ijlpr 2023; doi 10.22376/ijlpr.2023.13.3.L123-L133

International Journal of Life science and Pharma Research

ISSN 2250-0480

Research

Ayurveda For Protein Energy Malnutrition

# Efficacy of Ayurveda Interventions in Protein Energy Malnutrition in Children: A Systematic Review and Meta-Analysis

**Dr. Sumod Khedekar[1*] Dr. Renu Rathi[2], Dr. Bharat Rathi[3], Dr. Heramb Hattikar[4] and Dr. Suraj Patlekar[5]**

[1] *Ph.D. Scholar, Department of Kaumarbhritya, Mahatma Gandhi Ayurved College, Hospital and Research Centre, Salod (H). Wardha, Datta Meghe Institute of Higher Education & Research, Wardha, India.*

[2] *Professor & HOD, Department of Kaumarbhritya, Mahatma Gandhi Ayurved College, Hospital and Research Centre, Salod (H). Wardha, Datta Meghe Institute of Higher Education & Research, Wardha, India.*

[3] *Professor Department of Rasashastra, Mahatma Gandhi Ayurved College, Hospital and Research Centre, Salod (H). Wardha, Datta Meghe Institute of Higher Education & Research, Wardha, India.*

[4] *Assistant Professor, Department of Shalyatantra, Gomantak Ayurveda Mahavidyalaya and Research, Centre, Shiroda- Goa, India.*

[5] *Assistant Professor, Department of Shalakyatantra, Gomantak Ayurveda Mahavidyalaya and Research, Centre, Shiroda- Goa, India.*

**Abstract:** According to United Nations International Children's Emergency Fund (UNICEF), in India, around 46 percent of all children below the age of three are too small, and 35.7% are underweight and come under MAM (Moderate Acute Malnutrition). Protein Energy Malnutrition (PEM) can be correlated with *Karshya, Balashosha, Phakka, Parigarbhika, Sushka Revati, and Apatarpanjanya Vyadhi* based on similar clinical features. Multiple evidence-based clinical studies are conducted in this sector, but no comparative conclusion of results or systemic review is accomplished. The study aims to evaluate and compare Ayurveda interventions' efficacy in managing children's protein energy malnutrition and to assess the effect of Ayurveda Interventions on weight gain and serum protein values in children suffering from PEM. This systemic review was conducted according to the guidelines of the Cochrane Handbook of Systemic review of interventions and is reported following the Preferred Reporting Guideline for Systemic review and meta-analysis guidelines (PRISMA). All study groups showed significant p values within the group and insignificant p values in the fixed random effect model. Though the p-value is insignificant between the groups, one group among the four shows better results in the fixed effect model. In the primary outcome of weight, group 3, i.e., the category of drugs having *Bruhana* and *Pachana* combination, shows better results than other groups in the fixed effect model. In the outcome of serum protein values, BMI, and Head circumference, group 4, i.e., drugs with only *Bruhana* properties, show better results than other groups. Based on this review, few policies or treatment protocols can be hypothesized for managing PEM at the national level. The Ayurveda intervention combinations have worked better because they work on multiple aetiological factors and biological variations in PEM in Children.

**Keywords:** Ayurveda, pediatrics, *Kaumarbhritya*, PEM, Children, Systematic review Meta-analysis.

***Corresponding Author**

**Dr.Sumod Khedekar , Ph.D. Scholar, Department of Kaumarbhritya, Mahatma Gandhi Ayurved College, Hospital and Research Centre, Salod (H). Wardha, Datta Meghe Institute of Higher Education & Research, Wardha, India.**

**Received On** 10 November, 2022

**Revised On** 31 January, 2023

**Accepted On** 17 February, 2023

**Published On** 1 May, 2023

**Funding** This research did not receive any specific grant from any funding agencies in the public, commercial or not for profit sectors.

**Citation** Dr.Sumod Khedekar, Dr.Renu Rathi, Dr.Bharat Rathi, Dr.Heramb Hattikar and Dr.Suraj Patlekar , Efficacy of Ayurveda Interventions in Protein Energy Malnutrition in Children: A Systematic Review and Meta-Analysis.(2023).Int. J. Life Sci. Pharma Res.13(3), L123-L133 http://dx.doi.org/10.22376/ijlpr.2023.13.3.L123-L133

## 1. INTRODUCTION

According to World Health Organization, protein energy malnutrition (PEM) is "an imbalance between the supply of protein and energy and the body's demand for them to ensure optimal growth and function"[1] It is a significant public health problem in India. It mainly affects preschool children (<6 years) with dire consequences ranging from physical to cognitive growth and susceptibility to infection. It involves the child at the most crucial period of development, which can lead to permanent impairment in later life.[2] PEM in early childhood has serious long-term consequences because it impedes motor, sensory, cognitive, social, and emotional development [3-5.] India contributes to 1/3 of severely wasted children under five in the world[6]. According to NFHS-4 (National Family Health Survey), 38.4% of children were stunted, 43% were underweight, and 21% were wasted in the less than five years' age group, belonging to SAM (Severe Acute Malnutrition) variety.[7] It also costs lives about 50 percent of all childhood deaths, including urban and rural or 30,000 deaths each day in children under five years. According to UNICEF, in India, around 46 percent of all children below the age of three are too small for their age, 35.7% are underweight and come under MAM (Moderate Acute Malnutrition).[8] Food (*Aahara*) is one of the three sub-pillars of life as per Ayurvedic classics. It is also regarded as the best Medicine, as per *Acharya Kashyapa.*[9] According to Ayurveda, *Agnimandya* is the main causative factor, and *Vata dosha* is the main *Dosha* involved in inducing malnutrition in children[10]. PEM can be correlated with *Karshya, Balashosha, Phakka, Parigarbhika, Sushka Revati, and Apatarpanjanya Vyadhi* based on similar clinical features. Lack of appetite creates an accumulation of undigested toxic elements and blockages in microchannels[11]. There are many causes like improper nutrition, unhygienic, recurrent health problems with no quality care, etc. The ideal treatment is stimulating appetite and increasing microcirculation to remove supplements of nutrition, anti-helminths, and immune modulators.

### *1.1 Background*

#### *1.1.1. Description of the Condition*

Malnutrition is a range of conditions occurring when one or more nutrient intake doesn't meet the requirements. PEM is an essential nutritional problem among preschool-age children. The leading cause of PEM is food inadequacy. PEM was earlier attributed to the 'protein gap' (deficiency of proteins in diet). The food gap is the chief cause of PEM. It is not only the deficiency of proteins but inappropriate food (low in energy density, protein, and micronutrients - Vitamin A, Iron, Zinc) quantitatively and qualitatively. For all indicators of PEM, 80% of the children have been affected by life in Asia (mainly in southern Asia). 43% of children in developing countries are stunted. 50% of child deaths in developing countries are related to malnutrition. Factors associated with PEM are poor ante-natal and post-natal care, low birth spacing, improper feeding practices, unproportioned rural-urban distribution, infections & environment, literacy rate, and family socioeconomic status. WHO classification is based on Weight for height Z score.[12]

