


High adherence and its influencing factors on multiple micronutrient powders (MNPs)

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Abstract

Adherence to home fortification of foods with multiple micronutrient powders (MNPs) is an essential indicator of effective implementation of MNP programmes. A meta-analysis was conducted to evaluate the high adherence rate (HAR) to MNPs and further investigate the factors that influence HAR. We searched PubMed, Web of Science, Embase, CAB Abstracts, MEDLINE (OVID), Cochrane Library, China National Knowledge Infrastructure, Wanfang and VP, from the date of database inception to 9 November 2020. We included peer-reviewed observational studies that investigated adherence to MNPs. Data on the HAR to MNPs and influencing factors on HAR were extracted and then pooled together. A total of 10 studies were included. The pooled HAR to MNPs was 63.28% (51.12%–74.64%). Among HARs, rates were higher in middle-income countries (65.21%) than low-income countries (55.23%). Parental age over 30 years (maternal age OR = 1.25, 95% CI: 1.08–1.44; paternal age OR = 1.17, 95% CI: 1.04–1.32), children aged 18–36 months (OR = 1.45, 95% CI: 1.12–1.88), maternal educational attainment of college or above (OR = 1.38, 95% CI: 1.10–1.73), caregiver with the perception that other mothers use MNPs (OR = 1.52, 95% CI: 1.19–1.95), caregiver being aware of the importance of iron (OR = 1.42, 95% CI: 1.18–1.71), caregiver having correct knowledge of MNPs (OR = 1.36, 95% CI: 1.19–1.57) and caregiver reporting children have no side effects from MNPs (OR = 2.77, 95% CI: 2.46–3.11) were contributing factors to high adherence to MNPs. The overall HAR to MNPs was relatively low; hence, effective and trusted communication channels need to be established, along with more thorough dissemination of the knowledge of MNPs to caregivers, to improve MNPs adherence rates, especially in low-income countries.

KEYWORDS

adherence, influencing factors, meta-analysis, multiple micronutrient powders

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1 | INTRODUCTION

Good health and nutrition are essential to infants and young children for growth and development as they have lasting impacts on the health and well-being of individuals (WHO, 2013). However, the outlook on health and nutrition is not optimistic for children in low- and middle-income countries (LMICs), where low-income countries have per capita gross national income (GNI) below \$995 and middle-income countries have per capita GNI between \$996 and \$12,055, as classified based on criteria from the World Bank (World Bank, 2021). Evidence shows that 99% of malnourished children live in LMICs and may suffer from wasting (low weight-for-height), stunting (height-for-age) and being underweight (weight-for-age), which may jeopardize their health, growth, development and survival—all of which are largely irreversible (Black et al., 2013; Local Burden of Disease Child Growth Failure Collaborators, 2020). Due to limited access to, availability of, or adequacy of a balanced diet, children are unable to meet their daily requirements of micronutrients from complementary foods (Penny et al., 2005). Thus, adopting nutrient intervention with home fortified supplementary nutrients is an effective way to reduce anaemia and malnutrition and improve nutritional status in infants and young children in LMICs (Li, Li, et al., 2019; Suchdev et al., 2020; Xu et al., 2019).

Therefore, nutrition intervention of food fortification at home with multiple micronutrient powders (MNPs), which includes essential micronutrients such as iron, zinc and vitamins, has been established to achieve better nutrition and growth in infants and children (WHO, 2011). Nutrition intervention of food fortification at home was first developed in 1996 in Toronto, Canada, with an aim to prevent children's micronutrient deficiencies. These MNPs are single-dose sachets in powder form that can be easily sprinkled onto any semi-solid or soft foods and easily facilitate nutrient absorption (Zlotkin et al., 2005). Based on the scientific evidence and considerable health outcomes from implementation, in 2011, the World Health Organization (WHO) officially recommended food fortification at home with MNPs as a new strategy to improve the quality of young children's diets and to prevent and control anaemia during childhood (WHO, 2011).

Adherence to MNPs has gained importance over time as a solution for better implementation of MNP programmes, as research has demonstrated that high adherence can lead to better MNP outcomes. Evidence shows that higher adherence to MNPs can improve nutritional status of infants and young children, suggesting that adherence is a key factor in determining the effectiveness of the fortification strategy for MNP interventions (Black et al., 2013). Adherence is considered essential for successful treatment in clinical practices, with research demonstrating that high adherence patients often have better treatment outcomes (Munro et al., 2007; Villalva et al., 2017). Adherence is defined by WHO as 'the extent to which a person's behavior-taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider' (WHO, n.d. Regarding MNP implementation, adherence refers to the extent that caregivers follow the feeding

