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Assessment and Management of Acute Malnutrition in Infants Under Six Months: A Systematic Review

Review Article

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Abstract

Background: Acute malnutrition in infants under six months (u6m) is increasingly recognized as a serious public health concern, as the evidence from developing countries suggests that acute malnutrition affects around 8.5 million u6m infants. Despite this, the current evidence base on the management of acute malnutrition in under six months infants is sparse. The objectives of this paper were to present the burden and underlying risk factors associated with acute malnutrition and synthesize current evidence on various assessment and management approaches currently in use for infants u6m.

Methods: Two electronic databases, PubMed and Cochrane Library were searched between April 2020 and May 2020. We systematically reviewed the literature and identified 33 papers that fulfilled the inclusion and exclusion criteria. Results: One third of the identified studies (n=10, 30.3%) were secondary data analysis. The studies were geographically diverse (LICs + LMICs), of which six were multi-country studies. The review identified that South Asian countries bear the highest burden of acute malnutrition in u6m infants. In order to identify the u6m infants at the risk of mortality, severe underweight at 6 weeks of age could be a potential indicator (requires further evidence from different contexts). Majority of the studies identified maternal related factors to be mainly associated with acute malnutrition in u6m infants. Among preventive interventions, one with maternal nutritional supplementation (MNS) in addition to breastfeeding support showed promising improvement in anthropometric outcomes.

Conclusion: Health programmes, particularly in South Asia region require to focus on maternal related factors to avert and/or manage growth faltering in u6m infants. Further research on context specific burden of acute malnutrition and identification of underlying risk factors, is urgently required for shaping new programs and/ or for incorporating u6m in the existing malnutrition management programs.

Keywords: Assessment; Management; Acute malnutrition; Wasting; Infants under six months

Introduction

Childhood malnutrition is a global public health problem and it is known that majority of the children become susceptible to malnutrition during periods of vulnerability i.e., during the intrauterine period and the early years of life [1]. Wasting (acute malnutrition or wasting have been used interchangeably) in infants under six months (u6m) is increasingly recognized as a serious public health concern [2]. Evidence from developing countries reveal, an estimated 8.5 million infants aged u6m being wasted [3], of which nearly 4.7 million infants aged u6m being moderately wasted, and approximately 3.8 million as severely wasted [4]. These wasted u6m infants constitute an important proportion of all wasted children aged less than five (< 5) years [5]. More than half of all wasted < 5 children in the world live in southern Asia [6], and the age distribution of wasting in this region reveals that the highest prevalence is seen at birth and most of the infants experience their first wasting episode by three months of age [7,8].

When compared to the older children-the physiological processes, including thermoregulation, renal and gastrointestinal functions, are relatively immature in infants u6m [9], Infants are more susceptible to frequent and severe infections as their immune systems are still developing [1], they are less able to make their needs known and are more vulnerable to the effects of poor parenting [10], diagnosing oedema in infants might be more challenging, as most of the older children can stand, and gravity might influence in narrowing the location of the oedema to the limbs in the older children and also, evidence suggests that infants u6m face higher mortality risk during treatment of acute malnutrition [11].

There are several risk factors associated with wasting infants u6m. Some studies have broadly categorized these risk factors into infant-related, maternal-related, and household-related factors [7,12]. Most commonly, severe acute malnutrition in this age group is known to occur due to suboptimal feeding practices, especially breastfeeding practices [9,13]. As per WHO recommendations, infants u6m should be exclusively breastfed however [14], in low-income and lower-middle-income countries (LICs and LMICs), only 37% of children younger than 6 months of age are exclusively breastfed [15]. Studies have shown that even exclusively breastfed infants are susceptible to acute malnutrition [16,17].

Assessment of infants u6m is an essential step to identify acutely malnourished infants and accordingly enroll them into nutrition programmes. However, authors have reported that infants u6m are often excluded from nutrition surveys and marginalized in nutrition programmes [12]. The two anthropometric indicators commonly used for assessing severe acute malnutrition (SAM) in children aged 6-59 months are also being considered for infants u6m [9], namely weight-for-height z score (WHZ) and mid-upper arm circumference (MUAC). However, in order to compute WHZ, length/ height is required, which is especially difficult to measure in younger infants (u6m infants) [18]. Further, there are no standards for calculating weight-for-height (WFH) for those with length <45 cm [19].

It is challenging to manage malnutrition in u6m infants as it is complex and multifactorial [12,19]. Thus, in 2013, for the first time WHO guidelines on the management of SAM recognized u6m as a special group and included a chapter dedicated to management of infants u6m [9]. Facility-based management of these infants include the use of F-75 or diluted F-100 milk via a supplementary suckling technique until exclusive breastfeeding is re-established with/without antibiotic therapy during the stabilization phase [20]. Focusing only on facility-based strategies might lead to increased admissions, which might have serious implications on resources [21]. Hence, WHO mentions community-based management approach for uncomplicated cases/at-risk infants. Findings from a qualitative study in Senegal showed that community-based care for uncomplicated cases of acute malnutrition in infants u6m improved their access to care [22].

With paucity of evidence on actual burden and associated risk factors, also, with uncertainty in assessment and management approaches, it is difficult to design specific programmes focusing on u6m infants. Through this review we aim- to present the estimated burden of acute malnutrition in u6m infants and also explore and synthesize evidence on various assessment and treatment approaches used for infants u6m.

Objectives

- To explore and synthesize evidence on various assessment and treatment approaches used for infants u6m.
- To identify the current evidence on burden of acute malnutrition in infants u6m.
- To explore and identify underlying risk factors associated with acute malnutrition in infants u6m.

Methods

The methods for this review follow the criteria of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement [23].

Information Source and Search Strategy

The literature search was conducted on two electronic databases- PubMed and Cochrane Library. At the initial stage filter for language (English), species (Human), age (Infant: birth-23 months, Infant: 1-23 months, Newborn: birth-1 month) and publication date (2000-2020) were applied in PubMed database. For PubMed database both ‘controlled vocabulary’ and ‘free-text’ terms were used. Similar search terms were applied for both the databases, according to databases’ advanced search set-up. The final search strategy was run on 15th May, 2020.

Search Strategy: ((((“Infants”[Text Word] OR (“under”[All Fields] AND “six months”[Text Word])) OR ((((“infant”[MeSH Terms] OR “infant”[All Fields]) OR “Infants”[All Fields]) OR “infant s”[All Fields]) AND “under 6 months”[Text Word])) OR ((((“infant”[MeSH Terms] OR “infant”[All Fields]) OR “Infants”[All Fields]) OR “infants”[All Fields]) AND “aged 6 months”[Text Word])) AND (((((((((((((“management”[Text Word] OR “admission”[Text Word]) OR “admission profile”[Text Word]) OR “Discharge”[Text Word]) OR “discharge outcome”[Text Word]) OR “outcome”[Text Word]) OR “diagnostic criteria”[Text Word]) OR “prevalence”[Text Word]) OR “risk factor”[Text Word]) OR “support”[Text Word]) OR “breastfeeding support”[Text Word]) OR “F-100”[Text Word]) OR “diluted f-100”[Text Word]) OR “infant formula”[Text Word])) AND (((((((((((“severe acute malnutrition”[Text Word] OR “sam”[Text Word]) OR “severe malnutrition”[Text Word]) OR “acute malnutrition”[Text Word]) OR “wasting”[Text Word]) OR “wasted”[Text Word]) OR “MUAC”[Text Word]) OR “weight for age”[Text Word]) OR “WAZ”[Text Word]) OR “weight for height”[Text Word]) OR “WHZ”[Text Word]) OR “Anthropometry”[Text Word]).

Study selection

Screening: The selection of the studies was performed using two stage selection process using explicit inclusion and exclusion criteria- first based on title and abstract and later based on full-text. It was performed in EPPI-Reviewer software (version: 4.11.1.1) [24].

Inclusion Criteria

- Population: Infants u6m of age (Low birth weight infant, preterm infants, small for gestational age were included)
- Intervention(s)/Exposure(s): risk factor, diagnostic criteria, admission/ discharge criteria, formula feeding, F-100/ diluted F-100, counselling of mothers of u6m infants (prenatal as well as postnatal), postnatal interventions on mothers of u6m infants.
- Comparator: Any
- Outcome: any of the following- Weight-for-age (WAZ), Weight-for-height (WHZ), Mid Upper Arm Circumference (MUAC), morbidity, mortality due to malnutrition.

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- Context: Studies with a focus on LIC or LMIC, based on World Bank classification of country on income group, 2019 (in case of multi-country study, at least one country belongs to LIC/LMIC group) [25].
- Study design: observational, interventional and secondary data analysis studies

Exclusion Criteria: We excluded the articles that were qualitative, systematic reviews, trial protocols, case studies, or published in abstract form only. Articles where evaluation was done for congenital abnormalities, diseases, illness, hospitalization for reason other than malnutrition or HIV-exposed population was excluded. Articles with prime focus on overweight/obesity or stunting (chronic malnutrition) were also excluded.

Data Extraction

The extracted data included characteristics of the study population, brief description of-intervention (s)/ exposure (s), comparator if present in the study, outcome and context.

Quality Assessment

Quality assessment was performed for all the studies except for studies with secondary data analysis study design. Two checklists were used- for interventional studies, quality was assessed using 'Methods for the development of National Institute for Health and Care Excellence (NICE) public health guidance' [26], and for observational studies, the quality was assessed using- 'Quality assessment tool for observational cohort and cross-sectional studies and, quality assessment tool for case-control studies by National Institute of Health, National Heart, Lung, and Blood Institute (NIH, NHLBI)' [27].