#### *1.1.2. Description of the Intervention*

Based on similar clinical features, PEM can correlate with *Karshya* (emaciation). In *Karshya*, *Agnimandya*, i.e. (lack of appetite) is present, which creates *Ama* (~undigested toxic element) and *Srotorodha* (blockage in microchannels).[13] There are many causes of *Karshya*, like improper nutrition, un-hygiene, recurrent health problems with no quality care, etc.[14] The ideal treatment is stimulating appetite and increasing microcirculation to remove *Ama,* the supplement of nutrition, anti-Helminthes, and immune-modulators. [15] Several Ayurvedic interventions can be effectively utilized for the management of PEM, which have high nutritional value, act as anti-oxidants, immunomodulators, and prop up gastro-intestinal system.[16] Basti (~medicated enema), *Abhyanga* (~oleation therapy) and *Swedana* (~Sudation therapy) are the best available *Vatahara* (opposing Vata properties) and *Bruhana* (anabolic) external procedure mentioned in Ayurveda.[17]

#### *1.1.3. How the Interventions might work*

The intervention for PEM might work due to *Deepana-Pachana, and Agni Vardhak* properties, by enhancing metabolism, *Brimhana* properties, by *Snehana*, and nourishment of the body, by improving the digestive fire and thus the absorption of the food intake by the individual. However, the studies included in this study involved single or multiple drugs having properties of *Snighdha, Guru, Bruhana, Mansavardhana*, etc. few studies included panchakarma therapies, and few included drugs enhancing the digestive power and thus improving nourishment.

## 2. METHODS

This systematic review was conducted according to the guidelines of the Cochrane Handbook of Systematic review of interventions and is reported following the Preferred Reporting Guideline for Systematic review and meta-analysis guidelines (PRISMA). The review protocol is published. The trial was registered in PROSPERO with ID-CRD42021248005[18].

### *2.1. Eligibility criteria*

Studies fulfilling the criteria as per the inclusion criteria were eligible. The various areas sought for inclusion are 1. Study design: All comparative trials, including randomized clinical trials (RCTs), controlled clinical trials (CCTs), parallel-group trials, and multiple-arms clinical trials, case series, case reports. Postgraduate and Ph.D. dissertations and other unpublished clinical data if it contains sufficient data for critical evaluation. 2. Population: Studies with participants of both sex between 6 months to 6 years having classical signs and symptoms of *Karshya, Balashosha, Phakka, Yakshma, Kuposhanajanya Vyadhi* as explained in various classical texts of Ayurveda & Protein Energy Malnutrition will be included. Studies including Patients having PEM with Grade I and Grade II as per the WHO standards (MAM and Uncomplicated SAM)[19] 3. Intervention: Ayurveda treatment advised for *Karshya, Balashosha, Phakka, Yakshma, Kuposhanajanyavyadhi* as per the classical text of Ayurveda precisely in the form of *Samshamana* and *Shodhana Karma* line of treatment. In this study, Ayurveda treatment mainly comprises any internal or external application of herbal, mineral, polyherbal, or Herbo-mineral drug: single or compound, described in classical Ayurveda literature or a novel drug with ingredients described in Ayurveda texts. 4. Comparator: Ayurveda treatment with any form of drug, respective dosage form, dose, schedule, treatment other than Ayurvedic interventions, or combination of both, i.e., Ayurvedic and non-Ayurvedic interventions, conservative

treatment, placebo/ sham therapy, waitlist controls, no treatment.

### 2.2. Outcomes of interest

1. Primary outcomes: weight gain and Improvement in Laboratory parameters such as Serum protein values.2. Secondary outcome: Improvement in other anthropometric Parameters like BMI, HC, CC, and MAC.

### 2.3. Information Sources

Many different databases were searched, such as PubMed (Central), Cochrane central register of controlled trials (Central), AYUSH research portal (Govt. of India), DHARA portal, Google scholar, and online clinical trials registers (CTRI, clinicaltrials.gov) and WHO-ICTRP. There were no language restrictions for unpublished postgraduate (P.G.) and doctoral (Ph.D.) dissertation works, the Shodhaganga portal, the university/ institutional website, and other potential sources. More information was obtained from some studies' contact persons (authors) through e-mail or telephone.

### 2.4. Search

The key terms searched relating to or describing the intervention "*Ayurved*" and "Ayurveda" in combination with search terms describing the condition of the disease "*Balashosha*", "*Karshya*", "*Kuposhanajanyavyadhi*", "*Phakkaroga*," "*Shosha*," "*Yakshma*" "PEM." Specific filters were used to search terms in a database search by adaptation. The following search algorithm was adopted ["AYUSH" or "Ayurvedic medicine" or "Medicine, Ayurveda" or "Ayurved" or "Ayurveda" or "Ayurvedic" or "Ayurveda therapy" or "Ayurveda intervention" or "Ayurvedic drugs" or "Ayurveda Herbs" or "Ayurveda Plants" or "Ayurvedic Formulation" or "Ayurveda Panchakarma" or " Basti" or "*Santarpana*" or " *Brimhana*" or "*Rasayana*" or "CCRAS" or "Indian Traditional Medicine," or "*Kaumarbhritya*" or "*Balaroga*"] And ["PEM" or "pem" or "Protein Energy Malnutrition" or "Children" or "Clinical Trial" or "WHO" or "Immunomodulator" or "Indian Academy Of Pediatrics" or "Weight gain in Children" or " Anthropometry" or " Serum Protein," or "Z Score" or "SAM" or "MAM" or "ICDS" or "Supplementary Nutrition Programme"] as title/abstract/keyword.

### 2.5. Study selection and data extraction

Three review authors (SK, RR, BR) were earmarked to assess titles and abstracts of studies reanalyzed using the search strategy and those collected from other additional sources. After excluding duplicates from eligible articles, full-text articles were screened thoroughly to determine whether they fit the inclusion and exclusion criteria stated above. Any contradiction in deciding the eligibility of particular studies was resolved through discussion with the reviewer (HH). The selection process details for the study were shown in Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram. Three reviewers (SK, RR, BR) screened the eligibility of the searched studies individually based on inclusion and exclusion criteria. PICO format was followed to extract data from the included studies. The critical data points of included trails are shown in Table No.1.

### 2.6. Fixed effect Model

This study used a fixed-effect model to maintain the homogeneity of selected trials and avoid omitted variable bias. First, screened trials were divided into four subgroups depending upon their similarities of variables. After that, the data was subjected to statistical analysis, and the meta-analysis results were performed with the appropriate software.