Key messages

- Despite the proven importance of high adherence to multiple micronutrient powders (MNPs), the outlook on caregivers' high adherence to MNPs is not optimistic in low- and middle-income countries.
- Parents aged more than 30 years, children aged 18–36 months and maternal educational attainment of college or above predict higher adherence to MNP. Assessment of these characteristics before caregivers begin use of MNPs may allow for identification of other 'risk factors' to low adherence.
- Interventions to increase caregivers' adherence to MNPs should target caregivers' perceptions of MNPs' usage and caregiver knowledge of MNPs, given the evidence that these factors are good predictors of adherence.

guidelines and MNP consumption (Tumilowicz et al., 2017). High adherence has often been related to influencing nutritional and health status (Cardoso et al., 2016) and has been used as an essential indicator to evaluate the success of project implementation (López-Flores et al., 2012).

Previous systematic reviews of MNPs mainly describe intervention implementations or evaluate MNPs safety and its effects on nutrition and health outcomes (Wang et al., 2018). Furthermore, available evidence of MNP consumption and high adherence to MNPs is limited to results from intervention programmes (Roschnik et al., 2019). To date, there have been no large-scale efforts to statistically examine adherence to MNPs and influencing factors of adherence across LMICs. Thus, such research is needed to demonstrate the overall nature of MNP adherence and to offer policy directions for future implementation on MNPs.

Understanding the factors that influence adherence to MNPs could facilitate the identification of barriers and help programme designers and practitioners maximize exposure to factors for promoting adherence. The objective of this study is to conduct a meta-analysis of all open empirical studies focused on MNP adherence among infants and young children (6–36 months) and their caregivers by documenting the HAR to MNPs and identifying influencing factors of HAR. Conclusions from this meta-analysis provide suggestions for how to improve caregivers' adherence to MNPs, which can ultimately help support better health and nutrition in infants and children.

2 | METHODS

This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses

statement (Moher et al., 2009), and the protocol was registered with the PROSPERO (CRD42021233056).

2.1 | Search strategy and selection criteria

First, a comprehensive systematic literature search was conducted to identify the published studies from the date of database inception until 9 November 2020 across different databases including PubMed, Web of Science, Embase, CAB Abstracts and MEDLINE (OVID), Cochrane Library, China National Knowledge Infrastructure (CNKI), Wanfang and VP. The search terms were as follows: 'micronutrient powders', 'micronutrient sprinkles', 'multiple micronutrients in powder', 'adherence', 'accept*', 'willing*' and other related terms. The full list of search strategies is shown in Supplementary Table 1.

2.2 | Inclusion and exclusion criteria

The inclusion criteria were (i) studies that investigated adherence to MNPs; (ii) the studies that included original data to describe the characteristics of both high and low adherence groups; and (iii) the study population of children aged 6–36 months. In this meta-analysis, 'high adherence' to MNPs was defined as 'consumed ≥ 4 MNPs packages each week or (amount of consumed MNP envelopes/total amount of delivered MNPs envelopes) $\times 100\% \geq 75\%$ ' (De-Regil et al., 2013; Suchdev et al., 2020; Wu et al., 2017). In this meta-analysis, as some of the potential eligible studies were not explicit about the definition of high adherence, hence the decision was made according to the authors' description.

Studies were excluded from this meta-analysis based on the exclusion criteria: (i) Studies did not report original data for high adherence/low adherence group to MNPs; (ii) subjects in the studies were experimentally divided into the high adherence and low adherence groups; (iii) studies had duplicated publication data, abstracts or reviews, and the studies were missing key data.

2.3 | Screening, data extraction and quality assessment

After removing duplicates, two reviewers (RL and FQL) independently screened search results based on the eligibility criteria, and uncertainties were resolved by consensus. The reviewers collected data from included studies, involving basic information from the studies (e.g. first author and journal name), demographic characteristics (e.g. area and main sources of income), household characteristics (e.g. parent education [whether parents had completed primary school or below, middle school, high school or college or above], parental age, who the caregivers were and child gender) and MNP-related knowledge (e.g. mother's perception that other mothers in

the community also use MNPs and caregivers' skills/knowledge of MNPs). The Newcastle–Ottawa Scale suitable for observational studies was used to assess the quality of each study (Stang, 2010). The scale consists of eight items, including three parts: selection, comparability, and exposure or outcome. Star awarded was adopted for each quality item assessment with a full score equal to nine stars. The EndNote (Version X9) was used to manage the articles and citations.