Analysis

The analysis is presented in the form of a narrative synthesis. However, where the authors had stated significance of the finding, it is presented in the results table as P-values. The evidence is presented as- (percentage/mean/ratio/median) for the u6m population as one group or as a comparison between the intervention group (IG) and the control group (CG). Since this review involves a variety of interventions/exposures, this led to a methodological heterogeneity in the results. Thus, final results are presented under categories/ clusters, formed based on the type of intervention/exposure identified in the included studies.

Ethical Approval

The review protocol was submitted to the ethical committee at the Indian Institute of Public Health, Gandhinagar (IIPHG). The protocol was assessed by research ethics committee and an exemption was granted.

Results

Study Selection

Initial search identified 3,689 articles. Of these, 440 articles were removed as duplicates, the remaining 3,249 records were screened in stage-1. The screening based on title and abstract lead to exclusion of another 3,177 records. Remaining 72 records were included in stage-2 for full text assessment. Of these, 39 were excluded based on predetermined inclusion and exclusion criteria. Finally, 33 records were included for analysis (Figure 1).

Study Characteristics

Characteristics of the included studies are presented in Table 1. Among the included studies, one-third of the studies were secondary data analysis (SDA) followed by seven randomized controlled trials (RCTs) seven prospective cohort studies (PCS) [3,11,13,16,18,28-46)] (Table 1). Six studies were multi-country studies [3,11,18,30,32,36], followed by six studies from India [16,31,35,40,47,48] and three from each of these countries-Uganda [29,46,49], Bangladesh [38,42,43], Pakistan [39,45,50], Kenya [28,34,51].

Result of Studies

Interventions and Outcomes: Of 33 studies, 12 (36.4%) studies observed both prevalence and risk factors, seven (21.2%) studies focused on prevalence, six (18.1%) assessed preventive interventions, four (12.1%) focused on treatment of wasting and three (9.1%) assessed risk factors associated with malnutrition (table 1). One (3%) study focused on the assessment i.e., indicators used to assess acute malnutrition and predicting mortality in malnourished infants.

Of the total studies, anthropometry outcome was measured in 30 studies (90.9%), morbidity outcome in six studies (18.1%), mortality was observed in six studies (18.1%) and discharge outcomes in three studies (9.1%) [Table 1].

Effect of Interventions on Specific Outcomes: Anthropometry Outcomes: Of total 30 studies reporting outcomes on anthropometry, 26 reported WAZ and 21 reported WHZ. Of these, 12 focused on both prevalence and risk factors, seven focused on prevalence, six on preventive interventions and two on treatment aspect of acute malnutrition in u6m infants [Table 2].

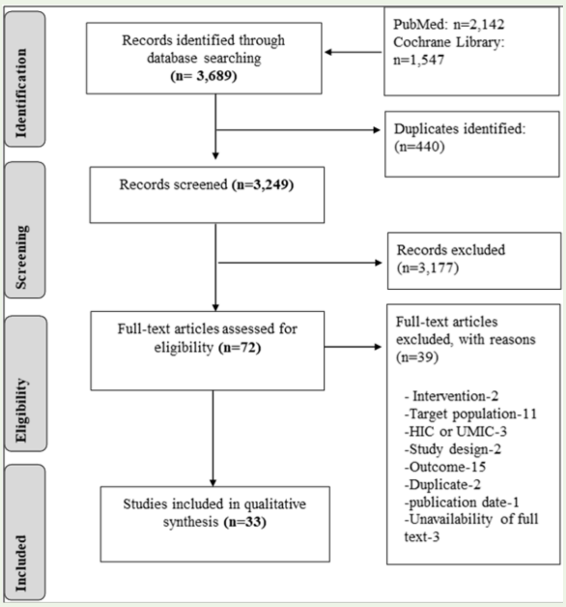

Figure 1: PRISMA Flow Diagram.

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Table 1: Characteristics of the included studies, n=33.

Author (Year†)	Country	Study Type/ Data Type	Target Population	Type of Intervention/ Exposure	Sample size (n is for infants u6m age)	Outcome				
						Anthropometry		Mortality	Morbidity	Discharge outcomes
						WHZ	WAZ			
Agrasada GV (2005) [33]	Philippines	RCT	Mother-infant pairs (Infants-term LBW at enrollment, followed until 6 mo of age)	Preventive Intervention	204		√	√	√	
Barennes H (2009) [52]	LaoPDR (Laos)	C-SS	Mother–infant pairs (infant aged less than 180 days)	Prevalence and Risk Factor	300	√	√			
Berkley JA (2016) [34]	Kenya	RCT	Children aged 60 days to 59 mo‡	Treatment	306			√		
Bhandari N (2003) [35]	India	RCT	Mother-infant pairs (infants followed up to 6 mo of age)	Preventive Intervention	1115	√			√	
Bhargava A (2000) [28]	Kenya	SDA	0-6 month infants	Risk factor	90		√			
Coles CL (2012) [40]	India	PCS	Infants under 6 mo of age	Prevalence and Risk factor	354	√	√			
Eide KT (2016) [29]	Uganda	SDA	Mother-infant pairs (infant followed until 24 weeks of age)	Risk Factor	639	√	√			
Engebretsen IM (2008) [49]	Uganda	C-SS	Mother-infant pairs (infants with 0–11 mo age§)	Prevalence and Risk Factor	412	√	√			
Engebretsen IM (2014) [36]	Burkina Faso, Uganda and South Africa	RCT	mother and infant pairs (infants followed up to 24 weeks of age)	Preventive Intervention	2579	√	√			
Espo M (2002) [41]	Malawi	PCS	Mother-infant pairs (followed until infant was 12 mo of age‖)	Prevalence	582	√	√			
Grijalva-Eternod CS (2017) [11]	10 developing countries	SDA	Children aged 0–60 months (focus on infants u6 mo of age)	Treatment	2939	√		√		√
Hautvast JL (2000) [53]	Zambia	C-SD	Children aged 0–12.5 mo‖	Prevalence	272		√			
Huynh D (2018) [37]	Vietnam	RCT	Mother-infant pairs (infants followed up to 12 weeks of age).	Preventive Intervention	228		√			
Islam MM (2019) [38]	Bangladesh	RCT	Infants under 6 mo of age	Treatment	153, F-100group (50), Diluted F-100 group (52), IF group (51)	√	√	√		√
Kerac M (2011) [3]	21 developing countries	SDA	Children aged 0-60 mo of age (Focus on Infants under 6 mo)	Prevalence	15534	√				
Lopriore C (2007) [18]	76 developing countries	SDA	Infants and children aged 0–5 mo, U3 and U5 years	Prevalence and Risk Factor	For 0–5months infants, ss was at least 100 infants	√	√			
Madeghe BA (2016) [51]	Kenya	C-SS	Mother-infant pairs (6–16 weeks-old infants)	Prevalence and Risk factor	200		√			

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Martorell R (2012) [30]	India and Guatemala	SDA	Children U5 year§ and mother (15-49 years)	Prevalence	India(3346) Guatemala (1031)	√				
Milton AH (2018) [42]	Bangladesh	PCS	Mother-infant pairs (followed until infant was 9 mo of age‖)	Prevalence and Risk Factor	120	√	√			
Nasreen HE (2013) [43]	Bangladesh	CCS	Mother-infant pairs (followed until infant was 6-8 mo of age)	Prevalence and Risk Factor	652	√	√			
Nigatu D (2019) [13]	Ethiopia	SDA	Mother-infant pairs (infants under 6 mo of age)	Prevalence	2080	√	√		√	
Oktaria V (2017) [44]	Indonesia	PCS	Mother-infant pairs (infant under 6 mo of age)	Prevalence	223	√	√		√	
Olusanya BO (2010) [54]	Nigeria	C-SS	Infants 0-3 mo of age	Prevalence and Risk Factor	5888	√	√			
Olusanya BO (2012) [55]	Nigeria	C-CS	Mother-infant pairs (Infants 0-3 mo of age)	Prevalence and Risk factor	Cases(918), Control (1836)	√	√			
Patwari AK (2015) [16]	India	SDA	Children aged 0-59 months (Focus on 0-6 mo infants)	Prevalence	3807	√	√		√	
Qazi SA (2003) [50]	Pakistan	C-SD	Infants under 6 months enrolled and followed up till 24 months of age	Prevalence and Risk Factor	553		√			
Rahman A (2004) [45]	Pakistan	PCS	Mother-infant pairs (followed until infant was 12 mo of age‖)	Prevalence and Risk Factor	265		√			
Rahman A (2008) [39]	Pakistan	RCT	Mother-infant pairs (infants followed up to 12 mo of age‖)	Preventive Intervention	IG (368), CG (359)		√			
Shroff MR (2011) [47]	India	C-SD	Mother infant pairs (3–5 mo old infants)	Risk factor	465	√	√			
Singh DK (2014) [31]	India	SDA	Infants under 6 mo of age	Treatment	108			√	√	√
Singh V (2017) [48]	India	PCA	Mother-child dyads (followed from birth to 18 months of age‖)	Preventive Intervention	IG (492), CG (450)		√			
Vesel L (2010) [32]	India, Ghana, Peru	SDA	Mother-infant pairs (Infants 0-12 mo of age¶)	Assessment	Ghana (2637), India (3718), Peru (2251)			√		
Wandera M (2012) [46]	Uganda	PCS	Mother-infant pairs (followed until infant was 3 weeks of age)	Prevalence and Risk Factor	519	√	√			

Notes: †Year is given as year when study was published, ‡age has separate category for 2-5 months, §age has separate category for 0-5 months, ||outcome is seen at 6 months, ¶age has separate category for 0-6 months.