**Table 1: Key data points of included trials.**

| Study Id/ Author | Year Of Publication | Sample Size | Groups | Group A | Group B | Group C | Dosage | Duration |
|---|---|---|---|---|---|---|---|---|
| Amrut Patil Ramgaunda Et Al[20] | 2016 | 20 | A & B | *Ashwagandhaghrita* | *Balawadi* Nutrition Programme, | | Not specified | 75 days |
| Renu Rathi Et. Al[21] | 2017 | 30 | A & B | *Shramahara Dashemani* Syrup (Sdk Syrup) | Sdk Syrup + *Sarvanga Snehan Sweden & Matra Basti* by *Dashmoola Taila* For 7 Days/Month | | 5ml-10ml | 90 days |
| Sheetal Et Al.[22] | 2017 | 30 | A & B | *Vidharikandadi churna* | *Balawadi* Nutrition Programme | | Increasing dose of 1gm per 1 year age of the child | 90 days |
| Babar Et Al.[23] | 2014 | 40 | A & B | *Rajivamrit Yoga* | Placebo | | 1gm/kg/day in 2 divided doses | 90 days |
| Ravindra R. Dhanawade | 2019 | 60 | A & B | *Shatavaryadi Churna* | *Vidaryadi Churna* | | Not specified | 60 days |
| Jagruti S. Kharatmal Et.Al[24] | 2018 | 60 | A & B | *Yashtyadyam Ghrita* | *Goghrita* | | 2-10 gms | 60 days |
| Renu Patel Et. Al | 1993 | 60 | A & B | Liv 52 | Placebo | | 1Tsp TDS | 180 Days |
| Rakesh Kumar et al. | 2020 | 121 | A & B & C | *Ashwagandha Ghrita* | *Ashwagandha* Granules | Placebo | 2.5-4 gm | 60 days |
| Dinesh [25]Et Al. | 2015 | 12 | Na | *Madhvashva Yoga* | Na | | 1-2 gm BD with milk | 90 days |
| Shiksha Kumari Et. Al.[26] | 2018 | 20 | Na | *Matra Basti* Of *Ksheerabal Taila* | | | 30-60 ml | 30 days |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Geeta Et. Al.[27] | 2009 | 37 | A & B | *Vidarikandadi Vati* | *Matra Basti* Of *Ksheerabal Taila* | 3.5-12.5 gm in divided doses | 30 days |
| Astha Sharma Et.Al[28] | 2017 | 30 | A & B | *Santarpan Manth* | Placebo | 200-400 mg per kg body weight | 90 days |
| Yogesh And Jai[29] | 2015 | 30 | A & B | *Godanti Bhasma* | *Balaposhaka Churna* | 4mg/kg body wt. BD | 120 days |
| Deepthi Viswaroopan Et Al[30] | 2016 | 10 | Na | *Ashwagandha Ghrita* | | Dose as per age | 45 days |
| Divya Et Al.[31] | 2019 | 40 | A & B | *Vidarikandadi Churna* Granules | Hyderabad Mix Granules | (1gm each a year and increased by 1 gm every year up to 1 gm year | 120 days |
| Niraj Kumar Joshi Et Al[32] | 2018 | 60 | A & B | *Shri Siddha Modak* | Placebo | 500mg/kg/day in two divided doses | 90 days |
| Rathore Lk et al. [33] | 2019 | 60 | A & B | *Indukantam Ghritam* | Placebo | 1ml/kg/day in two divided doses | 120 days |
| Dr. Parwati Rawat | 2020 | 30 | A & B | Standard Diet | Ayurveda Nutritional Compound | 1gm/kg/day in 2 divided doses | 90 days |
| Dr. Rajagopala S | 2019 | 100 | A & B | *Vidarikandadi* Granules | Hyderabad Nutrition Formula | 14-25 gms/day | 60 days |
| Vijayalaxmi Mallannavar et al. | 2017 | 106 | A & B | *Karshyahara Yoga* | ICDS Guidelines | 18 gms/day | 120 days |
| Saranya Sivaraj Et Al | 2019 | 27 | A & B | *Amritapraasha Ghrita* | Standard Diet | 6 ml twice daily with warm milk | 56 days |
| Chavada Et Al. | 2017 | 30 | A & B | *Ashwagandha* Granules | *Prinana Modaka* | As per Clark"s rule | 90 days |
| Saranya Sivaraj Et Al. | 2018 | 34 | A & B | *Amritapraasha Ghrita* | Standard Diet | 6ml twice daily | 56 days |
| Sumod Khedekar Et Al.[34] | 2021 | 60 | K&C | *Krishnadi* Granules | ICDS Guidelines | 2-3.5 gms in divided doses | 120 days |
| Eishan Jain | 2018 | 40 | A & B | *Vidarikandadi Churna* | Placebo | | 60 days |
| Kalpana Patni[35] | 2017 | 40 | A & B | *Ashwagandha Ksheerpaka* | *Ashwagandha Ksheerpaka* + *Ksheerbala Taila Abhyanga* | 100mg /Kg/day for each serving | 90 days |
| Rajkumar Harinkhede Et Al. | 2016 | 60 | A & B | *Sinhyadi Ghrita* | Hyderabad Protein Energy Rich Mixture | 4-12 ml/day in 2 divided doses | 90 days |
| Pradeep K. Et Al.[36] | 2020 | 60 | A & B | *Shiva Modaka* | Placebo | 5 gm /day | 90 days |

### *2.7. Risk of bias in individual studies*

The included randomized controlled trials (RCTs) study methodology was assessed using the revised tool available online (RoB 2) to evaluate the risk of bias in randomized trials[37]. A pre-defined algorithm was followed to set five domains of each study, i.e., randomization process, deviations from specified interventions, deleted outcome data, measurement of the primary and secondary outcome, and selection of the enlisted results. In case of any disagreement, it was resolved by discussion.

### *2.8. Synthesis procedures and statistical analysis*

For dichotomous data, the risk ratio was used with a 95% confidence interval; the treatment effect was by calculating the mean difference for continuous outcomes measure. A fixed-effects model was used as the data showed insignificant statistical heterogeneity. Meta-analysis was conducted using (RevMan) software tools to minimize the errors.

## 3. RESULTS

### *3.1. Study selection*

A total of 6455 studies were identified from various databases and other sources. After removing duplicate records, 6442 were screened based on title and abstract, of which 6415 records were excluded and 27 were retained. The full text of these 27 articles was assessed for eligibility. Thus 27 articles were included in the final review. The study selection is summarized in fig 1.

