

Developmental Origins of Health and Disease (DOHaD): Implications for health and nutritional issues among rural children in China

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Summary

In China, with fast economic growth, health and nutrition status among the rural population has shown significant improvement in the past decades. On the other hand, burden of non-communicable diseases and prevalence of related risk factors such as overweight and obesity has also increased. Among rural children, the double burden of malnutrition and emerging overweight and obesity has been neglected so far. According to the theory of Developmental Origin of Health and Diseases (DOHaD), malnutrition, including both undernutrition (stunting and wasting) and over-nutrition (overweight and obesity) during childhood is closely related to worsened health outcomes during adulthood. Such a neglected problem is attributable to a complicated synergy of social and environmental factors such as parental migration, financial situation of the household, child-rearing knowledge and practices of the primary caregivers, and has implications for public health. Based on literature review of lessons from the field, intervention to address malnutrition among rural children should be a comprehensive package, with consideration of their developmental environment and geographical and socioeconomic diversity. The scientific evidence on DOHaD indicates the probability and necessity of prevention of adult disease by promotion of maternal and child health and reducing malnutrition by provision of high-quality complementary foods, promotion of a well-balanced dietary pattern, and promotion of health literacy in the public would bring a potential benefit to reduce potential risk of diseases.

Keywords: Malnutrition, developmental origins of health and disease (DOHaD), non-communicable diseases (NCDs), children, rural, China

1. Introduction

In general, patterns of disease burden and malnutrition parallels and changes with socioeconomic development. Due to the socioeconomic gap, a huge difference between

urban and rural settings regarding children's health, nutrition and development has been widely observed in China. Traditionally, prevalence of overweight and obesity in the urban area is higher than that in the rural area; while nutrient deficiencies and wasting among rural children are much more common compared to their urban counterparts. In China, the geographical and socioeconomic situation diversifies the pattern of malnutrition: in some poor and remote rural areas of Midwestern provinces, the major nutritional problems among children tend to be nutrient deficiencies such as anemia and stunting (1-3), while overweight and obesity among rural children have also reported, especially

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in developed provinces (4,5). The double burden of malnutrition and emerging overweight and obesity among rural children has been neglected so far. Although compared to that in urban children, the prevalence of anemia and stunting in rural children is higher, overweight and its risk factors among rural children are emerging as well. In our interventional program, we also found that both wasting and overweight are relevantly prevalent among rural children in Shandong Province, a developed region in the country, and in particular those left behind by rural-to-urban migrant parents had a higher prevalence compared to their non-left-behind counterparts (Figure 1). Such a neglected problem is attributable to complicated social and environmental factors and has implications for public health.

Since the 1980s, when retrospective cohort studies implemented by David Barker and colleagues indicated that the incidence of certain adult diseases such as cardiovascular disease and type II diabetes may be linked to early-age development, the hypothesis "Developmental Origins of Health and Disease (DOHaD)" and its conceptual framework has been established (6). Based on the theory of DOHaD, the beginning stages of life including pregnancy, neonatal period and childhood provides an essential opportunity to mitigate the environmental insults that may increase an individual's sensitivity to, or risk of developing diseases later in life (7). In this brief review, we examine the current epidemiological characteristics of malnutrition among rural children, their developmental environment and possible interventions to address the double burden of malnutrition and potential disease burden of non-communicable diseases (NCDs) in view of the theory of DOHaD.

2. Interpretation of causes and prevention of NCDs based on the theory of DOHaD

Although it generated considerable skepticism and related mechanisms remain unclear, Barker's hypothesis has established an association between developmental origins and health at later life stages. Since then, more robust evidence from epidemiological work based on large cohorts of the population and laboratory studies to explore epigenetic mechanisms confirmed that nutritional and toxicant exposure in the early stages of life have a profound impact on the development of NCDs in adulthood and led to widespread acceptance of the association (8,9).