Abbreviations: WHZ: weight-for-Height z-score; WAZ: weight-for-age z-score; ss: sample size; C-SS: cross-sectional study; C-SD: cross-sectional data; SDA: secondary data analysis; PCS: prospective cohort study; CCS: community-based cohort study; RCT: randomized controlled trial; PCA: prospective cohort assessment; C-CS: case-control study; mo: months; BF: breastfeeding; CC: childcare; IG: intervention group; CG: control group; IF: infant formula.

Effect of intervention/Exposure on outcome (for details of each study refer table 2).

Prevalence (WHZ): Of the total 21 studies reporting WHZ, 15 studies presented prevalence of wasting in infants u6m. Of these, 11 considered prevalence based on WHO growth standards, two considered prevalence based on National Center for Health Statistics (NCHS) growth standards, while two studies compared prevalence based on both the standards. Prevalence of wasting was measured at different ages/ time points in different studies, however, all the studies measured prevalence among infants ≤ 6 months.

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Table 2: Result table presenting effects of intervention(s)/exposure(s) on anthropometry, morbidity, mortality and discharge outcome(s).

Sr. No	Author (Year†)	Target Population	Intervention/Exposure (includes I/E were outcome is seen in u6m infants)	Sample size (n is for infants u6m age)	Outcome
			Prevalence, n=7		
1	Espo M (2002) [41]	Mother-infant pairs (followed until infant was 12 mo of age‖)	**Prevalence:** WAZ, WHZ scores were calculated using NCHS Reference.	n=582	**Anthropometry:** Prevalence, at 6month (mo) Underweight: 9% Severely underweight: 1% Wasted: none
2	Hautvast JL (2000) [53]	Children aged 0–12.5 mo‖	**Prevalence:** WAZ score calculated using two references NCHS and breastfed data set (WHO).	n=272	**Anthropometry:** Prevalence, during first 6mo Underweight: 3-15% (NCHS) 19–28% (WHO)
3	Kerac M (2011) [3]	Children aged 0-60 mo of age. (Focus on Infants under 6 mo)	**Prevalence:** 21 countries were selected for analysis from a reference population of 36 that accounted for the majority of the global malnutrition disease burden and that had available DHS anthropometry data collected in the past 10 years. WHZ score was calculated using both NCHS and WHO standards.	n=15534	**Anthropometry:** Prevalence, NCHS Wasting: 1.1-15% (median 3.7%, IQR 1.8–6.5%) Estimated number, NCHS Wasted: 3 million Prevalence, WHO Wasting: 2.0–34% (median 15%, IQR 6.2–17%) Estimated numbers, WHO Wasted: 8.5 million Approximate numbers of infants u6m in all developing countries, as diagnosed using NCHS ref are (n=55.5 million), Severe wasting: 0.8 million Moderate wasting: 2.2 million Using WHO standards results in a large prevalence increase: Severely wasted: 3.8 million Moderately wasted: 4.7 million
4	Martorell R (2012) [30]	Children U5 year§ and mother (15-49 years)	**Prevalence:** for India, was calculated using NFHS-3 data and for Guatemala, using Reproductive Health Survey collected in 2008–2009. WHZ score was calculated using both 2006 WHO standard and 1976 WHO/NCHS reference	India (n=3346) Guatemala (n=1031)	**Anthropometry:** Prevalence, 0-5 mo Wasting: India 8% (NCHS) 30% (WHO) Guatemala: <2.3% (WHO)
5	Nigatu D (2019) [13]	Mother-infant pairs (infants u6m of age)	**Prevalence:** WAZ, WHZ were calculated using WHO Child Growth Standards. Morbidity was seen as presence of diarrhoea or ARI or fever in 2 weeks prior to assessment.	n=2080	**Anthropometry:** Prevalence, u6m Wasting: 14.2% Underweight: 10.8% **Morbidity:** Prevalence, u6m Diarrhoea: 9.0% Fever: 14.8% Symptoms of acute respiratory illnesses (ARI): 6.3% Had at least one of the above three outcomes: 20.6%
6	Oktaria V (2017) [44]	Mother-infant pairs (infant under 6 mo of age*)	**Prevalence:** WAZ, WHZ score were calculated using WHO growth reference. Morbidity: seen within 2 weeks prior to the assessment.	n=223	**Anthropometry:** Prevalence, at both time points (18-10 wks& 22-24 wks) Underweight: 5–6% Severely underweight: 1–2% Wasted: 3–5% Severely wasted: 1% **Morbidity:** Prevalence, at 8–10wks Had an episode of diarrhoea: 8% Had ARI symptoms with or without cough: 12.4% Prevalence, at 22–24wks Had an episode of diarrhoea: 9% Had ARI symptoms with or without cough: 26.6%

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7	Patwari AK (2015) [16]	Children aged 0-59 months (Focus on 0-6 month infants)	**Prevalence:** secondary analysis of NFHS-3 data was performed. Prevalence of u6m infants was compared with older children. WAZ, WHZ were calculated using WHO growth standards. Morbidity: 2 weeks prior to the assessment.	n = 3807	**Anthropometry:** Prevalence, u6m Wasting: 30.6%, of which Severely wasted: 13.1% Underweight: 29.6%, of which Severely underweight: 10.9% **Morbidity:** Prevalence, u6m Showed symptoms of diarrhoea: 10.6% Showed symptoms of fever: 11.7% Showed symptoms of ARI: 7%
Prevalence and Risk Factor, n=12					
8	Qazi SA (2003) [50]	infants under 6 months enrolled and followed up till 24 months of age	**Prevalence**: study was prospective observational and intervention, but data taken at time of enrolment, is used here to see prevalence of underweight. (WAZ <-2SD was taken as underweight). **Risk Factor:** correlation of family income and number (no.) of siblings with nutritional status of infants is mentioned.	n=553	**Anthropometry:** Prevalence, u6m (seen at enrollment) Underweight: 37.4% Compared to BF infants, exclusively bottle-fed infants were more underweight, RR: 2.15, (95% CI 1.51-3.07), (P = 0.0002) **Risk Factor:** Underweight: Higher in infants from low income families vs in infants from moderate income families, OR: 1.15, (95% CI: 1.03-1.29), (P = 0.017) Correlation between nutritional status and no. of siblings- statistically insignificant
9	Barennes H (2009) [52]	Mother–infant pairs (infant aged less than 180 days)	**Prevalence:** nutritional status of all infants given. WAZ, WHZ score calculated using WHO growth standards. **Risk Factor:** association of maternal restricted diets with infant's nutritional status is seen.	n=300	**Anthropometry:** Prevalence, Wasting: 10% Underweight: 3% **Risk Factors:** Prevalence, in infants of mothers with RD vs NRD, Underweight: 3.3% vs 0% Wasting: 9.9% vs 10.3% (P=0.09) But this difference was statistically insignificant
10	Coles CL (2012) [40]	Infants under 6 mo of age	**Prevalence:** WAZ, WHZ calculated using WHO growth standards. **Risk factor:** the study has seen effect of Spn colonization at ages 2 and 4 mo on growth at age 6 months.	n=354	**Anthropometry:** Prevalence, at 6mo Wasting: 21.3% Underweight: 37.4% **Risk Factors:** Adjusting for confounders, effect of nasopharyngeal carriage of pneumococci on **UNDERWEIGHT** at 6 mo, OR (95% CI), ref: no carriage Carriage at 2 mo only: 1.81 (0.80, 4.10), non-significant Carriage at 4 mo only: 1.48 (0.73, 3.01), non-significant Carriage at 2 & 4 mo only: 1.44 (0.70, 2.93), non-significant **WASTING** at 6 mo, OR (95% CI), ref: no carriage Carriage at 2 mo only: 0.83 (0.34, 1.99), non-significant Carriage at 4 mo only: 0.82 (0.39, 1.71), non-significant Carriage at 2 & 4 mo only: 0.90 (0.43, 1.87), non-significant **Adjusting for confounders, effect on WAZ:** Carriage at 2 mo alone: -0.35 (-0.70, -0.00), (P= 0.05), significant Carriage of invasive serotypes at age 4 mo or at ages 2 and 4 mo was not associated with any growth outcome.
11	Engebretsen IM (2008) [49]	Mother-infant pairs (infants with 0–11 mo age§)	**Prevalence:** WAZ, WLZ were calculated using WHO growth standards. **Risk Factor:** effect of pre-lacteal feeding is seen on wasting.	n=412	**Anthropometry:** Prevalence, for 0-5-mo subgroup Mean WLZ: +0.01 (95% CI -0.11 to +0.14) Mean WAZ: -0.41 (95% CI -0.53 to -0.30). **Risk Factors:** sub-group analysis for 0-5 mo infants, Association of pre-lacteal feeding with wasting: significant (OR 4.63, 95% CI 1.11–19.23)