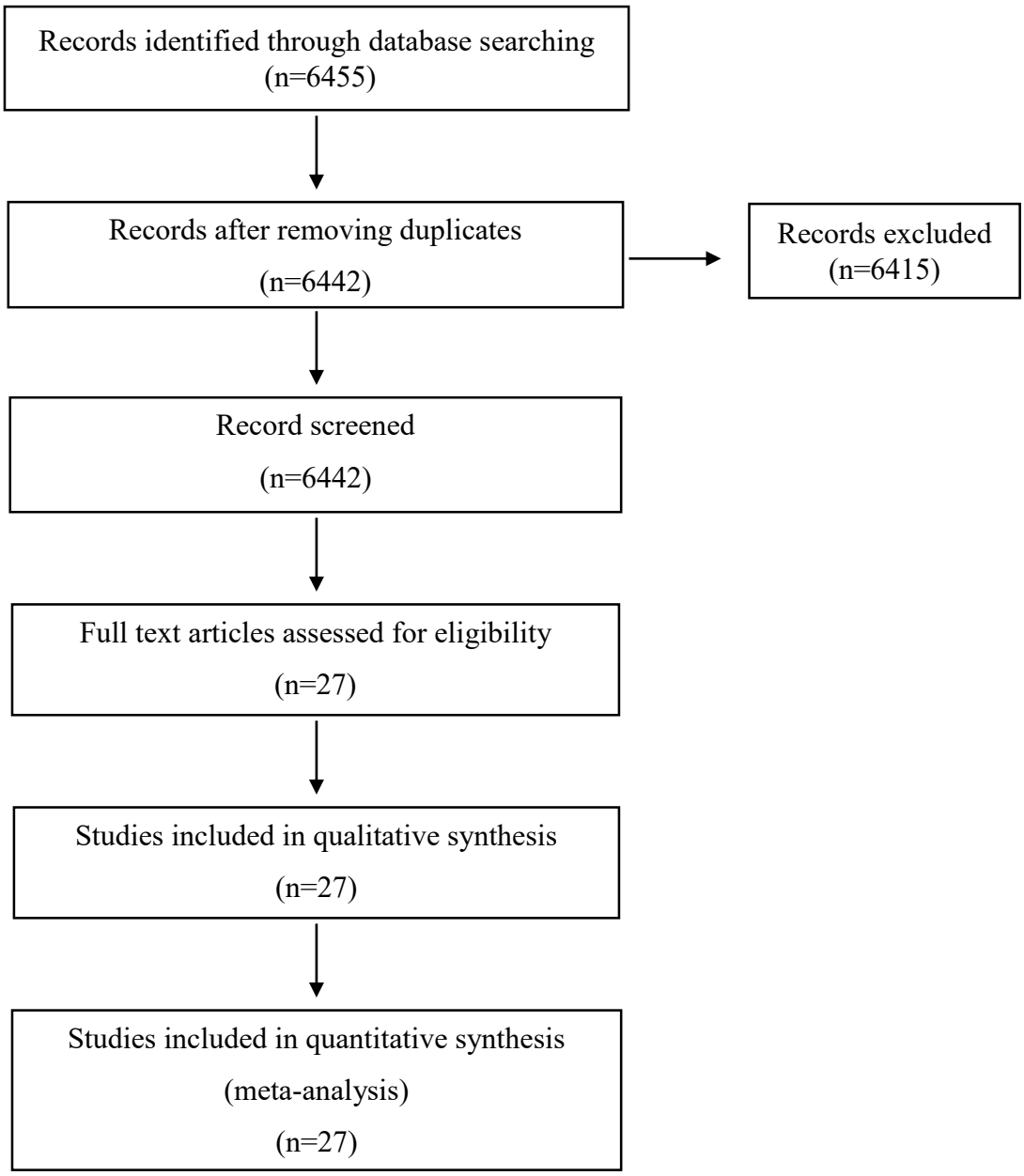



**Fig 1: Criteria of selection of studies**

### *3.2. Study characteristics*

Among these 27 selected comparative clinical trials, all were RCTs. All were included in the quantitative analysis. One trial had three arms, and 26 had two components. All studies were conducted in the outpatient department (OPD) and inpatient department (IPD) of various Ayurveda college hospitals and research institutes in India. All the studies reported subjective outcomes in the form of BMI, weight gain, head circumference, Chest circumference, Mid arm Circumference, and Skin fold thickness. Among objective parameters, serum protein value was considered in all the studies. Among the trial of 3 arms, the third arm was placebo. All these trials reported either partial or complete relief of symptoms at specific time points. Almost all studies didn't have any reporting on adverse events.

### *3.3. Interventions*

Among the included studies, 5 included ashwagandha as the chief component; seven used *Sneha Kalpana*, eight combined *Bruhana* drugs with *Pachana* drugs, and seven studies had the administration of only *Bruhana* drugs.

### *3.4. Risk of Bias in included studies*

The summary of 'Risk of bias' Randomized trials is shown in figs 2 and 3.