2.4 | Statistical analysis

The HAR to MNPs was pooled, and the 95% confidence interval (CI) was reported with variance transformed to a normal distribution by Freeman–Tukey double arcsine transformation (Barendregt et al., 2013). The odds ratio (OR) and its 95% CI were calculated to estimate whether the factors were associated with HAR. I^2 was used to evaluate the heterogeneity among each study, and the random-effects model was chosen when the $I^2 > 50\%$ showed high heterogeneity among the data; otherwise, a fixed-effects model was used (Ades et al., 2005). The funnel plot and Egger weighted regression were used to measure potential publication bias (Peters et al., 2006). Additionally, sensitivity analysis was conducted by serially excluding each study to estimate the effect of individual studies on overall pooled estimates. All data cleaning and analyses were performed using Microsoft Excel 2016 and R Version 3.2.3.

3 | RESULTS

3.1 | Search results

A total of 6463 records were identified through a database search. The titles and abstracts of 3577 published literatures were screened after duplicates were removed. Then, 96 articles were selected for detailed assessment. Among them, 86 studies were excluded: 59 studies with no original data for high/low adherence group to MNPs, 10 studies not involving children aged 0–36 months, 10 studies with duplicate publication data, abstracts or reviews and seven studies with trials or interventions (Figure 1). Finally, 10 studies with 16506 high adherence and 7796 low adherence caregivers were included to perform the meta-analysis in this study (Table 1).

3.2 | The pooled high adherence rate to MNPs

The overall pooled HAR to MNPs was 63.28% (95% CI: 51.12%–74.64%). Compared with the other countries included in this meta-analysis (Madagascar, Nepal and Peru), the pooled HAR to MNPs in China was higher at 70.85% (95% CI: 60.30%–80.37%) than