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12	Olusanya BO (2012) [55]	Mother-infant pairs (Infants 0-3 mo of age)	**Prevalence:** prevalence of severe underweight and severe wasting is seen among cases (n=918), using WHO, 2006 growth standards. **Risk factor:** determine the association between place of delivery and severe undernutrition in early infancy.	Cases n = 918, Controls n = 1836	**Anthropometry:** Prevalence, among cases Severely underweight: 32.8% Severely wasted: 22.9% **Risk factor:** % of infants delivered at residential homes in cases vs controls: 8.9% vs 4.9% In multivariate analysis, the risk of infant being severe underweight was associated with, adjusted OR (95% CI) Infants delivered at public hospitals, reference Infants delivered at residential homes: 2.98 (1.51–5.88), (P= 0.002), significant The risk of infant being severely wasted was associated with, adjusted OR (95% CI) Infants delivered at public hospitals, reference Infants delivered at residential homes: 2.90 (1.32–6.37), (P = 0.008), significant
13	Lopriore C (2007) [18]	Infants and children aged 0–5 mo, U3 and U5 years	**Prevalence**: WHZ, WAZ were calculated using 1977 NCHS/WHO reference. **Risk Factor:** correlation of underweight and maternal BMI was seen.	sample size in the age group 0–5 months was at least 100 infants	**Anthropometry:** Prevalence (overall), 0–5 mo Wasting: 6.7 Underweight: 7.3% Prevalence (highest in Asia): 0-5 mo Wasting: 7.8% Underweight: 10.5% **Risk Factor:** Prevalence of underweight in 0–5-mo-old infants was highly correlated with prevalence of low maternal BMI (Spearman rank correlation, r=0.78, n=41 countries)
14	Madeghe BA (2016) [51]	Mother-infant pairs (6–16 weeks-old infants)	**Prevalence**: All children with WAZ of-1SD, -2 SD and -3SD were considered underweight. **Risk factor:** effect of mother's PPD on infant's nutritional status is seen.	n=200	**Anthropometry**: Prevalence, 6-16 wks Underweight: 34% (95% CI 27.9–41.1%) **Risk factor:** Infants of women with PPD were significantly more likely than infants of women without PPD to be underweight (adjusted OR 5.79 (95% CI 2.14– 15.62), (P = 0.001)
15	Milton AH (2018) [42]	Mother-infant pairs (followed untill infant was 9 mo of age[ll])	**Prevalence:** WAZ and WHZ were calculated using WHO growth standards. **Risk Factor:** association between household arsenic exposure and under-nutrition during infancy is seen.	n=120	**Anthropometry:** Prevalence, at 3 mo Underweight: 25% Wasted: 23.3% Prevalence, at 6 mo Underweight: 10% Wasted: none **Risk Factors:** Association of household's arsenic exposure with Underweight at 3 mo (P=0.18) & 6 mo (P=0.19) Wasting at 3 mo (P=0.54) & 6 mo statistically non-significant
16	Nasreen HE (2013) [43]	Mother-infant pairs (followed untill infant was 6-8 mo of age)	**Prevalence:** WAZ, WHZ were calculated using WHO growth standards. **Risk Factor:** effect of maternal depressive symptoms on infant's growth status is seen.	n=652	**Anthropometry:** Prevalence, at 2–3 mo Underweight: 23.3% Wasted: 5.2% **Risk factors:** Effect of women's EPDS score during pregnancy and at 2–3 months postpartum on infant underweight at 2-3 months: non-significant (unadjusted analysis)

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17	Olusanya BO (2010) [54]	Infants 0-3 mo of age	**Prevalence:** WAZ, WHZ were calculated (WHO-MGR) growth standards. **Risk Factor**: Maternal and infant factors associated with undernutrition were explored with multivariable logistic regression analyses.	n=5888	**Anthropometry:** Prevalence, 0-3 mo Underweight: 13.8% Wasting (zBMI<-2): 10.0% Wasting (WHZ <-2): 11.4% Severe underweight: 5.4% Severe wasting (zBMI<-3): 3.7% **Risk factors:** Risk of infant being **Underweight** was significantly associated with (Maternal Factors), adjusted OR (95% CI) 1) Mother's childbearing age, ref: 20–35 yrs < 20 yrs: 1.86 (1.30, 2.66) >30 yrs: 1.33 (1.01, 1.75), (P<0.001) 2) Education, ref: tertiary Primary/ secondary: 1.12 (0.88, 1.43) None: 1.74 (1.10, 2.75), (P=0.058) 3) Place of delivery, ref: Hospital Out of hospital: 1.27 (1.08, 1.49), (P=0.004) 4) Multiple pregnancies, ref: No Yes:6.23 (4.50, 8.63), (P<0.001) (Infant Factors), adjusted OR (95% CI) 1) Gender, ref: female Male: 1.31 (1.12, 1.54), (P=0.001) 2) Chronological age, ref: 0-30d 31-60d: 2.67 (2.15, 3.30) 61-90d:3.55 (2.66, 4.74), (P<0.001) 3) Hyperbilirubinaemia, ref: No Yes: 2.20 (1.65, 2.92), (P<0.001) Factors associated with lower risk of infant being underweight were: 1) Parity, ref: primiparous Multiparous:0.67 (0.57, 0.79), (P<0.001) 2) Accommodation, ref: owned Rented:0.64 (0.45, 0.90), (P=0.011) **Risk of infant being Wasted was significantly associated with** (Maternal factors), adjusted OR (95% CI) 1) Mother's childbearing age, ref: 20–35 yrs < 20 yrs: 1.54 (1.01, 2.33) >30 yrs:1.30 (0.96, 1.75), (P=0.039) 2) Place of delivery, ref: Hospital Out of hospital:1.44 (1.20, 1.73), (P<0.001) 3) Multiple pregnancies, ref: No Yes: 2.00 (1.32, 3.03), (P=0.001) (Infant factors), adjusted OR (95% CI) 1) Gender:1.26 1.05, 1.50), (P=0.011) 2) Chronological age, ref: 0-30d 31-60d:1.98 (1.54, 2.55) 61-90d:3.81 (2.81, 5.17), (P<0.001) 3) Sanitation facilities, ref: shared Not shared: 1.95 (1.40, 2.71), (P<0.001) 4) Accommodation, ref: owned Rented: 0.45 (0.31, 0.65), associated with lower risk of wasting (P<0.001)
18	Rahman A (2004) [45]	Mother-infant pairs (followed untill infant was 12 mo of age[‖])	**Prevalence:** WAZ scores: calculated using NCHS/WHO international references. **Risk Factor:** study was conducted to see whether maternal depression is a risk factor for malnutrition.	n=265	**Anthropometry:** Prevalence, at 2 mo& 6 mo Underweight: 5% & 18%, respectively **Risk factors:** Estimates of simultaneous effects of maternal depression and other risk factors on underweight in 265 Infants at age 6 mo through multiple logistic regression Maternal depression OR (95% CI): 3.5 (1.5-8.6), (P<0.01) ≥5 Diarrhoeal episodes per year (P=0.05) OR (95% CI): 2.2 (1.0-4.7) Relative poverty (P<0.05) OR (95% CI): 2.3 (1.1-5.2)

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19	Wandera M (2012) [46]	Mother-infant pairs (followed until infant was 3 weeks of age)	**Prevalence:** WAZ, WHZ was calculated using WHO growth reference. **Risk Factor:** study examined the relationship between oral health indicators at 7 mo of gestational age and anthropometric status of infants 3 wks postpartum. Criteria used were; healthy (code 0), bleeding on probing observed (code 1), calculus detected during probing (code 2), pocket 4–5 mm (code 3) and pocket >5 mm (code 4)	n=519	**Anthropometry:** Prevalence, at 3 wks Wasting: 2.0% Underweight: 6.9% **Risk Factor:** Infant's WAZ, mean (SD) at 3 wks post-partum by maternal CPI score recorded at 7 mo of gestational age CPI=0: -0.32 (1.1) CPI≥1: -0.33 (1.1) Infant's WHZ, mean (SD) at 3 wks post-partum CPI=0: -0.31 (1.2) CPI≥1: -0.05 (1.3), significant (P<0.05)
Preventive intervention, n= 6					
20	Singh V (2017) [48]	Mother-child dyads (followed from birth to 18 months of age‖)	**Intervention:** INHP II program, enhanced version of the ICDS and RCH service package. **Intervention District:** Basic ICDS and RCH services plus age-specific BF and CF recommendations. **Comparison district:** Basic ICDS and RCH services. WAZ scores: calculated using WHO, 2006 growth standards.	IG, n=492 and CG, n=450	**Anthropometry:** Prevalence, at 6 mo (IG, n = 492 vs CG, n = 450) Underweight: 37.2% vs 44.4% Mean WAZ scores: -1.8 ± 1.1 vs -1.9 ± 1.3 However, this difference was non-significant. Odds of being underweight in the IG, at 6mo Adjusted OR (95% CI): 0.8 (0.5–1.2)
21	Rahman A (2008) [39]	Mother-infant pairs (infants followed upto 12 mo of age‖)	**Intervention:** Cognitive behaviour therapy. **IG:** sessions by community health workers for mothers with depression (no of sessions: 1 every week for 4 weeks in the last month of pregnancy, 3 in the first postnatal month, and 9 sessions monthly thereafter). **CG:** an equal number of visits in exactly the same way as those in the intervention group, but by routinely trained Lady Health Workers. WAZ scores were calculated using NCHS/ WHO international references.	Intervention group n=368, control group n=359	**Anthropometry:** Prevalence, at 6 mo(IG, n=368 vs CG, n=359) Underweight: 12% vs 12% Mean WAZ scores (SD): −0·83 (1·06) vs −0·86 (1·00) ICC=intra-cluster correlation coefficient: 0·017 Adjusted mean difference (95% CI): −0·02 (−0·18 to 0·14), (P=0·76), not significant
22	Engebretsen IM (2014) [36]	Mother and infant pairs (infants followed up to 24 weeks of age)	**Intervention:** community-based promotion of EBF. **IG:** EBF counselling by peer counsellors, mothers were offered at least five home visits. **CG:** separate team of peer supporters supported the families to obtain birth certificates and social welfare grants, this was believed not to interfere with BF behaviour.	n=2579	**Burkina Faso Outcomes** **Anthropometry:** Prevalence, at 24 wks(IG vs CG) Mean score differences (CI) WLZ: [-0.20(-0.39, -0.01)] WAZ: [-0.15(-0.34, 0.05)] Wasting PR(CI): [1.40(0.84, 2.32)], insignificant Underweight PR(CI): [1.23(0.88, 1.71)], insignificant **Uganda Outcomes** **Anthropometry**: Prevalence, at 24 wks (IG vs CG) mean z-scores difference (CI) WLZ: [-0.23(-0.43, -0.3)] WAZ: [-0.26 (-0.44, -0.08)] Wasting PR(CI): [2.36(1.11, 5.00)] Underweight PR(CI): [1.52(0.81, 2.88)] **South Africa outcomes** **Anthropometry** Prevalence, at 24 wks(IG vs CG) mean z-scores difference (CI) WLZ: [0.23 (0.03, 0.43)] WAZ: [0.09(-0.13, 0.30)] Wasting PR(CI): [1.12(0.30, 4.11)] Underweight PR(CI): [1.18(0.58, 2.38)]