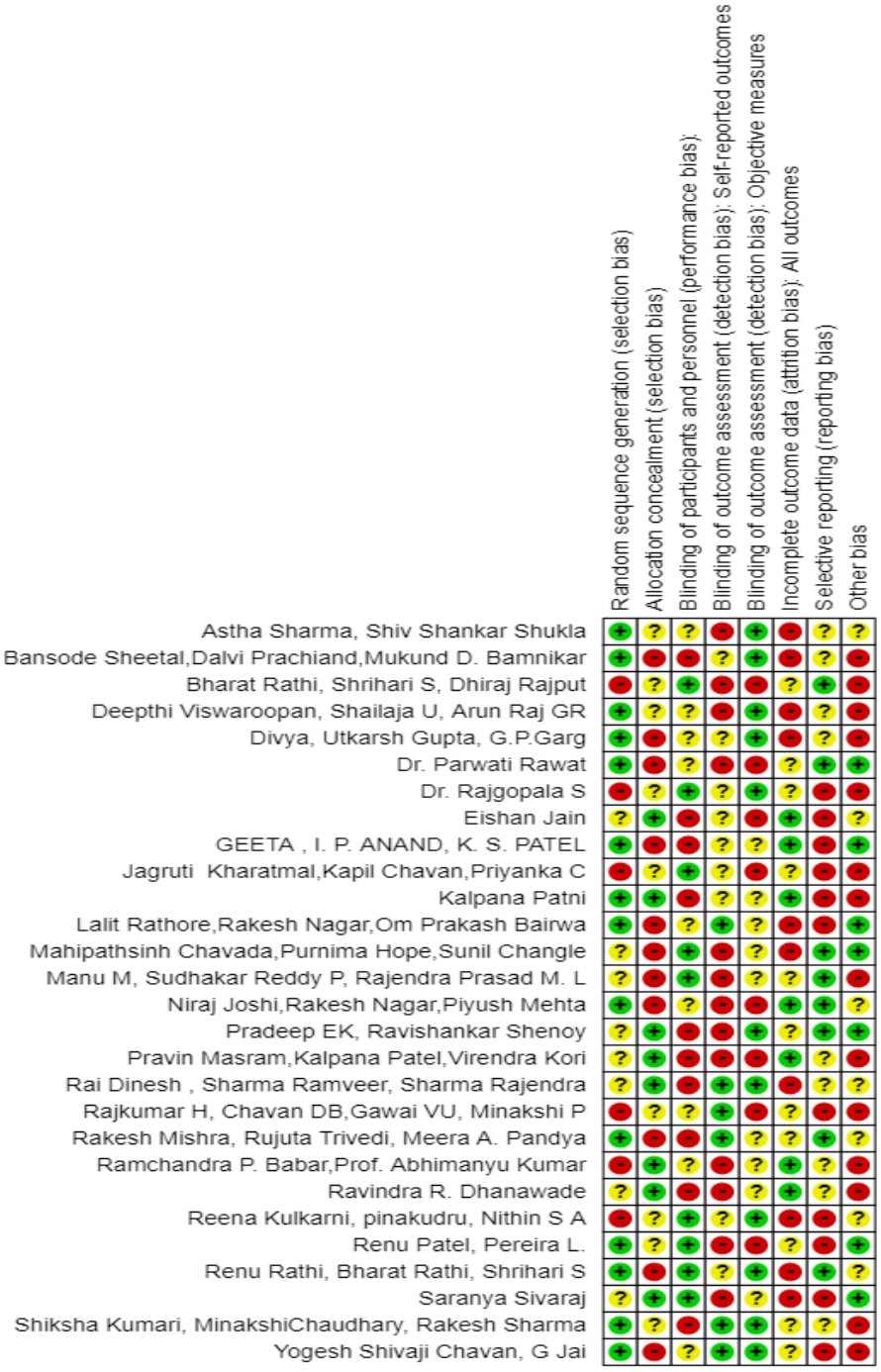



**Fig. 2. Risk of bias for randomized studies**

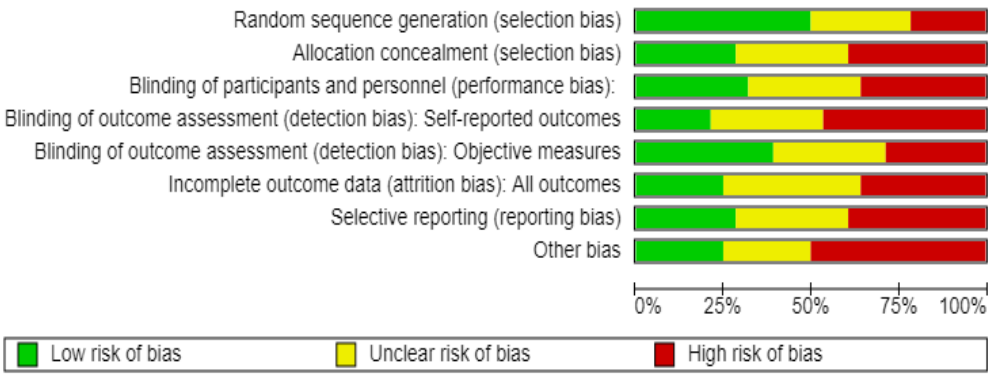



**Fig. 3. Assessment of Risk of bias**

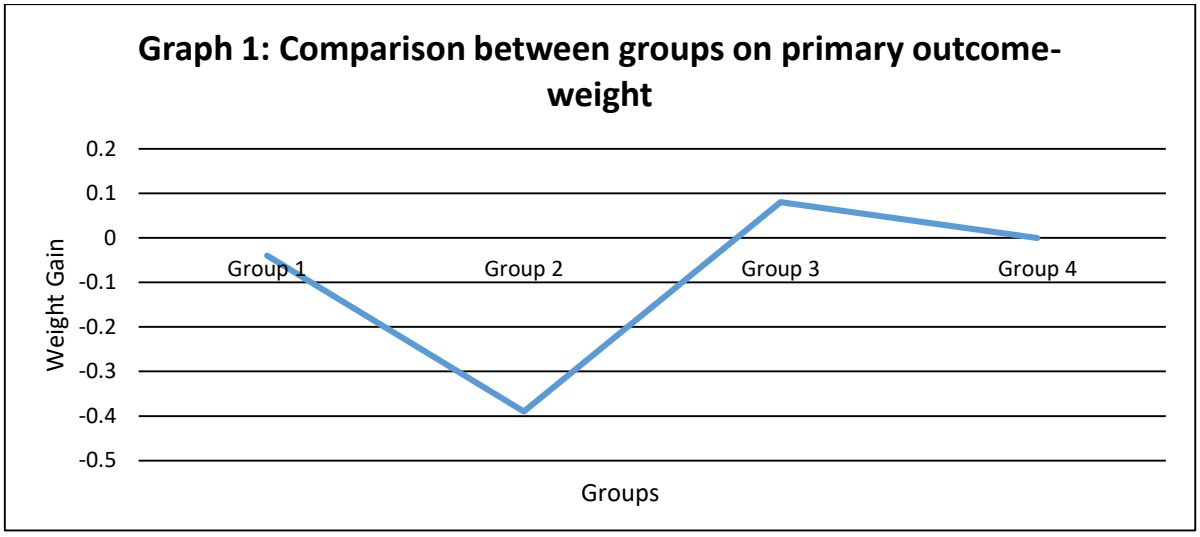
### 3.5. *Effects of intervention*

Primary outcomes: The data of the RCT is Homogeneous. So, it was considered appropriate to pool data according to the principles of interventions into 4 groups. Group 1- studies having Ashwagandha as the chief component; group 2- studies including *Sneha Kalpana* in its management; group 3- studies having a combination of *Bruhana* drug with *Pachana* drugs; group 4- studies involving administration of only *Bruhana* drugs. The primary outcome of the treatment was Serum Protein level, and weight gain, whereas secondary outcomes, were BMI, HC, CC, and MAC. p-value computed within the groups using Wilcoxon signed rank test, p-value calculated through fixed effects model with group 4 as the reference category where groups are set. The impact of the intervention on the primary outcome, like weight and serum protein values, is shown in table 2 and table 3.

**Table 2: Difference in groups on the outcome- weight**

| Parameter | N= available data points | Mean_b | Mean_a | Sd_b | SD_a | P value within Groups | P value between the Groups b | Est | Inference |
|---|---|---|---|---|---|---|---|---|---|
| Weight | 5 | 16.30 | 18.16 | 4.18 | 5.11 | 0.043 | 0.95 | -0.04 | Group 3 is doing better but needs to be statistically significant. |
| | 6 | 17.24 | 18.79 | 5.15 | 5.12 | 0.043 | 0.53 | -0.39 | |
| | 8 | 16.23 | 18.21 | 5.75 | 5.77 | 0.028 | 0.88 | 0.08 | |
| | 7 | 19.05 | 21.06 | 10.77 | 11.45 | 0.028 | - | | |

Table 2 reveals the difference between the four groups on the study's primary outcome, i.e., weight gain. The result shows that Group 3, i.e., studies combining *Bruhana* drug with *Pachana* drugs, is doing better than other groups but not statistically significant due to less sample size.



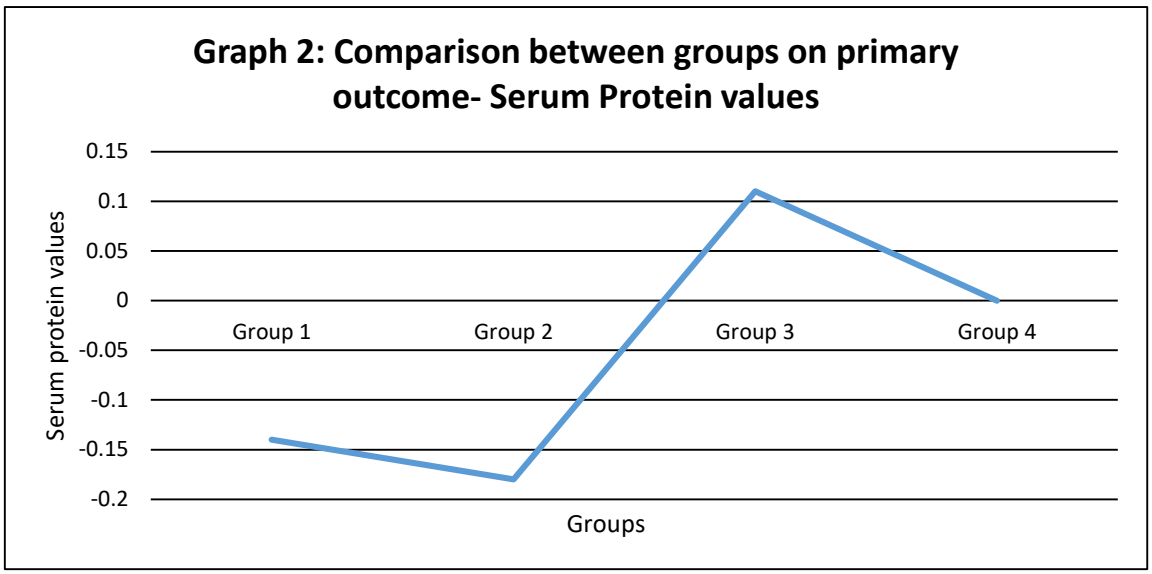

**Graph 1: Comparison between groups on the primary outcome- weight**

Graph 1 represents the comparative result between the groups on the primary outcome of weight gain. Though the results are not statistically significant, they show considerable differences within the groups.

