(88.9%)	46 85.2%)	0.03 (NS)	
BSI	55 (16.9%)	15(26.8%)	12(22.2%)	10 (18.9%)	4 (7.4%)	6 (11.1%)	8 (14.8%)		
TOLR	GI Sx (0,1)	200 (61.3%)	30 (53.6%)	30 (55.6%)	32(59.3%)	38(70.4%)	34 (63.0%)	0.031 (S)	
	GI Sx (≥2)	126 (38.7%)	26 (46.4%)	24 (44.4%)	22 (40.7%)	16 (29.6%)	18 (33.3%)		20(37.0%)
ENF Cost (USD/day)	1.13±0.96	1.18±0.94	0.77±0.42	1.59±0.85	1.26±0.96	1.75±1.14	0.25±0.15	0.000(S)	
TPN Cost (USD/ day)	51.8±16.2	57.0±22.9	50.2±12.4	50.9±11.1	50.3±15.9	50.9±16.3	51.0±15.3	0.2 (NS)	
H.ALB Cost (USD/day)	26.8±23.7	53.9±12.9	47.7±15.0	32.1±12.6	0.0±0.0	0.0±0.0	25.9±13.1	0.000 (S)	
CER (USD/ +1 g ALB/dl)	147.5±136.4	364.7±86.3	271.9±40.9	116.8±29.2	20.6±6.7	25.8±8.5	77.2±23.7	0.000 (S)	
TCR (Cal/kg/day)	21.10±5.32	22.34±7.04	21.06±5.49	20.33±3.33	21.55±4.89	20.93±5.22	20.40±5.17	0.36 (NS)	
TCR (Cal/day)	1449±388	1548±538	1423±325	1433±265	1446±371	1441±399	1398±369	0.43 (NS)	
%Goal Cal	79.4%±7.9%	81.8%±8.9%	78.8%±7.5%	81.5%±6%	77.9%±8.4%	77.1%±8.2%	79.3%±6.9%	0.15 (NS)	
Vol (ml/day)	78.2±96.0	194.8±156.4	124.8±68.8	54.2±28.9	18.6±14.2	23.4±15.2	48.8±29.7	0.000 (S)	
ENFs	%Cal TCR	5.5%±4.5%	11.2%±4.4%	8.8%±2.5%	7.3%±2.5%	2.4%±1.0%	1.3%±0.5%	1.6%±0.6%	0.000 (S)
	PRO (g/day)	5.75±3.99	7.19±5.72	5.43±2.94	4.71±2.5	5.58±4.26	5.71±3.72	5.86±3.57	0.34 (NS)
AA 10% vol (ml/day)	517.9±358.7	646.8±514.7	488.7±269.4	424.2±225.8	501.8±383.8	513.6±335.2	527.5±321.3	0.042 (S)	
IFE 20% vol (ml/day)	168.16±52.06	170.00±52.28	161.96±42.18	192.8±46.6	156.3±49.9	163.7±54.0	164.0±59.8	0.005 (S)	
DX 20% vol (ml/day)	751.0±277.8	846.4±365.1	738.7±260.1	751.5±169.3	761.4±289.8	713.6±310.9	690.9±207.9	0.066(NS)	
Dual TPN and EN days	9.03±1.78	8.93±1.57	9.40±2.31	8.87±1.44	9.20±1.81	8.71±1.73	9.22±2.13	0.057(NS)	
% PC_ TC	14.7%±5.5%	16.6%±6.5%	14.6%±4.1%	12.6%±4%	14.07%±6.1%	14.8%±5.3%	15.6%±5.5%	0.004 (S)	
% Carb Cal_ TC	35.2%±5.4%	36.9%±5.7%	35.2%±4.9%	36.2%±4%	35.8%±5.2%	33.3%±6.6%	34.0%±5.3%	0.005 (S)	
% Lipid Cal_ TC	29.5%±5.7%	28.3%±5.4%	29.1%±5.6%	32.8%±3.7%	28.0%±6.7%	28.9%±5.5%	29.6%±5.7%	0.000 (S)	
g Carb: g Lipid ratio	3.43±1.29	3.67±1.05	3.45±1.20	3.01±0.50	3.83±2.01	3.30±1.30	3.27±1.12	0.013 (S)	
Hospital Stay day(s)	15.02±2.39	17.82±1.27	16.59±1.46	14.89±2.57	12.56±1.49	13.44±1.51	14.74±0.65	0.000 (S)	
Overall 28-day Survival	246 (75.46%)	35 (62.5%)	38 (70.37%)	40 (74.07%)	47 (87.04%)	44 (81.48%)	42 (77.77%)	0.031 (S)	
Overall 28-day Mortality	80 (24.54%)	21 (37.5%)	16 (29.63%)	14 (25.93%)	7 (12.96%)	10 (18.52%)	12 (22.22%)		