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23	Bhandari N (2003) [35]	Mother-infant pairs (infants followed upto 6 mo of age).	**Intervention:** community-based counselling for EBF. **IG:** health and nutrition workers assessed infant's FP, identified difficulties, and provided information on the benefits of EBF, at multiple opportunities. **CG:** no specific intervention.	n=1115	**Anthropometry:** Prevalence, at 6 mo (IG, n=466 vs CG, n=411) Wasting: 3% vs 3% OR(CI): [0·83 (0·32 to 2·12)], (P= 0.695), insignificant Prevalence, infants with LBW (IG, n=159 vs CG, n=124) Wasting: 3% vs 5%, OR(CI): [–0·02 (–0·06 to 0·01)], (P= 0.195), insignificant **Morbidity:** Prevalence, at 3 mo (IG, n=483 vs CG, n=412). Diarrhoea in previous 7d: 22% vs 30%, OR(CI): [0·64 (0·44–0·95)], (P=0·028), significant. Diarrhoea episode in previous 3 mo for which treatment was sought outside home: 34% Vs 43%, OR(CI): [0·69 (0·56–0·84)], (P<0·0001), significant Prevalence, at 6 mo (IG, n=468 vs CG, n=412). Diarrhoea in previous 7d: 25% vs 28%, OR(CI): [0·85 (0·72–0·99)], (P=0·04), significant. Diarrhoea episode in previous 3 mo for which treatment was sought outside home: 43% vs 52%, OR(CI): [0.68(0.50-0.92)], (P=0·012), significant
24	Huynh D (2018) [37]	Mother-infant pairs (infants followed up to 12 weeks of age)	**Intervention:** MNS and BF support **IG:** received MNS (252 kcal/day) daily up to 12 weeks postpartum and 4 BF education and support sessions. **CG:** received standard care WAZ scores: calculated using WHO, 2006 growth standards. **Note:** 0.0500 ≤ p values ≤ 0.1000 considered a trend	n=228	**Anthropometry:** Growth from birth to 12 weeks postpartum (IG, n=104 vs CG, n= 100) Trends for WAZ score development over time, estimate (95%CI): [0.16 (-0.03, 0.36)], (P=0.0636), significant
25	Agrasada GV (2005) [33]	Mother-infant pairs (infant- term LBW at enrollment, followed untill 6 mo of age)	**Intervention:** homebased postnatal peer counselling. **IG1:** BF counsellor informed mothers the benefits of EBF the infants up to 6 mo, and assisted mothers in preventing and managing BF problems. **IG2:** childcare counsellors assisted mothers on infant care and increasing mother–infant interaction using activities such as infant massage and smile therapy. **CG:** did not receive any counselling.	n=204	**Anthropometry:** Prevalence, at birth Mean WAZ ± SD: BF group (n=68) = -1.96 ± 0.26 CC group (n=67) = -1.91 ± 0.18 Control group (n=69) = -1.91 ± 0.22 Prevalence, at 6mo Mean WAZ ± SD: BF group (n=68) = -1.10 ± 0.83 CC group (n=67) = -0.92 ± 0.93 Control group (n=69) = -0.92 ± 0.87 **Morbidity**: Prevalence, birth to 6 mo Rates of diarrhoea: BF group: 15%; CC group: 28.3% Control group: 30.5% **Mortality:** No infant in this study died.
			Risk Factor, n=3		
26	Bhargava A (2000) [28]	0-6-month infants	**Risk factor:** Maximum likelihood estimates of dynamic random effects model for WAZ scores based on NCHS reference explained by maternal nutritional status, and infant nutrient intakes.	n=90	**Risk Factors:** Factors significantly and positively associated with infant's WAZ score: Maternal BMI Maternal haemoglobin concentration, (P<0.05) Factors non significantly associated with infant's WAZ score: Infant morbidity index Maternal morbidity index
27	Eide KT (2016) [29,50]	Mother-infant pairs (infant followed until 24 weeks of age)	Risk Factor: secondary data analysis to see socioeconomic distribution growth outcomes among infants included in a trial, which promoted EBF by peer counsellors in Uganda. (linked to no.21, Engebretsen IM, 2014)	n=639	**Risk Factors:** At 12 weeks, socioeconomic distribution, Wasting: concentration index -0.213 Underweight: concentration index -0.301 (Significantly concentrated among the poor in the total population) At 24 weeks, socioeconomic distribution, n=641 Wasting: concentration index -0.253 Underweight: concentration index -0.226 (Significantly concentrated among the poor in the total population and intervention group)
28	Shroff MR (2011) [47]	Mother infant pairs (3–5-month-old infants)	Risk factor: Maternal autonomy was examined as a determinant infant growth in children 3 to 5 months of age. Maternal autonomy dimensions used: (1) household decision making, (2) decisions regarding child care, (3) mobility autonomy, (4) actual mobility, (5) financial autonomy, and (6) non-acceptance of domestic violence.	n=465	**Risk Factor:** After controlling for covariates, Effect of maternal autonomy dimensions seen with underweight **(WAZ)** Ability to make household decisions: (β = 0.167; 95% CI: 0.037, 0.297), significant With wasting **(WLZ)** Ability to make household decisions: (β = 0.263; 95% CI: 0.106, 0.421), significant Mobility autonomy (i.e. not needing permission to go out) (β = −0.202; 95% CI: −0.342, −0.063), significant
			Assessment, n=1		

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29	Vesel L (2010) [32]	Mother-infant pairs (Infants 0-12 mo of age¶)	Assessment: to determine the sensitivity and specificity of nutritional status indicators for predicting death during infancy. WHO and NCHS both references were used to see predictability.	Ghana (n =2637), India (n=3718), Peru (n=2251)	**Mortality:** In infants aged u6m, severe underweight at the first immunization visit as determined using WHO standards had the highest sensitivity (70.2%) and specificity (85.8%) for predicting mortality in India. No indicator was a good predictor of mortality at 6 months age in Ghana or Peru. Malnutrition indicators determined using WHO standards were better predictors of mortality than those determined using NCHS standards.
Treatment, n= 4					
30	Berkley JA (2016) [34]	Children aged 60 days to 59 months‡(were in the rehabilitation phase for treatment of SAM)	Treatment: daily co-trimoxazole prophylaxis in children without HIV being treated for complicated SAM. (Scheduled follow-up after enrolment: once per month up to 6 months, then once every 2 months from 6 to 12 months, without study medication) IG: 120mg (20mg trimethoprim/100mg sulphamethoxazole) for infants u6m old. CG: Placebo drug.	n=306	**Mortality:** <u>Mortality according to age group, 2-5 mo.</u> (IG, n=148 vs CG, n=158) Percentage of infants died: 21.62% vs 27.21% Incidence rate per 100 Child- years (95% CI):31.0 (24.8 to 39.0), (P< 0.0001), significant <u>In this trial, infants u6m, recruited using MUAC values</u>, comprised 17% of the participants & 29% of the deaths
31	Grijalva-Eternod CS (2017) [11]	Children aged 0–60 months (focus on infants u6m of age)	Treatment: inpatient therapeutic care programme for acute malnutrition. This was a secondary data analysis of datasets from 10 countries, that focused only on anthropometric and oedema data at admission and outcomes at discharge.	n=2939	**Anthropometry:** Prevalence At admission, 85.0% infants u6m were wasted (n=2069), of which 14.5% were moderately wasted and 70.6% were severely wasted. Mean WHZ score for infants u6m was (−3.89, 95% CI; −3.93, −3.85). **Mortality:** 4.60% infants u6m died before discharge. Infants u6m showed a greater risk of death (risk ratio 1.30, P< 0.01) during treatment, when compared to older children. **Discharge Outcomes:** 75.7% infants recovered and 10.2% were non-recovered. When compared to older children, significantly lower proportion of the infants u6m were discharged as defaulted [P<0.01].
32	Islam MM (2019) [38]	Infants under 6 mo of age	Treatment: Dietary management in the rehabilitation phase of SAM in infants u6m. Group1: F-100, Group2: F100D, Group3: IF	n=153 F-100 group n=50, Diluted F-100 group n=52, IF group n=51	**Anthropometry:** <u>Mean WLZ± SD scores at start of the trial</u> In F-100 (n=39): -3.8 ± 1.0 Diluted F-100 (n=39): -3.6 ± 0.6 IF groups (n=36): -3.7 ± 0.8 <u>Changes in mean WLZ± SD after completion of the trial</u> In F-100 (n=49): -2.7 ± 1.3 Diluted F-100 (n=48): -2.3 ± 0.8 IF groups (n=49): -2.8 ± 1.1 <u>Mean WAZ± SD scores at start of the trial</u> In F-100 (n=39): -5.1 ± 1.1 Diluted F-100 (n=40): -4.5 ± 1.3 IF groups (n=37): -4.6 ± 1.2 <u>Changes in mean WAZ± SD after completion of the trial</u> In F-100 (n=49): -4.4 ± 1.4 Diluted F-100 (n=50): -4.2 ± 1.4 IF groups (n=49): -4.3 ± 1.1 **Mortality:** <u>Percentage of infants died at end of the trial</u> F-100: 2% Diluted F-100: none IF group: none **Discharge outcome:** <u>Duration of Recovery (Days)- 'ITT' analysis,</u> MD (95% CI) F-100 vs Diluted F-100: −1.9 (−3.9 to 0.2), (P=0.07) F-100 vs IF: − 3.3 (−5.7 to −0.9), (P=0.008) Diluted F-100 vs IF: −1.4 (− 3.8 to 1.1), (P=0.26)