**Table 3: Difference in groups on the outcome- serum protein value**

| Parameter | N= available data points | Mean_b | Mean_a | SD_b | SD_a | P value within Group | P value between the Groups b | Est | Inference |
|---|---|---|---|---|---|---|---|---|---|
| Serum Protein Value | 5 | 4.09 | 4.79 | 0.27 | 0.88 | 0.043 | 0.71 | -0.14 | Group 3 is doing better but needs to be statistically significant. |
| | 5 | 5.38 | 5.80 | 1.39 | 1.42 | 0.043 | 0.59 | -0.18 | |
| | 6 | 5.09 | 5.64 | 1.18 | 1.18 | 0.027 | 0.74 | 0.11 | |
| | 6 | 5.58 | 6.15 | 1.41 | 0.87 | 0.075 | - | | |

Table 3 reveals the difference between the four groups on the study's primary outcome, i.e., serum protein values. The result shows that Group 3, i.e., studies combining *Bruhana* drug with *Pachana* drugs, is doing better than other groups but not statistically significant due to less sample size.




**Graph 2: Comparison between groups on the primary outcome- Serum Protein values**

Graph 2 represents the comparative result between the groups on the primary outcome, i.e., serum protein values. Though the results are not statistically significant, they differ considerably within the groups.

**Table No. 4: Difference in groups on the outcome- BMI**

| Parameter | N= available data points | Mean_b | Mean_a | SD_b | SD_a | P value within Group | P value between the Groups b | Est | Inference |
|---|---|---|---|---|---|---|---|---|---|
| BMI | 5 | 13.52 | 14.78 | 0.74 | 1.43 | 0.039 | 0.25 | -0.45 | Group 4 is doing better but needs to be statistically significant. |
| | 6 | 14.06 | 15.38 | 1.70 | 1.38 | 0.028 | 0.39 | -0.6 | |
| | 3 | 14.98 | 15.84 | 0.67 | 0.60 | 0.109 | 0.15 | -0.34 | |
| | 6 | 14.52 | 16.09 | 1.28 | 1.08 | 0.028 | - | | |

Table 4 reveals the difference between the four groups on the study's secondary outcome, i.e., BMI. The result shows that Group 4, i.e., studies involving the administration of only *Bruhana* drugs with a combination of *Bruhana* drugs with *Pachana* drugs, is doing better than other groups but not statistically significant due to less sample size.

**Table No. 5 Difference in groups on the outcome- HC**

| Parameter | N= available data points | Mean_b | Mean_a | SD_b | SD_a | P value within Group | P value between the Groups b | Est | Inference |
|---|---|---|---|---|---|---|---|---|---|
| HC | 5 | 101.76 | 102.86 | 30.03 | 30.60 | 0.068 | 0.15 | -1 | Group 4 is doing better but needs to be statistically significant. |
| | 5 | 102.21 | 103.81 | 31.58 | 32.40 | 0.043 | 0.45 | -0.5 | |
| | 6 | 97.09 | 97.58 | 46.40 | 47.20 | 0.042 | 0.05 | -1.5 | |
| | 5 | 74.86 | 76.59 | 37.09 | 37.25 | 0.043 | - | | |

Table No. 5 reveals the difference in the four groups on the study's secondary outcome, i.e., HC. The result shows that Group 4, i.e., studies involving the administration of only *Bruhana* drugs with a combination of *Bruhana* drugs with *Pachana* drugs, is doing better than other groups but not statistically significant due to less sample size.

**Table No. 6: Difference in groups on the outcome- CC**

| Parameter | N= available data points | Mean_b | Mean_a | SD_b | SD_a | P value within Group | P value between the Groups b | Est | Inference |
|---|---|---|---|---|---|---|---|---|---|
| CC | 3 | 57.53 | 57.59 | 12.88 | 12.84 | 0.317 | 0.44 | -0.45 | Group 3 is doing better but needs to be statistically significant. |
| | 5 | 51.50 | 51.91 | 2.87 | 3.84 | 0.5 | 0.77 | 0.15 | |
| | 5 | 54.17 | 54.90 | 3.29 | 3.10 | 0.043 | 0.42 | 0.18 | |
| | 6 | 55.55 | 56.08 | 8.60 | 8.36 | 0.043 | - | | |

Table No.6 reveals the difference in the four groups on the study's secondary outcome, i.e., CC. The result shows that Group 3, i.e., studies combining *Bruhana* drug with *Pachana* drugs, is doing better than other groups but not statistically significant due to less sample size.

**Table No. 7: Difference in groups on the outcome- MAC**

| Parameter | N= available data points | Mean_b | Mean_a | SD_b | SD_a | P value within Group | P value between the Groups b | Est | Inference |
|---|---|---|---|---|---|---|---|---|---|
| MAC | 5 | 14.53 | 12.31 | 1.50 | 6.42 | 0.5 | 0.12 | -2.7 | Group 2 is doing better but needs to be statistically significant. |
| | 7 | 13.58 | 14.44 | 0.99 | 0.81 | 0.018 | 0.76 | 0.48 | |
| | 6 | 14.56 | 15.13 | 1.35 | 0.98 | 0.027 | 0.96 | 0.08 | |
| | 7 | 12.46 | 15.16 | 7.00 | 3.89 | 0.028 | - | | |

Table No.7 reveals the difference in four groups on the study's secondary outcome, i.e., MAC. The result shows that Group 2, i.e., studies including *Sneha Kalpana* in its management, is doing better than other groups but not statistically significant due to less sample size.

**Table No.8: Difference in groups on the outcome- Skin Fold Thickness**

| Parameter | N= available data points | Mean_b | Mean_a | SD_b | SD_a | P value within Group | P value between the Groups b | Est | Inference |
|---|---|---|---|---|---|---|---|---|---|
| Skin Fold thickness | 5 | 8.18 | 8.96 | 0.40 | 0.43 | 0.042 | 0.68 | 0.07 | Group 2 is doing better but needs to be statistically significant. |
| | 7 | 8.39 | 9.20 | 0.26 | 0.13 | 0.017 | 0.19 | 0.21 | |
| | 8 | 8.33 | 8.98 | 0.17 | 0.24 | 0.011 | 0.92 | 0.01 | |
| | 6 | 8.34 | 8.97 | 0.31 | 0.40 | 0.028 | - | | |

Table No.8 reveals the difference between the four groups on the study's secondary outcome, i.e., Skin fold thickness. The result shows that Group 2, i.e., studies including *Sneha Kalpana* in its management, is doing better than other groups but not statistically significant due to less sample size.