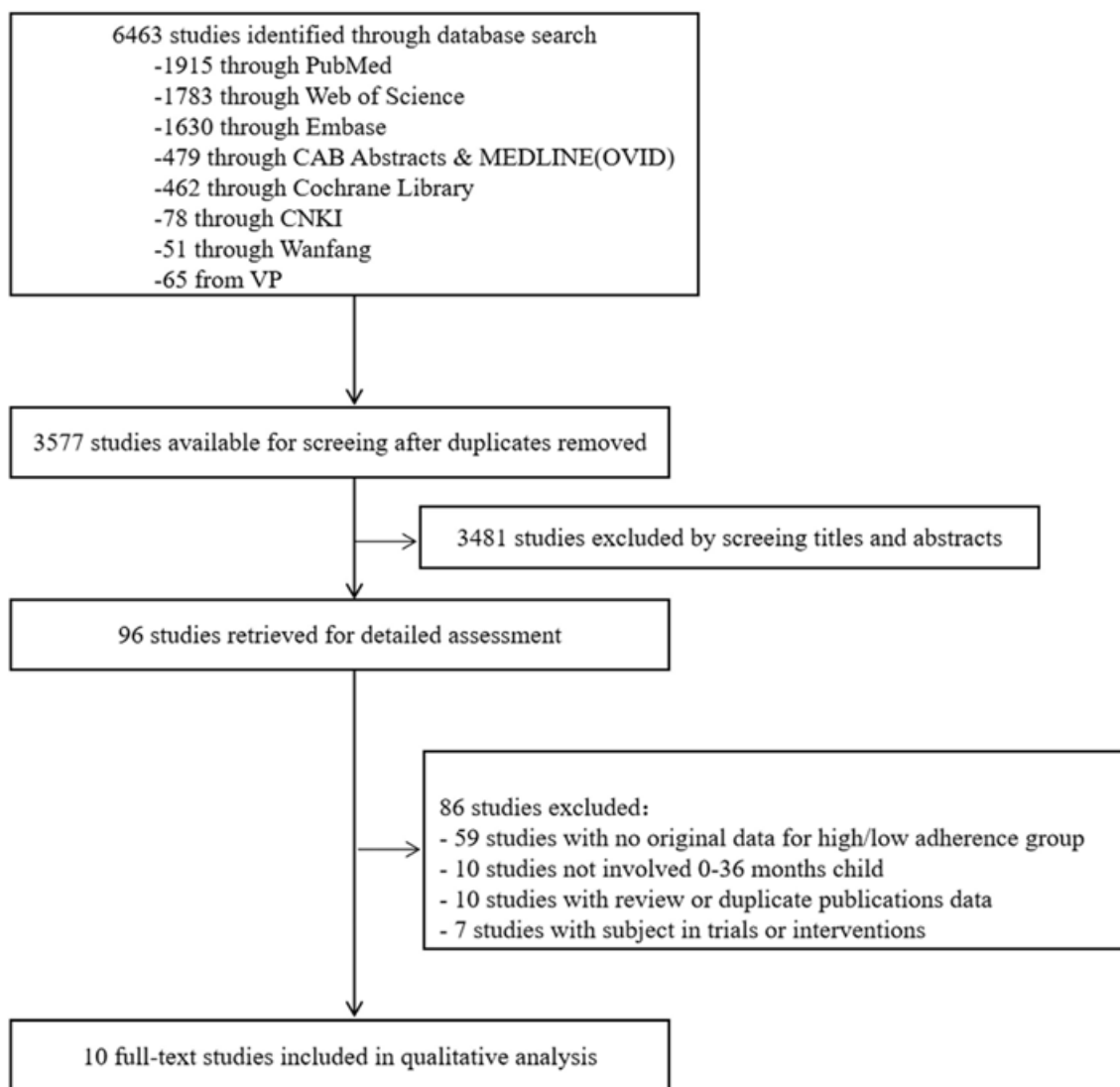


FIGURE 1 Flow diagram of the study selection process for this meta-analysis

in the other countries at 44.54% (95% CI: 22.06%–68.26%). Similarly, the pooled HAR to MNPs was higher in middle-income countries, with 65.21% (95% CI: 51.11%–78.06%), compared with HAR of 55.23% (95% CI: 53.38%–57.07%) in low-income countries (Figure 2).

3.3 | The household characteristics association with the high adherence to MNPs

Parents aged 30 years and older were found to be an influencing factor for high adherence to MNPs, as both maternal age (OR = 1.25, 95% CI: 1.08–1.44) and paternal age (OR = 1.17, 95% CI: 1.04–1.32) influence HAR. Children aged 18–36 months were associated with high adherence (OR = 1.45, 95% CI: 1.12–1.88), whereas children aged 6–11 months were associated with low adherence to MNPs (OR = 0.52, 95% CI: 0.33–0.82).

Paternal educational attainment of primary school or below was a negative factor (OR = 0.53, 95% CI: 0.29–0.95), whereas maternal

educational attainment of college or above was a positive factor for high adherence to MNPs (OR = 1.38, 95% CI: 1.10–1.73). Moreover, whether the children's caregivers were their parents or grandparents, there was no impact on the children's adherence to MNPs (Figure 3).

3.4 | The association between knowledge of MNPs and high adherence to MNPs

Caregivers with the perception that other mothers in the community also used MNPs (OR = 1.52, 95% CI: 1.19–1.95), those aware of the importance of iron (OR = 1.42, 95% CI: 1.18–1.71), those with correct knowledge of or skill with MNPs (OR = 1.36, 95% CI: 1.19–1.57) and caregivers reporting children had no side effects from MNPs (OR = 2.77, 95% CI: 2.46–3.11) were positive factors for high adherence. The caregivers with no perception of the beneficial effects of MNPs (OR = 0.42, 95% CI: 0.31–0.58), those with incorrect knowledge of MNPs (OR = 0.73, 95% CI: 0.64–0.84) and those who

TABLE 1 The studies and characteristics included in this meta-analysis

Study ID	Journal name	Published year	Study period	Sample size	Age of children	Study country	Economic status	Study quality
Wang et al., 2017	PLoS ONE	2017	2017	823	6–23 months	China	Middle	6
Munares-García & Gómez-Guizado, 2016	Rev Bras Epidemiol Jul-Set	2016	2014	2024	6–35 months	Peru	Middle	7
Locks et al., 2017	Nutrients	2017	2013	847	6–23 months	Madagascar	Low	6
Mirkovic et al., 2016	Matern Child Nutr	2018	2010	2576	6–23 months	Nepal	Low	7
Zhou et al., 2017	Journal of Hygiene Research	2017	2015	6762	6–24 month	China	Middle	6
Wang et al., 2018	Journal of Hygiene Research	2018	2013	910	6–12 month	China	Middle	6
Li, Jiang, et al., 2019	Chinese Journal of Child Health Care	2019	2017–2018	2120	6–24 month	China	Middle	6
Li, Fang, et al., 2019	Maternal and Child Health Care of China	2019	N/A	3188	6–24 month	China	Middle	5
Zhang et al., 2015	Chinese Journal of Women and Children Health	2015	2013	5824	6–24 month	China	Middle	6
Niu et al., 2017	Journal of Hygiene Research	2017	2014	334	6–24 month	China	Middle	6

reported their children had side effects from MNPs (OR = 0.37, 95% CI: 0.33–0.41) were negative factors for high adherence to MNPs (Figure 4).

3.5 | Publication bias and sensitivity analysis

The shapes of the funnel plots were relatively symmetric (Supplementary Figure 1). Egger weighted regression was also conducted, and the p -value was 0.2914 ($p > 0.05$), which indicated that no obvious publication bias was found. The results of the sensitivity analysis showed that the meta-analysis was stable and that no single study altered the pooled proportion estimates (Supplementary Figure 2).