Recently, it has been widely recognized that NCDs are the long-term outcome of physiological adaptations to the environment, and the complicated process referred to as "programming" (10). The process of programming is a complex interaction between genetic make-up and environmental adaptation. During early stages of development, when cells are differentiating and tissues are developing, the organism responds

to exposure in the environment such as nutrient and physiological factors, drugs and environmental chemicals, by molecular pathways including DNA methylation, histone covalent modification and non-coding RNA expression, and such epigenetic modification can be passed from one cell generation to the next (11). The mechanisms result in permanent changes in physiology and metabolism of the infant. The early stages of development, including intrauterine, neonatal and infant life and early childhood, is the time when epigenetic marks undergo critical modifications, and the epigenetic system gradually becomes less plastic and sensitive to environmental alterations as the process of development finishes (12). Epigenetic mechanisms allow the organism to adapt to changing environments in order to maintain or improve reproductive capability; on the other hand, developmentally plastic processes can also have adverse consequences on disease risks later in life (13). Animal models provided robust evidence on epigenetic mechanisms involved in the theory of DOHaD.

It has been proven that malnutrition, not only over-nutrition (overweight and obesity) but also undernutrition (stunting and wasting) during childhood are closely related to worsened health outcomes in adulthood (14). Maternal malnutrition, such as under-nutrition, obesity, excessive weight gain and gestational diabetes in pregnancy influence disease risks in the next generation (13). Besides antenatal issues, growth in childhood is another major influence on programming, as recent studies also suggested that epigenetic changes in metabolic pathways may not be limited to malnutrition in the prenatal stage, but also in the postnatal period. Lower birth weight coupled with a higher body-mass index in childhood, which is now common in developing countries undergoing the nutritional and epidemiologic transition to Western styles of diet, sedentary behavior, obesity, and chronic diseases, appears to be associated with the highest risks of obesity, insulin resistance, the metabolic syndrome, type II diabetes, and ischemic cardiovascular disease (15). Stunting and growth failure due to malnutrition, which remains at a high level in developing countries, is difficult to reverse after 36 months of age and rapid weight gain in later childhood increases the risk of metabolic symptoms (14,16). In developing countries such as Pakistan, it has been observed that poor early growth due to malnutrition and later obesity often co-exist (17), and looking back to the nutritional and growth status of childhood, those who developed NCDs in adulthood tended to have below-average height, weight and BMI in early life with rapid weight gain in later childhood (14). Based on findings in epidemiological studies so far, the relevantly high burden of malnutrition in early childhood would increase the risk of epidemic and a high burden of NCDs in their adulthood in the future.

3. The developmental environment for children's health and development in rural China

The rural area of China recently has experienced an epidemiological and nutritional transition. With the rapid economic growth, health and nutrition status among the rural population has shown significant improvement in the past decades. On the other hand, NCDs such as cardiovascular diseases (CVD), type II diabetes mellitus and hypertension, as well as a prevalence of related risk factors such as overweight and obesity in adults and children have also increased in rural China (1,18,19). The shift of the disease and nutrition pattern is attributable to life style, health-related behaviors and diet (20). Recently in the rural area, health-related behaviors including diet and physical activities of adults, particularly the primary caregivers of children, affects health and nutritional status of not only themselves, but also children. A matter of great concern requiring urgent action is to prevent and control NCDs by removing unhealthy various risk factors in daily life by both population-wide interventions and targeted measures for individuals at high risk (21).

Social and environmental factors contributing to the emerging nutritional problem of rural children are complicated, and the underlying common background is a profound social mobilization with rapid economic growth. During the past decades a relevant amount of the rural migrant population moved to the urban area and left their children behind to grandparents. It is estimated that the amount of rural-to-urban migrant population has increased from 70 million to 221 million during the period from 1990 to 2010, accounting for 16.5% of the overall population in China, and continues to increase. Population mobilization has put huge pressure on public services in the urban area such as, education, medical insurance, employment, and social welfare. A relevantly large number of rural-to-urban migrant populations tend to not be covered by those public services and left their children at the villages. Consequently, the population of rural left-behind children increased rapidly as well, accounting approximately for 30% of rural children and 22% of the total number of children in the country. Having separated from their parents, more than half of those left-behind children are raised by their elderly grandparents.