## 4. DISCUSSION

### *4.1. Summary of main results*

This review summarises findings from 27 studies and includes 6,442 participants. All the studies included in this review were RCTs and assessed the impact of various interventions for the management of PEM on objective and subjective parameters. Studies including patients having PEM with grade I and grade II as per the WHO standards (MAM and Uncomplicated SAM) were included in this study. Primary outcomes were assessed on weight gain and improvement in laboratory parameters such as serum protein values.[38-39] As these were primarily present in all study articles, this two help determine PEM's prognosis. The study's secondary outcome included improvement in other anthropometric Parameters like BMI, HC, CC, MAC, and SFT. These anthropometric parameters were mentioned in most of the selected studies. Also, assessing the patients with these parameters in every follow-up is easy.[40] It was found that all the study groups showed significant p-value within the group and insignificant p-value in the fixed random effect model. Though the p-value is not significant between the groups, one group among the four shows better results in the fixed effect model. In the primary outcome of weight and serum protein values, group 3, i.e., the category of drugs having *Bruhana* and *Pachana* combination, shows better results than other groups in the fixed effect model. In the outcome of BMI and Head circumference, group 4, i.e., drugs having only *Bruhana* properties, are showing better results than other groups. In the outcome of Chest Circumference, group 3, i.e., the category of narcotics having *Bruhana* and *Pachana* combination, shows better results than other groups in the fixed effect model. In the outcome of mid-arm circumference and skin fold thickness, group 2, i.e., the category of drugs having *Snehana Kalpana*, shows better results than other groups in the fixed effect model. Recent studies reveal that protein is an essential nutrient typically assimilated efficiently following the action of gastric, pancreatic, and small intestinal enzymes. After hydrolysis, protein digestion products in amino acids and small peptides undergo mucosal uptake by distinct transport mechanisms. Although gastric and pancreatic enzymes are necessary; the small intestine is the critical rate-limiting tissue in this process. Impaired intake, assimilation, or excessive enteric protein loss may occur with several diseases leading to protein-energy malnutrition.[41] This supports our study results that intervention involving *Brihmana* and digestion correction has a better result than other treatment protocols. Observing different treatment protocols for these conditions mainly focused on three areas, i.e., Diet, Digestion, and Measures to prevent/treat the infection. Thus PEM is one of the diseases interrelated to *Annavaha Srotas*. While describing the importance of *Agni*, Acharya *Charaka* affirms that *Bala* (Strength/Immunity), *Aarogya* (Health), *Aayu* (life expectancy), and *Prana* (liveliness/vitality) are depended on one factor *Agni* (Digestion). In addition, it is mentioned that with the fuel of food, *Agni* is stimulated, and its absence leads to an abate state of *Agni*, leading to diseases or death.[42]

### *4.2. Quality of the evidence*

The quality of evidence was intense as all the 27 trials selected were RCTs with high homogeneity in the data. There are four grades of assessment of PEM. All the trials included in the study had grade 1 and 2 categories of patients. i.e., the mild and moderate categories of malnutrition.

### *4.3. Limitations of this review*

There are different causative factors of PEM, according to Ayurveda. Based on etiology in conservative medicine, the appropriate group intervention can give good results. Also, the number of subjects included in each trial was less and unequal, which may be the reason for the statistically insignificant result in the fixed effect model.

## 5. CONCLUSION

This systematic review and Meta-Analysis help us to conclude that the Efficacy of Ayurveda Interventions, specifically on Weight Gain in the Management of Protein Energy Malnutrition in Children, group 3, i.e., the category of drugs having *Bruhana* and *Deepana, Pachana* combination is showing better results than other groups in fixed effect model. These Ayurveda intervention combinations are better because they work on multiple aetiological factors and biological variations in the case of PEM in Children. Although different trials are being carried out for the management of PEM through Ayurveda interventions, there is a need for high-quality studies in Ayurveda to confirm the potential beneficial effect of *Brumhana* and *Deepan, Pachan* Medicines to combat Protein-energy Malnutrition in Children through Ayurveda.

## 6. AUTHOR'S CONTRIBUTION STATEMENT

Dr. Sumod Khedekar conceptualized the study. Dr. Sumod Khedekar, Dr. Renu Rathi, and Dr. Bharat Rathi designed the treatment protocol. Dr. Sumod Khedekar, Dr. Heramb Hattikar, and Dr. Suraj Patlekar did screening for the eligibility of the searched studies individually based on inclusion and exclusion criteria. Dr. Sumod Khedekar and Dr. Renu Rathi statistically analyzed the data collected; Dr. Sumod Khedekar, Dr. Renu Rathi, Dr. Bharat Rathi, Dr. Heramb Hattikar, and Dr. Suraj Patlekar discussed the study. All the authors contributed to designing the manuscript. All the authors read and approved the final version of the manuscript.

## 7. CONFLICT OF INTEREST

Conflict of interest declared none.