4 | DISCUSSION

Adherence is an important indicator used to evaluate nutrition improvement programmes; however, few studies have focused on this topic. This meta-analysis systematically pooled and analysed data from all open empirical studies on adherence to MNPs, which included data from 16,506 high adherence and 7796 low adherence caregiver pairs from four LMICs (China, Madagascar, Nepal and Peru), to evaluate HAR to MNPs and investigate the influencing factors of HAR. We observed that pooled HAR was relatively low, especially in the low-income countries, when compared with other studies that find HARs of 70%–83% in LMICs (Angdembe et al., 2015; Lundeen et al., 2010; Wu et al., 2017). Parents aged 30 years and older, children aged 18–36 months and maternal educational attainment of college or above were contributing factors to high adherence to MNPs. Additionally, caregivers with the perception that other mothers use MNPs, caregivers who were aware of the importance of iron, caregivers with correct knowledge of MNPs and those who reported their children had no side effects from MNPs all served as positive effects on high adherence to MNPs. The results of this study provide the scientific basis for developing effective intervention measures to improve adherence to MNPs.

The HAR to MNPs was estimated as 70.85% in China, which is higher than HAR from other included countries. This HAR lies in the range of studies that reported HAR from 12% (Vietnam) to 88% (Mongolia) (Nguyen et al., 2016; World Vision Mongolia, 2005). In China, Yingyangbao (YYB) is a home fortification of food with multiple MNPs, including calcium, iron, zinc, vitamins and, in some formulations, folic acid to provide additional calories and protein (Wang et al., 2017). It was first used as a fortified complementary food to improve child nutrition as a pilot intervention project from 2001 to 2003 in five poor counties of Gansu Province. This pilot intervention project provided evidence that MNPs could improve anaemia status among infants and young children (Cai, 2005). After implementation of the MNP supplementation programme by the United Nations Children's Fund in the earthquake-affected areas of the 2008 Wenchuan earthquake, evidence showed that childhood anaemia in affected