A child's quality of life and developmental outcomes are affected by the environment where he or she grows up (22). Parental migration tends to have a profound impact on both positive and negative aspects of a child's growth. Positively, parental migration from rural areas to urban areas often leads to a higher income and enhanced socioeconomic status (23). On the other hand, under a special developmental environment of lack of parents' involvement, such a large population suffers from various problems in their physical and

psychological health, nutritional status and development (24-26). A further concern is that 'left-behind' children will also be at risk of inappropriate food intake and malnutrition because of lack of nutritional knowledge among elderly caregivers (27), rather than lack of access to foods. In the rural area, when the financial situation of the household is improved, children can easily access high-fat or non-nutrition-based foods including snacks and sugar-sweetened beverages, which significantly affect overall energy intake and nutrient balance (28). In our surveyed rural children, inappropriate consumption of snacks and sugar-sweetened beverages, picky eating and unbalanced nutrient intake in meals is prevalent, particularly among those left-behind children raised by their elderly grandparents. Such a dietary pattern exposes children to the double burden of malnutrition. For most rural households, recently when food availability is no longer a problem with improved income, how to eat healthily tends to be a new issue.

Previous studies suggested that the impact of parenting style on a child's health and development often depends on the characteristics of the primary caregiver, such as education, income, child-rearing beliefs, and behavior, rather than status of separation from parents or not (29). Most primary caregivers of left-behind children are their grandparents, whose educational level tends to be low and knowledge related to children's health, nutrition and development are poor, profoundly affecting child-rearing beliefs and practices. This kind of population often tends to be exposed to high risks for NCDs as well, as a national surveillance showed that those who are older, who live in eastern or central China or who are poorly educated tended to more likely be exposed to multiple risk factors for NCDs, such as insufficient intake of fruit and vegetables, overweight and obesity, raised blood pressure, physical inactivity, raised total serum cholesterol, and raised blood glucose (30). Therefore, in rural China, it should be highlighted that in such a population it is crucial to not only control NCDs at the community level, but also to address the double burden of malnutrition of rural children. Promotion of health-related behaviors including diet, physical activity and child-rearing beliefs and practices is expected to bring benefit to the population for different generations.

4. Effective solutions for double-burden of malnutrition among rural children in China

To tackle both nutrient deficiency and overweight among rural children, effective health and nutritional intervention for rural children in China is urgently needed. So far, previous studies implemented in developing countries suggested some effective interventions to solve specific problems of children's malnutrition and growth, such as multiple micronutrient supplementation (including iron, zinc, and vitamins), behavior change for complementary

feeding, and universal salt iodization (2031). Most of those interventions proven effective and considered cost-effective are for prevention of undernutrition, while the impact of those to prevent overweight and obesity and related NCDs remain uncertain (32). Moreover, what is already known is that comprehensive and multifaceted interventions rather than a single intervention would be more effective to tackle various nutritional problems among children living in developing countries. In a population with sufficient food, education about complementary feeding improves children's growth; while in a population with insufficient food provision of food supplements works. (2031). As young children's nutritional status results from a complex interaction of various factors such as food consumption, knowledge and practices of caregivers, and health system strengthening, an integrated strategy is necessary for their growth and development (31,33).

It should be highlighted that the malnutrition issue faced by children living in rural China is unique and within the country nutritional epidemiology is diversified by regions. Except those living in remote and poor western regions, food is now sufficient for a relevantly large amount of the population and even a rapid nutrition transition to a high-fat, high-energy-density and low-fiber diet is ongoing (34,35). Therefore, interventions targeting the undernutrition issue among vulnerable children in less developed countries are suggestive for those poor regions where underweight and stunting is still common, but may be not an appropriate solution for affluent regions. Both at the global and national level, strategies to prevent and control malnutrition have focused on nutritional deficiency and need to be re-examined and aligned with measures to fight against overweight and obesity (26).