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33	Singh DK (2014) [31]	Infants under 6 mo of age	Treatment: data was collected and analysed to see outcome of 108 infants u6m with SAM admitted in NRC at a teaching hospital.	n=108	**Morbidity:** Prevalence, while admission Acute diarrhoea: 35.2% **Discharge outcome:** Of 108 infants with SAM, 1.69.4% infants- Cured after nutritional rehabilitation. 2.Of the 75 infants cured- 20 cured with correction of positioning and attachment, 32 with SST, (i.e., 48 % infants showed good weight gain after proper counselling or supplementary suckling technique alone) 23 with F-100D 3.26.8 % were non responders 4.Relapse=1 **Mortality:** 3 infants died.

Notes: †Year is given as year when study was published, ‡age has separate category for 2-5 months,§age has separate category for 0-5 months, ||outcome is seen at 6 months, ¶age has separate category for 0-6 months.

Abbreviations: WHZ: weight-for-Height z-score; WAZ:weight-for-age z-score; mo: month; wks: weeks; d: days; ref: reference; yrs: years; I/E: intervention/ exposure; NCHS: National Center for Health Statistics; WHO: world health organization; NFHS: National Family Health Survey; OR: odds ratio; RD: restricted diets; NRD: non restricted diets; spn: streptococcus pneumoniae; WLZ: weight-for-length z-score; FAO: Food and Agriculture Organization of the United Nations; PPD: postpartum depression; LBW: low birth weight; WHO-MGR: World Health Organisation'sMulticentre Growth Reference; CPI: Community Periodontal Index; INHP: integrated nutrition and health program; ICDS: integrated child development services; RCH: reproductive and child health; BF: breastfeeding; CF: complementary feeding; NCHS/ WHO: National Center for Health Statistics/World Health Organization; PR: prevalence ratio; RR: Relative Risk; FP: feeding practices; EBF: exclusive breastfeeding; LBW: low birth weight; MNS: maternal nutritional supplementation; F100D: diluted F-100 ; IF: infant formula; SAM: severe acute malnutrition; MD: Mean Difference; ITT: Intention To Treat; NRC: Nutritional Rehabilitation Centres; SST: Supplementary suckling technique.

Figure 2 presents prevalence reported as per WHO/ NCHS growth standards in the studies, except one study that reported mean WHZ score [49], Which is not presented in this figure. As per WHO growth standards, highest prevalence of wasting was observed in an India based study- 30.6% infants u6m reported as wasted [16]. Lowest prevalence was reported as 2% in Uganda [46]. As per NCHS standards, highest prevalence was reported as 6.7% by a multi-country study [18]. Lowest prevalence was reported as 0% in Malawi [41] (Figure 2). While severe wasting was reported by Nigeria based case-control study- among all the cases of 0-3 months infants with undernutrition, 22.9% (0-3 mo) infants were reported to be severely wasted [55].

Prevalence (WAZ): Of the total studies, 17 had reported underweight prevalence. Of which, 13 studies measured prevalence of underweight based on WHO growth standards, three studies measured underweight based on NCHS standards and one study reported prevalence based on both the standards. Prevalence of underweight was measured at different ages/time points in different studies, however, all the studies measured prevalence among infants ≤ 6 months of all the studies reporting underweight prevalence, a Zambia based study reported prevalence in the form of range (19-28% as per WHO standards and 3-15% as per NCHS) and another Uganda based cross-sectional study reported mean WAZ score (-0.41) [49,53]. Results of remaining 14 studies are shown in **figure 3**- as per WHO standards, highest prevalence of underweight was observed in two studies, one was India based study and another was Pakistan based study [40,50]. A case-control study conducted in Nigeria reported very high prevalence (%) of severe underweight among cases of 0-3 months infants with under nutrition(55)Risk factors (WAZ / WHZ) (for details of each study refer Table 2): Of the total 15 studies focused on risk factors, 13 studies reported factors associated with WAZ/ underweight and nine studies reported factors associated with WHZ/ wasting in infants u6m. Various risk factors identified from these studies are presented below:

- Maternal BMI: Two studies reported maternal BMI [18,28] as a significant factor correlated (Spearman rank correlation coefficient, r=0.78) [26] /associated with underweight/ WHZ in infants u6m (P< 0.05) (28).
- Maternal depression: Three studies reported maternal depression as a factor associated with infant's underweight.

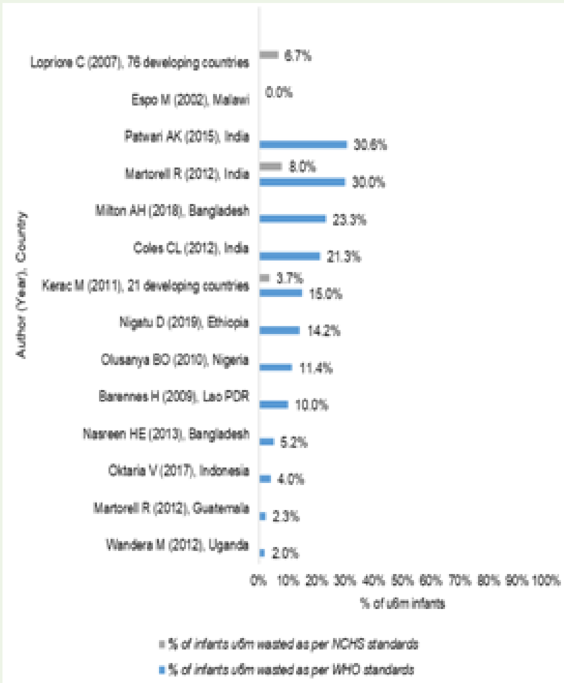

Figure 2: Prevalence of wasting in u6m infants.

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Two studies found significant association of maternal depression with underweight in infants u6m (45, 51). Rahman et al. (OR 3.5; 95% CI: 1.5-8.6; P<0.01) (45), and Madeghe et al. (adjusted odds ratio- AOR 5.79; 95% CI: 2.14 –15.62; P = 0.001) (51), however one study focused on both prenatal as well as postnatal depression and other study reported only postpartum depression [45,51]. On the other hand, Nasreen et al. found non-significant association of maternal depressive symptoms (during pregnancy and 2-3 mo postpartum) with infant's underweight at 2-3 mo [43].

Place of Delivery: Two studies (Nigeria based) found place of delivery as a factor significantly associated with underweight or wasting in infants u6m (54, 55). Of these two studies, one was a case-control, which found that infants delivered at residential homes compared with the public hospitals had almost threefold odds of being severely underweight (AOR 2.98; 95% CI: 1.51–5.88; P= 0.002) or severely wasted (AOR 2.90; 95% CI: 1.32–6.37; P = 0.008), when controlled for potential confounders [55]. The other study which was cross-sectional in nature reported infants born out of hospital had higher odds of being underweight (OR 1.27; 95% CI: 1.08, 1.49; P=0.004) or wasted (OR 1.44; 95% CI: 1.20, 1.73; P<0.001) compared to those born at hospitals [54].

Socioeconomic Status: Three studies observed association of indicators related to socioeconomic status of the family with underweight or wasting in infants u6m [29,45,50]. The Uganda based study performed secondary data analysis to see socioeconomic distribution of underweight or wasting, and found that prevalence of underweight (at 24 wks: concentration index -0.226, at 12 wks: concentration index -0.301) or wasting (at 24 wks: concentration index -0.253, at 12 wks: concentration index -0.213) was significantly concentrated among poor [29]. Another study from Pakistan, reported family income as a factor associated with underweight and found that higher proportion of infants from low income families were underweight when compared to infants in moderate income families (OR 1.15, 95% CI: 1.03-1.29, P = 0.017) [50]. Rahman et al found relative poverty as a factor significantly associated with underweight (OR 2.3; 95% CI: 1.1-5.2; P< 0.05) in infants u6m [45].

Other Factors

Maternal Factors: Maternal haemoglobin concentration and mother's education status were significantly and positively associated with underweight. Mother's periodontal health was significantly associated with infant's WHZ. Factors like maternal autonomy [28,54,46,47], mother's childbearing age and having multiple pregnancies were significantly associated with underweight or wasting in infants u6m. While, association of restricted maternal diets, during postpartum period with infant's underweight or wasting was found to be negative, but insignificant [52,54].