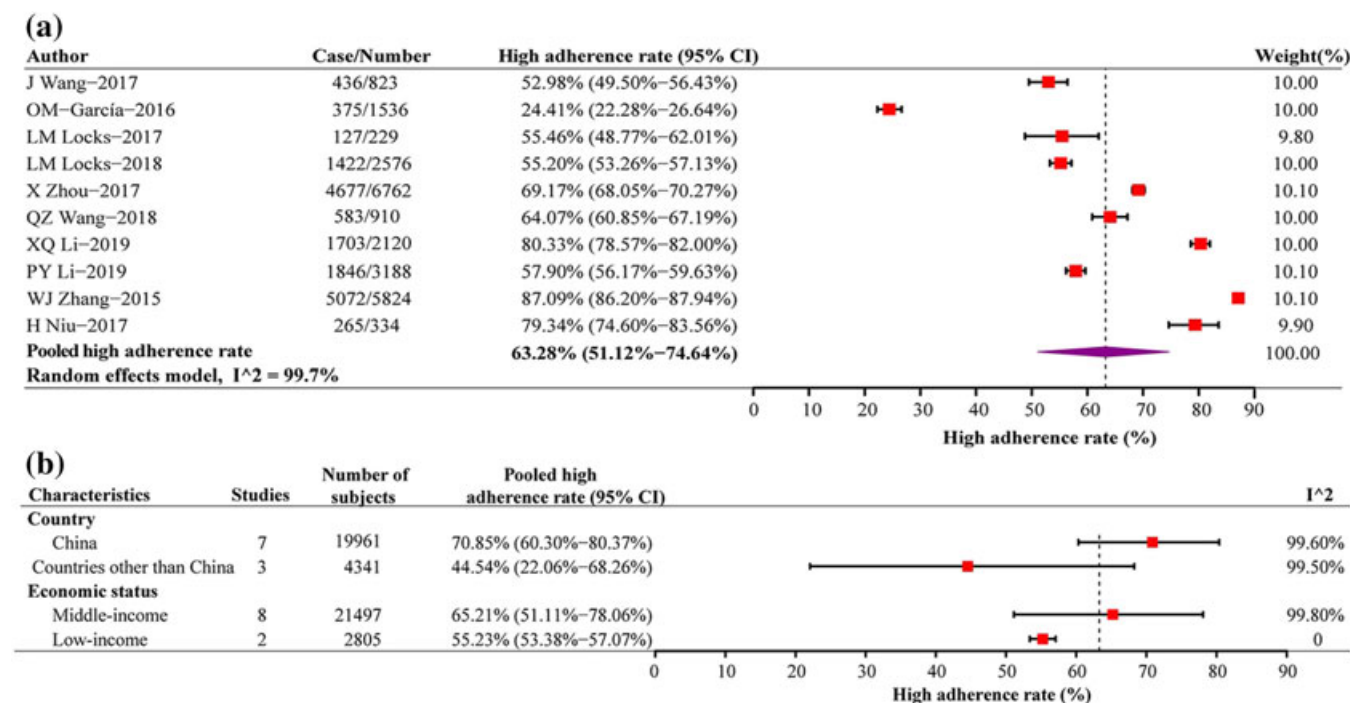


FIGURE 2 Forest plots of meta-analysis of pooled HAR rate to the MNPs. (a) The pooled HAR rate to the MNPs. (b) The pooled HAR rate to the MNPs by subgroups

areas was reduced by 60% (UNICEF, 2015). Given the high prevalence of anaemia and stunting among children aged 6–24 months in rural areas, and evidence from pilot projects that addressed the importance of MNPs, the Chinese government officially launched the Nutrition Improvement Program on Children's Health in Rural Areas in 2012 (National Health and Family Planning Commission, 2012). Under this programme, MNPs were purchased by local governments and then distributed to children free of cost. These efforts aimed to promote scientific feeding knowledge and skills among caregivers and improve the nutrition and health status of children in poor areas. Unified procurement and free distribution of MNPs to caregivers in China under this programme may have contributed to higher adherence rates than those from other countries (Sarma et al., 2020). Another possible reason for HAR being slightly higher in middle-income countries than in low-income countries may be that MNPs must be mixed into complementary foods, but such foods are not always available in low-income countries (Tripp et al., 2011). A final point worth noting is that in comparison with low-income countries, MNPs are distributed free of cost in middle-income countries and better economic status often leads to better implementation outcomes (Schauer et al., 2017).

Lower levels of educational attainment for fathers and higher levels of educational attainment for mothers were negative and positive factors of high adherence to MNPs, respectively. These results are similar to those in previous studies (Mirkovic et al., 2016; Zhang et al., 2015). Parents' educational attainment is associated with children feeding decisions, with highly educated parents more likely to make the right feeding decisions (Zhou et al., 2017). Parents with less education may encounter more obstacles to reading MNPs and

understanding published information about MNPs and MNPs' usage, often misinterpreting the benefits of MNPs for children. Additionally, parents who had knowledge on the importance of iron and correct knowledge of MNPs were positively associated with high adherence to MNPs. In Wang et al.'s study, the views and perception of people around caregivers were also important factors contributing to adherence to MNPs (Wang et al., 2018). The more information the caregiver receives about the benefits of MNPs for children, the more it reinforces parents' intentions to using it (Geltman et al., 2009). Therefore, effective advocacy, promotion and interpretation of correct MNPs' knowledge are all important factors when designing and conducting MNP projects. Furthermore, sharing a successful example from the family or community that resulted in better health status in children after feeding MNPs could also improve the willingness of other caregivers in the same community to practice on using MNPs (Locks et al., 2017).

The results also showed that the age of parents and children could influence the adherence of MNPs. Mothers older than 30 years was found to be the protective factor for HAR to MNPs, which may be related to parents' feeding experience and the fact that older parents might have better knowledge on how to feed their children than younger parents (Li, Jiang, et al., 2019). Children older than 6 months need to be gradually fed Supplementary semi-solid foods to meet their daily diet requirements. Many studies have reported that when MNPs are added as the supplementary food to children, some children might have uncomfortable symptoms in the beginning, including diarrhoea or loose stools and vomiting (Tumilowicz et al., 2017). Thus, many caregivers who choose to stop using MNPs due to the concern