Data are presented as Mean±Standard deviation and are analyzed by using ANOVA test (at p-value< 0.05).

S: Significant (P-Value <0.05).  
 NS: Non-significant (P-Value >0.05).  
 N: Number of study's hospitalized patients.  
 ALB: Albumin level.  
 H.ALB: Human albumin.  
 Group I: Hospitalized patients on TPN supplemented partially by Ensure®.  
 Group II: Hospitalized patients on TPN supplemented partially by Resource® Optimum.  
 Group III: Hospitalized patients on TPN supplemented partially by RenaMent®.  
 Group IV: Hospitalized patients on TPN supplemented partially by ArgiMent®.  
 Group V: Hospitalized patients on TPN supplemented partially by PROSource®.  
 Group VI: Hospitalized patients on TPN supplemented partially by reconstituted WP 100%.

ENFs: Enteral nutritional formulas.  
 GI: Gastrointestinal.  
 TPN: Total parenteral nutrition.  
 EN: Enteral nutrition.

Sx: Symptoms.  
 BSI: Blood stream infection.  
 TOLR: Tolerance.  
 PRO: Protein.  
 PC: Protein Cal.  
 Carb: Carbohydrates.  
 Cal: Calories.  
 USD: United State Dollar.  
 AA: Amino acid.  
 IFE: Intravenous fat emulsion.  
 DX: Dextrose.  
 Vol: Volume.  
 TCR: Total calorie requirements.  
 TC: Total calorie.  
 CER: Cost effectiveness ratio.

This high variety in CER among analysis groups came mostly from significant differences in H.ALB cost which was lowest in Group IV and Group V followed by Group VI, Group III, Group II, and lastly Group I (0.0±0.0 USD and 0.0±0.0 USD, 25.9±13.1 USD, 32.1±12.6 USD, 47.7±15.0 USD, and 53.9±12.9 USD, respectively) taking into consideration that this significant CER differences included only ENFs cost, TPN cost, and H.ALB cost and not included other cost expenditures especially hospital LOS. There were significant differences in GIT ENF tolerance among the six groups in which the incidence of <2 Symptoms (Sx) (e.g. bloating, cramping, ↑ gastric residual volume (GRV), and dyspepsia) was highest in Group IV followed by Group V, Group VI, Group III, Group II, and lastly Group I (38(70.4%), 36 (66.7%), 34 (63.0%), 32(59.3%), 30 (55.6%), and 30 (53.6%), respectively). This GIT tolerance was directly correlated with ENFs volume administered per day in which it was significantly lowest in Group IV followed by Group V, Group VI, Group III, Group II, and lastly Group I (18.6±14.2 ml/day, 23.4±15.2 ml/day, 48.8±29.7 ml/day, 54.2±28.9 ml/day, 124.8±68.8 ml/day, and 194.8±156.4 ml/day, respectively). The Risk of enteric GNB translocation which was assessed indirectly by the positivity of any Enterobacteriaceae family in blood culture during and up to 3 days after discontinuation of dual TPN and EN was significantly lowest in Group IV followed by Group V, Group VI, Group III, Group II, and lastly Group I (4 (7.4%), 6 (11.1%), 8 (14.8%), 10 (18.9%), 12(22.2%), and 15(26.8%), respectively). Demographics, admission diagnostics and wards, anthropometrics, infectious, and nutritional indices comparative data of the study's malnourished hypoalbumenic hospitalized ill patients on dual TPN and trophic EN feeding are fully summarised in Tables 2-3.