To promote child-rearing practices of the primary caregivers, we implemented an interventional program during the past year targeting primary caregivers of 735 rural children aged 3 to 6 years old who have not yet been admitted to the preliminary school in two counties of Shandong Province, a developed region in China. The program aimed to improve rural children's health and growth status, especially that of left-behind children, involving primary caregivers (including children's parents and grandparents). Left-behind children's parents who were working out of the villages were invited to the intervention when they went back during a vacation as well. The intervention was conducted every two-months, consisting of a set of free-style educational and consulting programs on children's health and nutrition targeting primary caregivers, and an interaction of children, primary caregivers, kindergarten teachers and local community administrators. Such intervention was developed and provided by academic and clinical experts in various fields such as pediatrics, nutrition, and developmental psychology, with the main components focusing on children's growth and development, nutrition

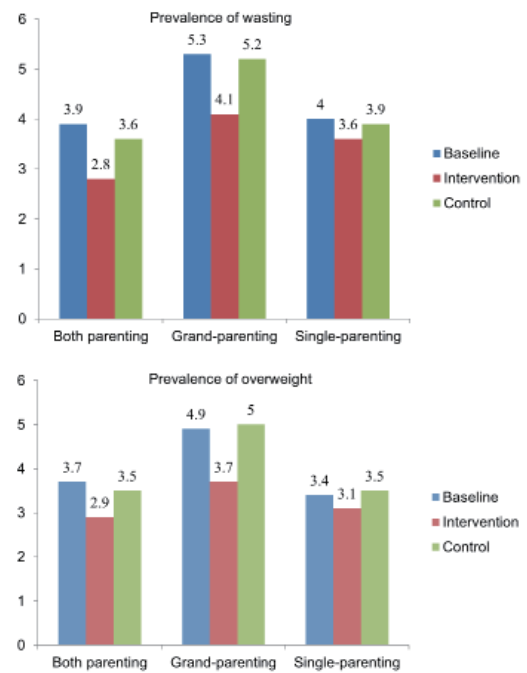


Figure 1. Prevalence of overweight and wasting among rural children, in the field of Shandong Province, China.

and feeding, prevention and treatment of common diseases, vaccination, and education and communication with children. In the results, when knowledge and feeding practices of the primary caregivers and the dietary pattern of children (assessed by 3-day food records and factor analysis) were improved after the intervention, the prevalence of both wasting and overweight was reduced significantly in the intervention group compared to that in the control group, and the program particularly showed a positive effect for the left-behind children (Figure 1). Improvement of health literacy and feeding practices of the primary caregivers contributed to alleviation of the double burden of malnutrition among rural children.

Our field attempt provided a preliminary solution to empower the primary caregivers and to improve the developmental environment of rural children. The approach is especially appropriate for affluent rural regions in China, where household income is able to ensure availability of food. For poor and under developed regions, provision of complementary food supplements combined with knowledge enhancing the primary caregivers still plays a major role for improving feeding practices. Taking these facts into consideration, interventions for Chinese rural children should be a comprehensive package, with consideration of their developmental environment and geographical and socioeconomic diversity.

Similar to other developed and developing countries of the world, emerging nutritional problems and non-communicable diseases occurred first in higher socioeconomic groups and later shifted to the less advantaged in China. The rural area is a high priority for prevention and control of NCDs in the country. Recently,

the incidence of NCDs and the disease burden in the rural area has been much higher than that in the urban area. Among rural residents, major risk factors such as overweight and obesity, inadequate physical exercise, and high-fat and energy-dense diet are also emerging and prevalent. So far, most community-based interventions such as promotion of diet and lifestyle have focused on adults and most investment has been injected into secondary prevention and treatment, whereas the major disease burden caused by non-communicable diseases such as cardiovascular disease and type II diabetes have their origins in transition from malnutrition in early childhood (9). The latest evidence shows overweight or obese children who were obese as adults had increased risk of type II diabetes, hypertension, dyslipidemia, and carotid-artery atherosclerosis and the risk is not changed whether they became obese or not by adulthood (26), suggesting early intervention during childhood could be more effective (38). The scientific evidence on DOHaD indicates the probability and necessity of prevention of adult disease by promotion of maternal and childhood health (9).

Without effective measures to tackle the double burden of malnutrition among rural children, it is not possible to attack the epidemic of NCDs in the near future. Although the long-term outcome of maternal and infant intervention to prevent related NCDs remain uncertain because of the absence of high-quality cohort data in a short time period, the current recommendations based on the theory of DOHaD presume that reducing malnutrition by provision of high-quality complementary foods, promotion of a well-balanced dietary pattern, and promotion of health literacy in the public would bring potential benefits to reduce the potential risk of diseases. In this respect, a cross-sectional endeavor to improve the developmental environment of rural children will have a vital role to play.

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