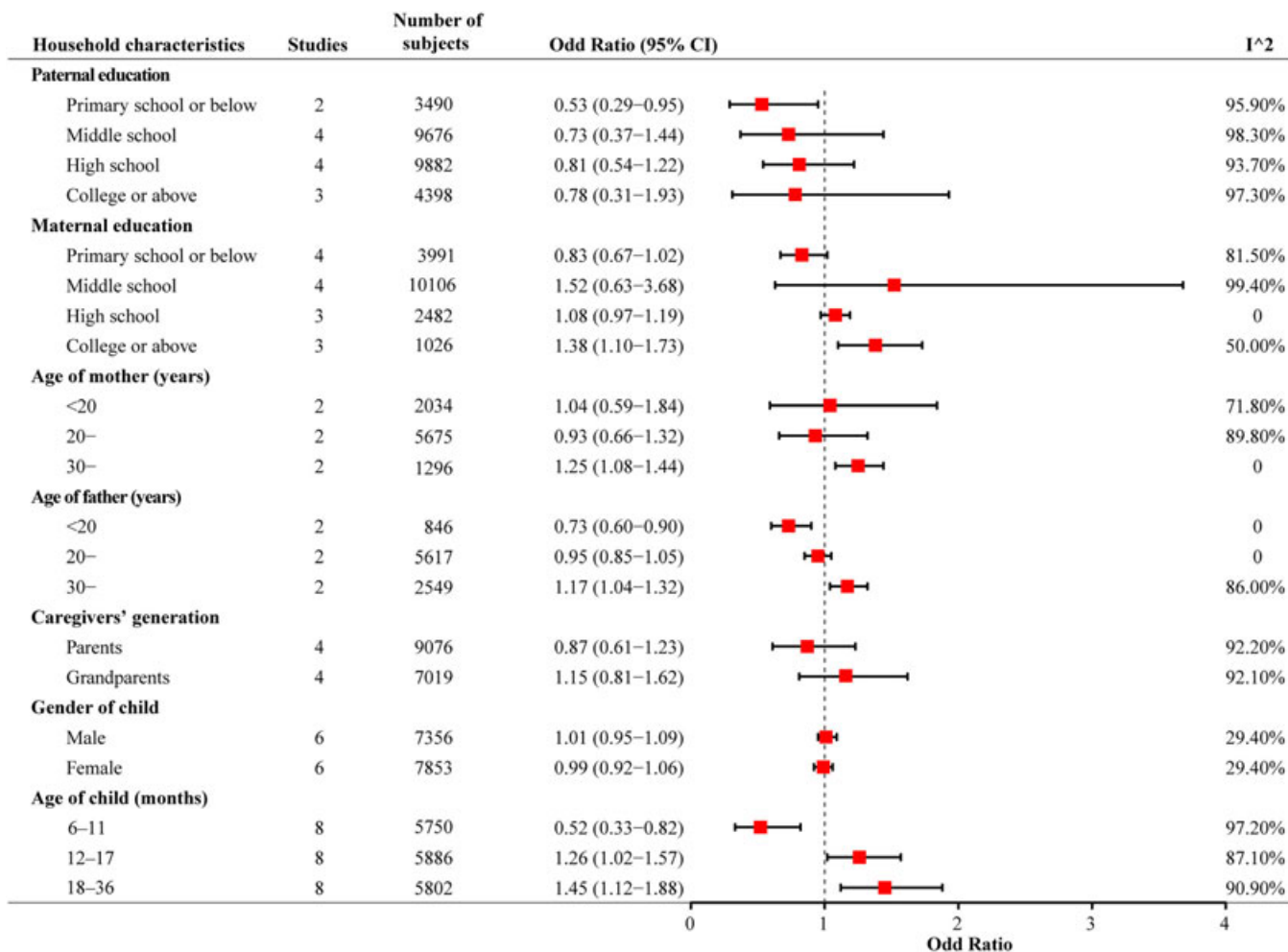


FIGURE 3 Forest plots of household characteristic association with the HAR to MNPs

