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Abstract

Introduction: M e a 3.5 e a d c e de e d e eac ea c e d e de g de . Ma e e a c a ed c c a c e de ce ce . l e decade e e e ca a e ed ac e de ead c e de ce ce . We e a e a ed e ec M c e P de (MNP) e ea c e e a d c e .

Methods: We e a ca e e ed e a e b ed N e be 2012 de d e de c b g e e ec e e MNP. We ed a a da d ed ab ac a d ad g a e a e e ec MNP b a g e a da d C d Hea E de g Re e e ce G (CHERG) .

Results: We c ded 17 d e e . MNP g ca ed ced e e a ce a e a b 34% (RR: 0.66, 95% CI: 0.57-0.77), de c e c a e a b 57% (RR: 0.43, 95% CI: 0.35-0.52) a d e de c e c b 21% (RR: 0.79, 95% CI: 0.64, 0.98). I a g ca ed e e g b e e (SMD: 0.98, 95% CI: 0.55-1.40). W e e e e a ca g ca ac b e ed e e a d c de ce c . O a a ac MNP a a e c c e c d g g (RR: 0.92, 95% CI: 0.81, 1.04), a g (RR: 1.13, 95% CI: 0.91, 1.40), de g (RR:0.96, 95% CI: 0.83, 1.10), HAZ (SMD: 0.04, 95% CI: -0.13, 0.22), L]8 de ed a IDD. I e a ed a e- d

(VAD) affects at least 2.80 million preschool children in over 60 countries, and sub clinical VAD is considered a problem for at least 251 million that includes school-age children and pregnant women [8].

Micronutrients play a critical role in cellular and humoral immune responses, cellular signaling and function, learning and cognitive functions, work capacity, reproductive health and even in the evolution of microbial virulence [9,10]. Infants, children and pregnant women have high demands for vitamins and minerals because of increased growth and metabolic requirements and yet their dietary intake often fails to meet these requirements [3,11]. In children these micronutrient

that is attributable to heterogeneity rather than to chance, a low p-value (less than 0.1) or a large chi-squared statistic relative to its degree of freedom and I^2

Table 2 Quality Assessment by Hematologic Outcome

		Qua... A... e...					Su... F...		
		D... e...		N... e...					
N...	De...	L... a...	C... e... c...	Ge... ab... ... e...	Ge... ab... e... e...	I... e...	C...	RR / SMD (95% CI)	
Anemia: Moderate outcome specific quality of evidence									
E... e	RCT	S... ca... e... e... ... ... ec... de... ed...	S... e... de... be...	A... de... e... c...	T... ed... de... ... ed... 12... a... e... e... 10...	1081	1443	RR: 0.66 [0.57, 0.77]	
Iron deficiency Anemia: Moderate outcome specific quality of evidence									
Se... de... (da... e)	RCT	S... ca... e... e... ... ... ec... de... ed...	F... de... be...	A... de... e... c...	T... ed... de... ... ed... 2-12...	404	986	RR: 0.43 [0.35, 0.52]	
Hemoglobin: Moderate outcome specific quality of evidence									
F... de... (F... da... e)	RCT	S... ca... e... e... ... ... ec... de... ed...	N... e... be...	A... de... e... c...	S... de... ... ed... d... 2-12...	4571	3783	SMD: 0.98 [0.55, 0.40]	
Serum Zinc: Moderate outcome specific quality of evidence									
T...	RCT	S... ca... e... e... a... ... ec... de... ed...	O... d... be...	A... de... e... c...	O... d... a... c... d... ced... c...	761	788	SMD: -0.22 [-0.52, 0.09]	
Serum Retinol: Moderate outcome specific quality of evidence									
T...	RCT	S... ca... e... e... a... ... ec... de... ed...	O... d... be...	B... de... I... da...	S... d... d... a... ... ed... 6-8...	464	504	SMD: 1.66 [-1.60, 4.92]	
Serum Ferritin: Moderate outcome specific quality of evidence									
F...	RCT	S... ca... e... e... ... ... ec... de... ed...	T... ee... de... be...	A... de... e... c...	S... de... ... ed... d... 6... 12...	850	884	SMD: 1.78 [-0.31, 3.88]	
Zinc Deficiency: Moderate outcome specific quality of evidence									
T...	RCT	N... ca... e... e... ... ed... ec... de... ed...	N... e... d... be...	A... de... e... c...	T... e... d... d... ... ed... 6-8...	258	272	RR: 1.02 [0.87, 1.19]	
Retinol Deficiency: Moderate outcome specific quality of evidence									
T...	RCT	N... ca... e... e... ... ed... ec... de... ed...	N... e... d... be...	A... de... e... c...	T... e... d... d... ... ed... 6-12...	111	145	RR: 0.79 [0.64, 0.98]	

less than six years of age, except two studies [30,39] that included children over 6 years of age although the subgroup analysis for children under five did not show any difference in the findings. Clinical heterogeneity was observed due to variations in type of intervention (number of micronutrients used ranged from 3 to 15), duration of the intervention (2-24 months), target population and different time intervals for follow-up. All the MNPs used contained iron in their composition.