Infant Related Factors: An India based study found that nasopharyngeal carriage of streptococcus Pneumococci (spn) in infants (at 2 mo) was significantly associated with WAZ score but not with WHZ (at 6 mo) [40]. Another study reported that infant's gender (i.e. when compare to female, male infants had higher odds of being underweight- OR 1.31, 95% CI 1.21, 1.54, P=0.001 or wasted-OR 1.26, 95% CI 1.05, 1.50, P=0.011, adjusting for covariates) and this association was found to be significant, however history of hyperbilirubinemia was associated with underweight only [54]. Two studies observed infant's morbidity status as a risk factor [28,45]. Of these, one study reported that ≥ 5 diarrhoeal episodes per year was significantly associated with underweight [45], while the other reported no significant association of infant's morbidity index with underweight [28].

Household Factors: A Bangladesh based longitudinal study observed association of household (HH) arsenic exposure on infant's underweight or wasting, but found it to be insignificant [42]. Another study reported, living in rented accommodation vs owned was associated with a lower risk of infant being underweight (OR 0.64; 95% CI: 0.45, 0.90; P=0.011) or wasted (OR 0.45; 95% CI: 0.31, 0.65; P<0.001) [54].

Preventive Intervention (WAZ): All the six studies with focus on preventive intervention reported anthropometric outcomes. Of these, five studies reported WAZ/ underweight [33,36,37,39,48] (for details of each study refer table 2). Of these five studies, two were community-based studies, where counseling on EBF was given through home visits. However, one study had peer counselors selected from the same village [36], while the other one had two intervention groups with breastfeeding (BF) counselors or childcare (CC) counselors [33]. At end of the trial both the studies found only small changes in WAZ scores of IG vs CG, which were non-significant [33,36]. A prospective cohort assessment was conducted in India to evaluate a program that in addition to government services, involved age specific recommendation of BF and CF in the intervention arm. The results showed that the proportion of underweight in IG (37.2%) was lower than CG (44.4%), but this difference was insignificant [48]. On other hand, Vietnam based RCT in conjunction with a breastfeeding support program also used maternal nutritional supplementation (MNS) in the intervention arm and at the end of the trial, trends for WAZ score development over time (birth to 12 weeks postpartum, estimate 0.16; 95% CI: -0.03, 0.36, P=0.0636) were significantly higher in the intervention group [37]. Only one study had the intervention focused on mothers with depression, which involved home-based cognitive behavior therapy sessions in the intervention arm, at the end of the trial differences in infant's WAZ score (adjusted mean difference - 0.02; 95% CI: −0.18 to 0.14, P=0.76) was non-significant [39].

Preventive Intervention (WHZ): Of six studies, only two reported WHZ/wasting [35,36]. Both the studies had community-based counselling of EBF as intervention. Of the two, an India based study found that prevalence of wasting in IG vs CG was 3% vs 3% and for LBW infants it was 3% vs 5%, with this difference being non-significant [35]. The other study was a multi-country trial, which showed the differences in wasting prevalence ratios between two groups were small and non-significant in Burkina Faso and South Africa, while in Uganda prevalence of wasting in IG vs CG was 7.56% vs 3.16%, and was significant [36].

Treatment (WAZ / WHZ): Of the four studies focusing on treatment aspect, only two had reported anthropometry outcomes [11,38]. First was a study on the dietary management in the rehabilitation phase of SAM in infants u6m, which described three interventions F-100, diluted F-100 (F-100D), and Infant Formula (IF). Positive impacts on WAZ scores and WLZ scores in all the three groups were reported at the end of the trial, but significance of these changes was not reported [38]. However, duration of recovery was reported to be significantly better with F-100D (median duration in days: F-100 vs Diluted F-100 -1.9, 95% CI -3.9 to 0.2, P=0.07; F-100 vs IF: - 3.3, 95% CI -5.7 to -0.9, P=0.008; Diluted F-100 vs IF: -1.4, 95% CI - 3.8 to 1.1, P=0.26) [38]. The other study was on inpatient therapeutic care programme for acute malnutrition, which reported 85.0% infants u6m being wasted at admission, of which 14.5% were moderately wasted and 70.6% were severely wasted and mean WHZ score for infants u6m was -3.89 [11].

Morbidity outcome(s): Of total six studies reporting morbidity outcomes, three were prevalence studies [13,16,44], Two studies focused on preventive intervention [33 35], and one study focused on treatment component of acute malnutrition/ wasting in infants u6m [31] (Table 1).

Effect of intervention/Exposure on outcome (for details of each study refer table 2).

Prevalence: Three studies that reported morbidity prevalence in infants u6m are shown in figure 4. Highest prevalence of diarrhea was reported by India based SDA [16], while highest prevalence of fever was reported by a SDA performed in Ethiopia and highest prevalence of ARI symptoms was reported by a study conducted in Indonesia [13,44].

Preventive intervention: Both the studies assessed community-based counseling on EBF as intervention and no specific intervention was provided to the control group. One was Philippines based RCT

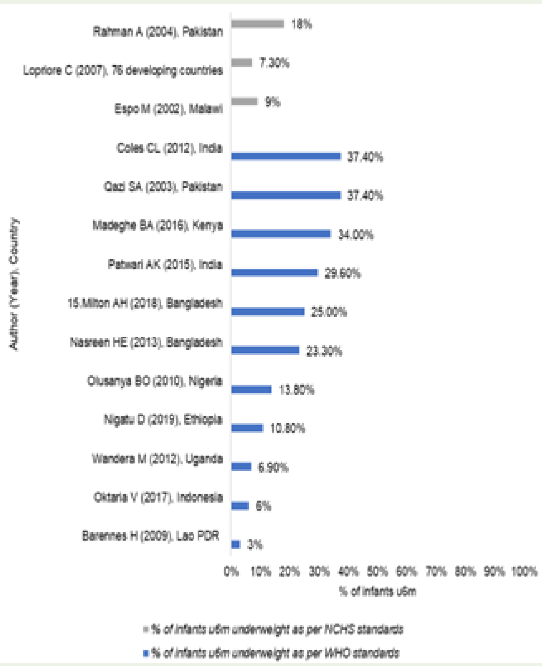

Figure 3: Prevalence of underweight in infants u6m.

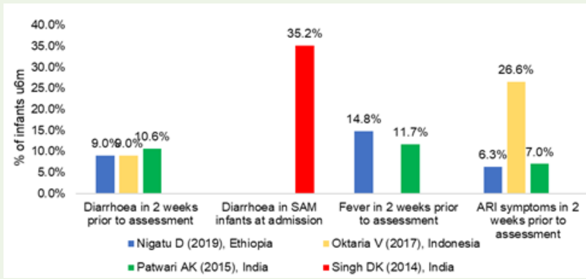

Figure 4: Prevalence of Diarrhoea, Fever and ARI symptoms in infants u6m.

that reported IG2: childcare group and CG: control groups had higher rates of diarrhea (IG2=28.3% and CG=30.5%) than the IG1: breastfeeding counselled group (IG1=15%) [33]. The other study was India based RCT, which reported prevalence of diarrhea at 6 months in IG vs CG was (25% vs 28%), i.e., significantly lower in intervention group (P=0.04) [35].

Treatment: One study observed admission profile of infants u6m with SAM admitted in Nutrition rehabilitation centre (NRC) in India, and reported- at admission most common symptom that the infants presented with, was acute diarrhoea [31] (Figure 4).

Mortality outcome(s): Of the six studies reporting mortality outcome, four focused on treatment [11,31,34,38]. Among remaining two, one was based on preventive intervention [33], and other on assessment aspect [32] (Table 1).

Effect of intervention/Exposure on outcome (for details of each study refer table 2).

Treatment: Among the four studies, two studies were SDA [11,31], one was India based study, that analysed data to see discharge outcomes of 108 infants with SAM admitted in NRC and reported death of 3 infants [31]. Other study was based on data from 10 countries and reported death of (4.60%) infants u6m before discharge, also infants u6m were found to have a greater risk of mortality (risk ratio 1.30, P< 0.01) during treatment, when compared to older children [11]. Mortality in IG vs CG was reported by two RCTs [34,38]. One RCT with intervention- daily co-trimoxazole prophylaxis given to children without HIV being treated for complicated SAM, reported (21.62% vs 27.21%) 2-5 months old infant deaths in IG vs CG [34]. Other study, compared three diets for dietary management in the rehabilitation phase of SAM in infants u6m- Group1: F-100, Group2: F100D and Group3: IF, and death at the end of trial was reported in F-100 group only (2%) [38].

Assessment: A multi-country study, determined the sensitivity and specificity of nutritional status indicators for predicting death during infancy and reported that- at 6 weeks of age, underweight or wasting in India was associated with an increased risk of death before 6 months of age, while no indicator was a good predictor of mortality at 6 months age in Ghana or Peru [32].

Discharge outcome(s): Of the four studies that focused on treatment, three reported discharge outcomes [11,31,38]. A study with three IGs (F-100 vs F-100D vs IF) reported duration of recovery

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i.e., infants who received F-100 recovered more quickly than infants who received infant formula (P = 0.016) but not more quickly than infants who received diluted F-100 (P =0.09) [38]. Another study reported percentage of infants admitted in NRC that were cured i.e., 69.4%, while percentage of infants u6m non-recovered were 26.8% [31]. Of those cured, 42.6% were cured using supplementary suckling technique (SST), 30.6% cured using F-100D and 26.6% cured with correction of positioning and attachment only [31]. The study based on SDA of datasets on inpatient therapeutic care programme for acute malnutrition from 10 countries reported- 75.7% infants as recovered, while 10.2% as non-recovered [11] (refer table 2 for details).