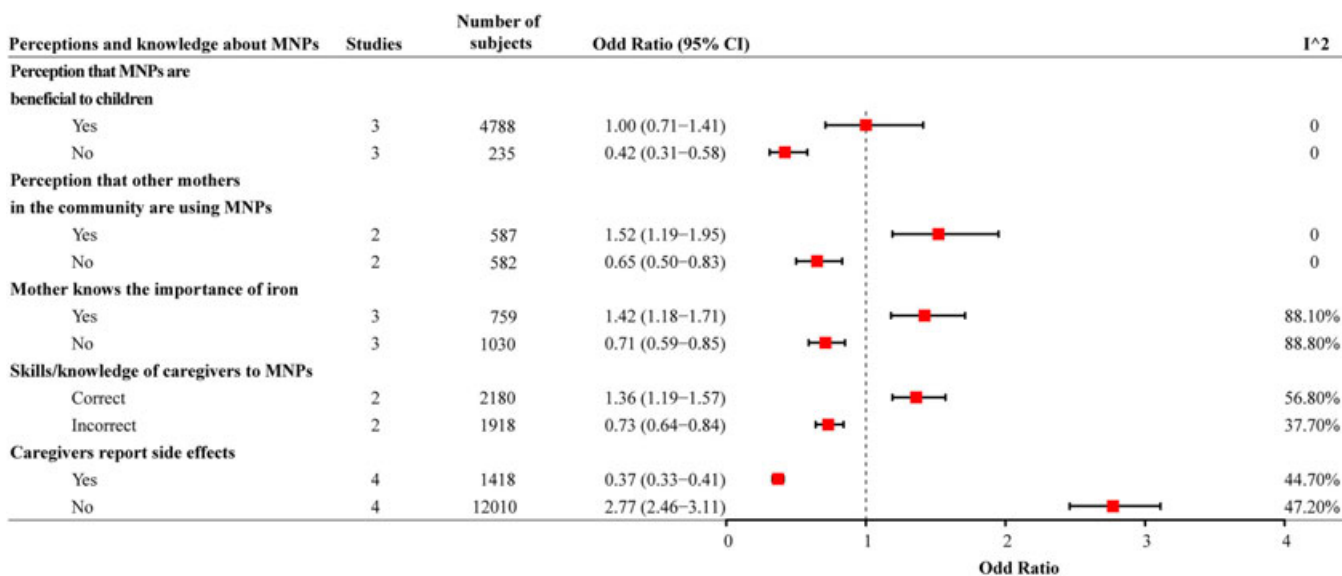


FIGURE 4 Forest plots of MNPs' knowledge association with the HAR to MNPs

that these symptoms are adverse side effects may actually harm children's health (Wu et al., 2017). However, these side effects can subside as children become more used to MNPs after first-time use (Li, Jiang, et al., 2019). Consistent with our results, caregivers reporting these types of side effects was a risk factor for the high adherence to MNPs; conversely, caregivers not reporting side effects, thus perceiving these side effects as positive, would increase adherence (Jefferds et al., 2015). Previous studies demonstrated that if caregivers were informed in detail about side effects before administering MNPs to their children, the caregivers better understand that these side effects are normal and may consider them positive signs that MNPs have observable effects on their child (Loechl et al., 2009). Therefore, effective and trusted communication channels need to be established, along with timely guidance for caregivers.

This study expounded on HAR influencing factors from the demand side and provided suggestions that can be directly used by health officers and project practitioners to improve the efficiency of MNP programmes. High adherence also depends on the supply side, which can be improved by maintaining routinely distribution and effective communication channels between caregivers and health providers, including counselling received by caregivers from frontline health providers or non-health platform workers, along with publicity and social mobilization (Ruel & Alderman, 2013). The maximization on the utility of MNP projects and reinforcement of successful programme outcomes that provide better nutritional support to eliminate infant malnutrition outcomes depend on both supply and demand sides. To this end, there is an even stronger need to end all forms of malnutrition by 2030 (United Nations, 2015).

4.1 | Strengths and limitations

This study is the first meta-analysis of all open empirical studies on adherence to MNPs. We provide comprehensive evidence and summary of adherence to MNPs and the factors that influence HAR from 16506 high adherence and 7796 low adherence caregivers from LMICs. These preliminary results could provide evidence-based suggestions for improving caregivers' adherence to MNPs, thus achieving better health and nutrition status for infants and children in LMICs, where 99% of malnourished children live (Black et al., 2013).

In addition to this strength, this study has several limitations. First, some of the included studies did not have clear definition of HAR. Therefore, the definition of HAR in this study was determined by the authors, which may lead to increased heterogeneity in the pooled HAR to MNPs. Thus, plausible and scientific guidance of MNP consumption and the definition of adherence still need to be addressed in future studies. Second, a limited number of countries and studies have reported data of HAR to MNPs. In the future, it would be better to incorporate as many studies as possible with a broad geographic scope to obtain a more comprehensive understanding of adherence to MNPs. Third, high statistical heterogeneity was found, which may be related to the diverse study regions, study populations, study periods and sample sizes. To account for

these differences, a random-effects model was used for the meta-analysis.

5 | CONCLUSIONS

This is the first meta-analysis that summarizes the adherence to MNPs and its influencing factors of 16506 high adherence and 7796 low adherence caregivers from four countries. The pooled HAR to MNPs was estimated as 63.28% in middle-income countries, which was higher than the HAR to MNPs of low-income countries. Parents aged 30 years and older, children aged 18–36 months, maternal educational attainment of college or above, caregivers with positive perception that other mothers in their community used MNPs, those with awareness on the importance of iron, those with correct knowledge of MNPs and caregivers reporting their children having no side effects of MNPs were all identified as positive factors for high adherence to MNPs. Thus, effective and trusted communication channels need to be established, along with timely guidance for caregivers. The findings are useful for developing effective intervention measures to improve adherence to MNPs in the future.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

CONTRIBUTIONS

HZ designed the study. RL and RY and CS did the literature search. RL, RY, FL, CS and QW did the literature screening and data extraction. RL did the data synthesis and wrote the manuscript. HZ revised the manuscript from preliminary draft to submission. HZ supervised the study. All authors have read and approved the manuscript.

DATA AVAILABILITY STATEMENT

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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