## 8. REFERENCES


1. Onis MD, Blossner M. WHO global database on child growth and malnutrition. WHO; 1997. [Last retrieved on 2010 Oct 01]. Available from: http://whqlibdoc.who.int/hq/1997/WHO_NUT_97.4.pdf.
2. Gragnolati M, Shekar M, Gupta MD, Bredenkamp C, Lee YK. India's malnourished children: A call for reform and action. Washington, DC: World Bank; 2005.
3. UNICEF. The state of the world's children. Adolesc Child Disabil. 2013. [Last retrieved on Aug 10, 2013].
4. Park K. Parks textbook on preventive and social medicine. 19th ed. Jabalpur: Banarsidas Bhanot; 2007. Nutrition and health. p. 507.
5. Paul V, Bagga A, Ghai. Essential pediatrics. 7th ed. Nutrition. New Delhi: CBS publishers; 2009. p. 57-8.
6. Parthasarathy A, Menon PSN, Mehta MN. 4th ed. Vol. 1, Protein-energy malnutrition: chapter 4. New Delhi: Indian Academy of Pediatrics; 2010. p. 136-7.
7. National Family Health Survey-4, India's factsheet by Ministry of Health, Family Welfare, IIPS, Mumbai. Available from: http://www.mohfw.nic.in/. Vol. 2; 2016-17.
8. [last accessed on 8/7/2022 at]. 4.19 PM www.mohfw.nic.in. Available from: https://www.unicef.org/uganda/IMAM_Guidelines_final_version.pdf.
9. Jeevak V, Pandit Hemaraj S, Tewari PV. English translation of Kasyapa Samhita, 1st edi, Edition1996, Khila Sthana [Chapter]- 4. Varanasi: Chaukhambha Bharati Academy.
10. Krishna GG, editor: chapter 11, verse 6.p.52. Ashtang Hriday of acharya Vagbhata. Maharashtra Sahkari Mudranalaya; Pune. In: Sutrasthan; Doshadividyniya Adhyay. 7th ed; 1983.
11. Tewari PV, editor. Kashyapa Samhitha of Vriddha Jivak. Chaukhambha Visvabharati, Varanasi. 1st ed. 2008, Phakka Chikitsasthan; Phakka Chikitsadhyaya: chapter;17, verse12-20:243.
12. Wu G, Fanzo J, Miller DD, Pingali P, Post M, Steiner JL, et al. Production and supply of high-quality food protein for human consumption: sustainability, challenges, and innovations. Ann N Y Acad Sci. 2014 Aug;1321(1):1-19. doi: 10.1111/nyas.12500, PMID 25123207.
13. Tewari PV, editor. Kashyapa Samhitha of Vriddha Jivak. Chaukhambha Visvabharati, Varanasi. 1st ed. 2008, Phakka Chikitsasthan; Phakka Chikitsadhyaya: chapter;17, verse12-20:243.
14. Tewari PV, editor, chapter 17, verse 41.p. Kashyapa Samhitha of Vriddha Jivak. Chaukhambha Visvabharati, Varanasi. In: Chikitsasthan; Phakka Chikitsadhyaya. 1st ed. Vol. 244; 2008.
15. Shastri K, editor, chapter 21, verses 29-33. Charak Samhita of Agnivesha. Chaukhambha Sanskrit Sansthan, Varanasi. In: Sutrasthan, Ashtaunindit Adhyaya, Purvardha. 4th ed; 1994. p. 282-3.
16. Sharma PV. Dravyaguna. 2nd ed. Vol. 2. Varanasi: Chaukhambha Bharati Academy; 1996. p. 51, 275, 339, 350, 370, 503.
17. Tripathi RD, Shukla VD, editors. Reprint ed. Charak Samhita of Agnivesha. Chaukhambha Sanskrit Pratishthan, Varanasi: 2015. Chikitsasthan, Vatavyadhi Adhyaya; chapter no. 28, verse104-5. p. 705-6.
18. Khedekar S, Rathi R, Rathi B, Hattikar H, Patlekar S, Karambhe A. Efficacy of Ayurveda interventions on weight gain in managing protein energy malnutrition in children: A systematic review protocol. J Pharm Res Int. 2021;33(52B):252-8:Article no. JPRI.76033. doi: 10.9734/jpri/2021/v33i52B33624.
19. Ghai OP. Essential Pediatric editor Vinod K Paul and Arvind Bagga, chapter 7, Nutrition, CBS Publishers & Distributors Pvt Ltd. page no. 93-95.
20. Viswaroopan D, Shailaja U, AR GR, Mallannavar V, KT. www. ijrap. net.
21. Rathi R, Rathi B, Shrihari S, Rajput D. Management of childhood Protein Energy Malnutrition through Ayurvedic interventions. J Indian Syst Med. 2017 Jul 1;5(3):196.
22. Sheetal B, Prachi D, Bamnikar M. Role of Vidarikanadi churana in managing Karshya W.S.R To malnutrition in children. 2017;6(2):965-78.
23. Babar RP, Kumar A. A Clinical Study of 'Rajivamrit Yoga'in the Management of Balshosha wsr to Marasmus. J Ayurveda. 2014 Jan;8(1).
24. Kharatmal JS, Chavan KR, Chabukswar PA. Study the effect of Yashtyadyam Ghrita in managing balashosha WSR to undernutrition. 2018;5(3):63-8.
25. Rai Dinesh K, Ramveer S, Sharma Rajendra K, Sharma Shiva K. A clinical study on the effect of Madhwashwayoga (kalpita yoga) on balashosha wrf malnutrition. Pharm Sci Monit. 2015;6(1):190-5.
26. Kumari S, Chaudhary M, Sharma R. A Clinical Study to evaluate the effect of Kshirbala Taila Basti in the

management of Karshya in school-going children. J Ayurveda Integr Med Sci. 2018 Feb 28;3(1):5-8. doi: 10.21760/jaims.v3i01.11632.
27. Anand IP, Patel KS. A Comparative Study on the Effect of Vidarikandadi vati and Kshirabala Taila Basti in managing Karshya in Children. AYU (An Int Q J Res Ayurveda). 2009 Jan 1;30(1):73.
28. Sharma A, Shukla SS. A pilot study to evaluate the role of Santarpan Manth in Protein Energy Malnutrition (PEM). Int J Ayurvedic Med. 2017 Jul 1;8(3):110-4. doi: 10.47552/ijam.v8i3.991.
29. Chavan YS, Jai G. A randomized controlled trial of Godanti Bhasma against Balaposhaka Churna in Management of Balashosha w.s.r. to Protein Energy Malnutrition. Int J Ayu Pharm Chem. 2015;4(1):40-58.
30. Viswaroopan D, U S, Gr AR, Kt JR, Patil S. Ayurvedic management of underweight in children at A Tertiary Care Teaching Hospital of Southern India: A pilot clinical study. Int J Res Ayurveda Pharm. 2016;7(4):46-9. doi: 10.7897/2277-4343.074131.
31. Divya GU, Garg G. Clinical Evaluation of the Effect of Vidarikandadi Churna in Balshosh w.s.r. to Protein Energy Malnutrition in Children. 2019;11(2):239-54.
32. Joshi NK, Nagar RK, Mehta PS. Clinical Study on the Efficacy of Shri Siddha Modak in the management of Balshosh w.s.r. to Protein Energy Malnutrition in Children. 2018;12(1):30-8.
33. Rathore LK, Nagar RK, Bairwa OP. Clinical study to evaluate the efficacy of Indukantam Ghritam (S.Y.) in the management of Balshosha W.S.R. to PEM (Protein Energy Malnutrition). J Ayurveda. 2019;13(2):36-45.
34. Karambhe AD, Khedekar SS, Karambhe PA, Gulhane CM. Critical review on Mandabuddhitva in children and role of Samvardhana Ghrita in treatment. J Ayurveda Integr Med Sci. 2019 Dec 31;4(06):88-92.
35. Patni K. A clinical study to evaluate the Paka and Kshirabala taila Abhyan wsr to Pem. International Ayurvedic. Med J. 2017;5(6):1838-46.
36. Pradeep EK, Shenoy R. Evaluation of the efficacy of Shiva Modaka on hematological, biochemical and immunological parameters in the management of malnutrition among school going children. 2020;5(1):6-9.
37. Eldridge S, Campbell M, Campbell M, Drahota-Towns A, Giraudeau B, Higgins J, et al. Revised Cochrane risk of bias tool for randomized trials (RoB 2.0): additional considerations for cluster-randomized trials;2016.
38. Collins N. Protein-energy malnutrition and involuntary weight loss: nutritional and pharmacological strategies to enhance wound healing. Expert Opin Pharmacother. 2003 Jul 1;4(7):1121-40. doi: 10.1517/14656566.4.7.1121, PMID 12831338.
39. Chowdhury MSI, Akhter N, Haque M, Aziz R, Nahar N. Serum total protein and albumin levels in different grades of protein energy malnutrition. J Bangladesh Soc Physiol. 2008;3:58-60. doi: 10.3329/jbsp.v3i0.1799.
40. Omran ML, Morley JE. Assessment of protein energy malnutrition in older persons, part I: History, examination, body composition, and screening tools. Nutrition. 2000 Jan 1;16(1):50-63. doi: 10.1016/s0899-9007(99)00224-5, PMID 10674236.
41. Freeman HJ, Kim YS, Sleisenger MH. Protein digestion and absorption in man: normal mechanisms and protein-energy malnutrition. Am J Med. 1979 Dec 1;67(6):1030-6. doi: 10.1016/0002-9343(79)90645-4, PMID 117704.
42. Agnivesha SK, Gorakhnath C, Samhita C. Sutra Sthana. Part j, Varanasi [reprint]. 2004:27/337.