The intervention was mostly reported to be acceptable by the mothers and children and there was no major loss to follow-up reported due to the intervention in any of the included studies. There have been no adverse events identified by any study except one [38] that reported increased diarrhea in the intervention group compared to control.

This review shows that MNPs raise serum hemoglobin levels and reduce anemia significantly, but the evidence on growth is weak, as relatively few studies have evaluated

Table 3 Quality assessment by anthropometric and morbidity outcomes

Stunting: Moderate outcome specific quality of evidence									
T d (ee da a e)	RCT	N g ca e e g e e , ed e ec de ed m	N e e d g e be e	A de e de e g m c e			810	838	RR: 0.92 [0.81, 1.04]
Wasting: Moderate outcome specific quality of evidence									
T d (ee da a e)	RCT	N g ca e e g e e , ed e ec de ed m	N e e d g e be e	A de e de e g m c e			263	234	RR: 1.13 [0.91, 1.40]
Underweight: Moderate outcome specific quality of evidence									
T ee de (da a e)	RCT	N g ca e e g e e , ed e ec de ed m	N e e de g g ca be e	A e de de e g c m e	A de c ded e a 3 c e . T e m de a g ed m d a 4-12 m m		671	679	RR: 0.96 [0.83, 1.10]
HAZ: Moderate outcome specific quality of evidence									
T ee	RCT	N g ca e e g e e , ed e ec de ed m	N e e de g g ca be e	A de a e A ca m	A de c ded e a 3 c e . T e m de a g ed m d a 6-12 m m		271	253	SMD: 0.04 [-0.13, 0.22]
WAZ: Moderate outcome specific quality of evidence									
T ee	RCT	N g ca e e g e e , ed e ec de ed m	N e e de g g ca be e	A de m A ca	A de c ded e a 3 c e . T e m de a g ed m d a 6-12 m m		271	253	SMD: 0.05 [-0.12, 0.23]
WHZ: Moderate outcome specific quality of evidence									
T ee	RCT	N g ca e e g e e , ed e ec de ed m	N e e de g g ca be e						

Figure 3 F e P m ac MNP e m b c e

this outcome. Improved hemoglobin and anemia status could be attributable to the iron component in all the MNPs used. Some studies have reported benefits on other developmental outcomes like walking by 12 months but not on growth [22]. This could be due to relatively shorter duration of the intervention to show actual long term impacts. These findings also suggest that multiple micronutrient interventions alone might not improve growth outcomes. To ensure long term impacts and sustainability, health education that aims to modify food habits would be necessary to improve child growth rates. Also, if the intervention initiation coincides with the child's diet transition from breast feeding to complementary feeding, the results may show improved growth.

The finding of significantly increased diarrhea is potentially alarming. It is mainly based on the significant increase in diarrhea observed in one large trial [38]. The association between increased diarrhea with iron supplementation is well recognized in the literature and is also reported in a review on iron supplementation by Gera [40]. However, our finding of excess morbidity and negligible growth benefit cannot be ignored in settings where large scale use of MNPs is being considered. The increased diarrhea burden could be one of the potential explanations for reduced growth benefits of MNPs.

The evidence is weak for any effect of MNPs on growth, as there were very few studies pooled for each outcome. More research is needed and studies need to report the outcomes of stunting, wasting, morbidity and mortality consistently to strengthen the evidence and evaluate its actual impact on growth and morbidity. A major research gap identified was that there were no studies evaluating the impact on women as all the studies targeted children only.

Conclusion

Our analysis of the effect of MNPs in children suggests benefit in improving anemia and hemoglobin however there is lack of impact on growth. Evidence of increased diarrhea requires careful consideration before recommending the intervention for implementation at scale.

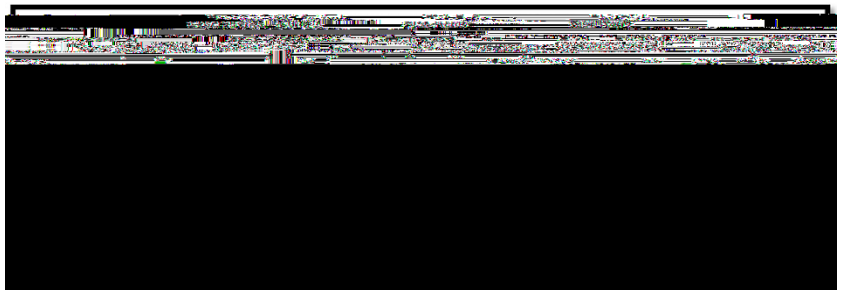

Figure 4 F e P m ac MNP d a ea c e