Discussion

Summary of Evidence

The review included 33 studies that were focused on different aspects related to acute malnutrition in u6m infants. These studies had varied methodology and were from different countries belonging to LICs or LMICs [25]. Majority (n=22) of the included studies focused on prevalence and risk factors associated with acute malnutrition. However, the target population was diverse in these studies, with some having sole focus on u6m infants while others incorporating sub group analysis for this age group.

Only one study focusing on assessment of u6m infants with acute malnutrition met the inclusion criteria. The study reported that, to identify infants at higher risk of mortality at 6 months age, severe underweight at 6 weeks age (i.e., age of routine immunization) could be considered as better indicator when compared to low WLZ score [32]. Similar findings were reported by Lelijveld N et al., in a review of methods to detect cases of severely malnourished infants u6m, the author rated WFA, MUAC as indicators over WLZ, for acute malnutrition and associated mortality in infants u6m [56]. The probable explanation for this could be the fact the WLZ has poor predictive value or low sensitivity to predict infant's death and many WLZ values are incalculable using current WHO growth standards [56,57,58]. WHO's current recommendations for u6m infants adopted the same criteria used for older children (i.e., use of WLZ for identifying mortality risk), however these recommendations were made in absence of quality evidence and recently emerging evidence has reported WLZ as poor indicator for u6m infants [9].

Four studies focusing on the treatment aspect were identified in this review [11,31,34,38]. The included studies found that u6m infants had a higher risk of mortality during treatment compared to the older children. However, u6m infants showed less default rate than the older children at discharge [11,34]. The higher vulnerability of these u6m infants could be one of the reasons explaining their higher mortality rate, when compared to older children (6- 59 months age).

In the study by Singh et al., majority of the inpatient infants were treated by simple interventions like- counselling, SST, correction of breast positioning and attachment [31]. These findings suggest that simple interventions could be easily incorporated in outpatient programs and a considerable case load of u6m could be managed in community itself, reserving the inpatient admissions for complicated cases (cases with oedema and danger signs).

For inpatient management of u6m infants with SAM, WHO guidelines based on earlier evidence stated F-100 to be unsafe for u6m infants with SAM, owing to high renal solute load and risk of hypernatraemic dehydration [9]. However, recent evidence from a study conducted by Islam et al., suggested that for infants who are gaining weight rapidly in a hospital environment with well-controlled preparation of feeds, F-100 is safe and that there is no need to prepare an alternative type of feed for infants u6m [38]. These contrasting findings highlight the need of further research in this field to generate concrete evidence.

The review also explored postnatal/ postpartum interventions that prevent growth faltering in u6m infants. Studies (n=4) mainly involved community-based promotion of breastfeeding practices as the intervention [33,35,36,48]. These interventions successfully improved breastfeeding practices in the intervention group and two studies, reported significantly less diarrhea prevalence in IG [33,35]. However, this improvement was not translated to infant's anthropometric outcomes at 6 months. This review observed outcomes at 6 months only. Thus, it is possible that improvement in anthropometry might have occurred, when follow up was carried out at later ages.

A study by Huynh et al, incorporated MNS in the intervention, in conjugation with BF support. This intervention reported significant trends for higher WAZ score development over time (birth to 12 weeks postpartum) in the infants of IG [37]. This finding explains the importance of incorporating mother's nutritional component in the interventions addressing the prevention of growth faltering in u6m infants.

Another study that offered cognitive behavioral therapy (counseling sessions) for mothers with depression presented no significant differences in underweight prevalence between IG vs CG, but other significant benefits of this intervention were reported [39].

Risk factors associated with acute malnutrition in u6m infants were reported by (n=15) studies in this review. The factors that were reported as significant were grouped into three categories- maternal related, infant related and HH/ sociodemographic related. Majority of the studies reported maternal related factors. Factors like maternal autonomy, mother's childbearing age, place of delivery, and parity were significantly associated with either underweight or wasting. While, maternal BMI, mother's mental health (depression), maternal education, maternal hemoglobin concentration were factors significantly associated with infant's underweight/WAZ score. On the other hand, mother's periodontal health (low CPI score) was found as a significant risk factor associated with infant wasting/WHZ score.

A systematic review by G.J. Carlson et al., reported similar findings in terms of, positive association between maternal autonomy and child's nutritional indicators in developing countries [59]. This review considered broad age group of children (0-60 months age) as target population, however there were studies that incorporated u6m infants as well.

The review also identified many infant-related risk factors, like infant's gender and chronological age, which were found to be significant risk factors associated with both underweight or wasting.

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While, nasopharyngeal carriage of pneumococci (spn) in infants at 2 mo age, history of hyperbilirubinemia, ≥5 diarrhoeal episodes per year, were the risk factors significantly associated with underweight/ WAZ score. In addition, acute malnutrition in u6m infants was more concentrated among poor and low-income families.

Some factors that were reported as non-significant by the authors were- HH arsenic exposure, maternal restricted diets in pospartim period, number of siblings, maternal and infant's morbidity index, and others. However for HH arsenic exposure, author reported no association of HH arsenic exposure with underweight or wasting but found association with stunting, indicating a chronic long term effect of HH arsenic exposure [42].

This review also identified burden of acute malnutrition in u6m infants. Studies reporting the prevalence of wasting and underweight were from three regions according to World Bank classification, i.e., South Asia, Sub-Saharan Africa, and East Asia & Pacific [25]. The highest prevalence of both wasting and underweight as per WHO growth standards was found in the South Asia region. With 30.6% and 30.0%, two India based studies reported the highest wasting prevalence followed by Bangladesh with 23.3% [16,30,42], with both the countries falling in a critical situation as per WHO cut-off values for public health significance. Similar findings were reported in a one-day consultation organized by UNICEF on wasting in South Asia, which reported that more than one in three children in India have wasting (WHZ <-2 SD) during the first three months after birth [8]. When looking at underweight prevalence found in this review, as per WHO cut-offs, very high underweight prevalence was reported from both India and Pakistan (37.4%), followed by Kenya (34%), and high prevalence was reported from Bangladesh based study (23% to 25%).

Limitations and Strengths of the study

The findings of this review should be interpreted with the following limitations. For screening based on title & abstract, studies where age group was not mentioned or had a broader age group (<1, <2, <5 years or <11, <23 months, etc.), inclusion for full-text screening was considered if sub-group analysis was mentioned in the abstract or based on the reviewer's judgment. During the initial search some filters were applied in the search strategy, this could have led to a bias in the total number of records found initially. Due to the broad scope of this review, there was considerable heterogeneity in the interventions and outcomes. A large number of studies were included based on the full text; hence details of individual studies could not be discussed. A qualitative tool was used for quality appraisal, which could have led to reviewer bias. Another limitation is that the review did not look at the interventions given to mothers prenatally, and likewise, interventions that had seen outcome at the age beyond 6 months were not considered in the review.

In spite of these limitations, this review also has some considerable strength. To our knowledge, this is the first review that presents burden and risk factors of acute malnutrition in u6m infants along with the preventive interventions, assessment, and treatment approaches used for u6m infants with acute malnutrition in LICs and LMICs.

Implications for Practice and Research

The review identified high burden of acute malnutrition in u6m infants in LICs and LMICs which recognizes an urgent need to plan programs and invest resources for management of acute malnutrition in u6m. The review also identified various risk factors associated with acute malnutrition in u6m and knowledge about these factors would help in planning the strategies to prevent growth faltering in infants of this age group. Evidence from this review could be helpful in strategizing community-based support of breastfeeding mothers as a treatment option for uncomplicated cases (without oedema and danger signs) of malnutrition in infants u6m.

Routine immunization visits shortly after birth could be utilized as an effective platform for anthropometric assessment of u6m infants to identify wasted infants at a higher risk of death and thus targeted interventions could be planned accordingly. In addition, as mother's mental health is found to impact infant's health, training of community/ frontline health workers could be considered for early screening and identification of depression symptoms in mothers. Detecting and treating maternal depression and child malnutrition simultaneously could be an effective approach and programs can integrate a psychosocial component into existing maternal and child health interventions.

Research Gaps Identified in the Study

Of all the 33 included studies, only 17 studies had prime focus on u6m infants, while rest were studies that had a component of sub-group analysis in u6m infants. Majority of the studies that reported prevalence and risk factors had SDA as study design. Thus, considerable gap was observed in context specific primary studies with a focus on u6m infants.

The number of studies that measured the impact of preventive interventions on anthropometry and morbidity outcome was very limited, as most of the studies focus only on measuring the improvement in breastfeeding practices.

The review also found that the number of studies focusing on assessment and treatment aspect were very limited. In future studies presenting evidence on the feasibility and accuracy of using MUAC to identifyu6m infants at higher risk of mortality is required. Also, research to identify effective choice of therapeutic milk for infants u6m and follow-up of malnourished non-breastfed infants.

Studies exploring psychosocial support activities to manage depression in pregnant and lactating women and its effects on improving infant's nutritional status, require urgent consideration.

Conclusion

The review systematically synthesized evidence on burden, risk factors, different preventive interventions in practice, assessment and treatment strategies to manage acute malnutrition in infants u6m from LICs and LMICs. Burden of acute malnutrition in u6m infants in LICs and LMICs is very high, especially in South Asia region. Risk factors identified in the review were mainly maternal related and MNS component along with BF support is identified as an effective strategy to prevent growth faltering in u6m infants. The review also identified that there is paucity in current evidence on assessment and management of acute malnutrition in u6m infants.

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In addition, further research on context specific burden of acute malnutrition and identification of underlying risk factors, can help shaping new programs and/ or in incorporating u6m in existing malnutrition management strategies.

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