## DISCUSSION

This study included wasted hypoalbumenic hospitalized patients who had received TPN with TF of various six ENFs at an average volume of amino acid (AA) 10%, intravenous fat emulsion (IFE) 20%, and dextrose (DX) 20% of 517.9±358.7 ml/day, 168.16±52.06 ml/day, and 751.0±277.8 ml/day, respectively. The average volume of TF ENFs in this study was 78.2±96.0 ml/day which represented around 5.5%±4.5% from average TCR of 1449±388 Cal/day. To the best of our knowledge, this is the first study in the world which directly compare the positive clinical and economic impacts of standard ENFs versus specialized MFs versus MPFs as supplemental EN at TF dose in hypoalbumenic hospitalized patients who were mostly dependent on TPN in order to rehabilitate the GIT gradually for weaning from PN as soon as possible and to mitigate the PN associated complications.<sup>[13-17]</sup>The TF dose that we adopted in our study was 10 ml/hr from standard ENFs for 16 hours which is approximately around to 160 ml/day, 160 Cal/day, or 5g protein (PRO)/day. In this study, we supplement TPN by TF dose of ENFs to target at least 5 g PRO/day (if tolerated) regardless of ENFs CD and PD. According to our proposed concept, ENF with higher PD requires lower volume per day to achieve this target and this explain the higher GIT tolerance in Group IV, Group V, and Group VI in compared with Group I, Group II, and Group III when we commenced the target enteral PRO daily dose which was insignificant different among the six tested groups. Patients who are not taking any EF may decrease the integrity of enterocytes and colonocytes which subsequently increase the risk of bacterial translocation and GIT related enterobacteriaceae sepsis.<sup>[18,19]</sup>Enterocyte integrities are highly

sensitive to EF itself and to availability of enterocyte-specific nutrients.<sup>[18]</sup>Short chain fatty acids (SCFAs) are the end active metabolite of bacterial fermentation for non-digestible, non-absorbable, but fermentable soluble fibers.<sup>[20-22]</sup>These SFAs can yield around 2 Cal/g for enterocytes but dependently on prebiotic bacteria for fermentation so that this processes can be affected by using antibiotics that are commonly used in hospitalized patients.<sup>[23,24]</sup>Other important enterocyte-nutrient is GLT which is independent on prebiotics for activation and so not affected by broad spectrum antibiotics. The GLT theory might also explain the significant higher ENF GIT tolerance and positive clinical outcomes in improving the ALB, GIT related systemic inflammatory response syndrome (SIRS), and GIT related enterobacteriaceae sepsis in Group IV, Group V, and Group VI in compared with Group I, Group II, and Group III.<sup>[25-27]</sup> Across all analysis variables in our study, ArgiMent<sup>®</sup> had the highest significant positive clinical and economic outcomes due to the unique formulation characteristics of very high PD (≈26 g/100 Cal), High PRO quality (10 g of whey protein (WP)), high CD (≈2 Cal/ml), enrichment of immune-enhancing nutrients (IENs) of GLT, arginine (ARG), and vitamin C, enrichment of prebiotic galacto-oligosaccharides (GOS or Bimuno), and enrichment of zinc which might also explain the significant highest liver ALB synthesis in short bowel syndrome (SBS) or other TPN indication scenarios in hospitalized patients with highly suspected zinc deficiency.<sup>[28-31]</sup>In summary, using TF dose of ENFs in TPN dependent wasted hypoalbumenic hospitalized patients may have great positive clinical and economic outcomes especially if the ENF have a unique nutritional characteristic of higher PD, CD, and GLT, prebiotic, and zinc enrichments. This study is limited by its retrospective design and the use of single-centre data. Nonetheless, our centre is an experienced and high-volume unit, so our data may be useful for other centres. A larger, multisite, prospective study is needed to control for multiple confounders.

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