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Perspective

Comprehensive understanding of developmental origins of health and disease concepts: Early intervention to non-communicable diseases in China

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Introduction

Mortality due to various kinds of non-communicable diseases (NCDs) has become an increasing focus of attention in recent years.[1] With rapidly increasing globalization, lifestyles in low- and middle-income countries increasingly include high-fat diets and inadequate physical exercises are resulting in an increased worldwide burden of NCDs.[2,3] A study by the International Diabetes Federation (IDF) showed that about 382 million people had diabetes in 2013, and this will rise to 592 million by 2035. The number of people with type 2 diabetes is increasing in every country, and 80% of people with diabetes live in low- and middle-income countries. The burden of NCDs and the prevalence of related risk factors such as overweight and diabetes have also increased in China over the past decades. In 2005, NCDs accounted for an estimated 80% of deaths and 70% of disability-adjusted life-years lost in China.[4] In 2010, the leading causes of death among Chinese women were cardiovascular and cerebrovascular diseases and cancer, which together accounted for nearly 70% of all deaths.[5] The incidence of hypertension increased from 5.1% to 33.5% between 1958 and 2010, while the prevalence of diabetes increased by 9.7% and the estimated prevalence of pre-diabetes was 15.5%, accounting for 92.4 million adults with diabetes and 148.2 million adults with prediabetes.[6,7] The prevalence and burden of NCDs in China is creating a significant economic and social load on society, so epidemiological, demographic and socio-economic transitions has been made to prevent and control NCDs in China.

Theory of developmental origins of health and disease and NCDs

In the 1980s, retrospective cohort studies implemented by David Barker and colleagues indicated that

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the incidence of certain adult diseases such as cardiovascular disease (CVD) and type 2 diabetes may be linked to the intrauterine environment.[8,9] Based on Barker hypothesis, the theory of "Developmental Origins of Health and Disease (DOHaD)" and its conceptual framework has been established: stating that an offspring with susceptibility to chronic diseases in later life may be programmed in early life development.[10,11] Initial studies on the DOHaD focused on the impact of maternal under-nutrition, and demonstrated that low birth weight was associated with an increased risk of obesity, CVD and metabolic disorders in later life. Small at birth and thin at two years of age and gaining weight rapidly thereafter is a pattern of growth during childhood associated with insulin resistance and coronary problems in later life.[12] Children born from preeclamptic pregnancies were more prone to hypertension, insulin resistance and diabetes mellitus, neurological problems, stroke, and mental disorders throughout life.[13] Recent evidence on the effect of over-nutrition showed that fetal exposure to a diabetic environment in utero is associated with an increased incidence of hypertension and glucose and lipid metabolism disorders in adulthood.[14,15] A case–control study by identification and prevention of dietary- and lifestyle-induced health effects in children and infants (IDEFICS) showed that parental body mass index (BMI) and gestational weight gain were the key risk factors of childhood obesity at the age of nine years.[16] Moreover, maternal obesity (BMI > 30 kg/m^2) and high-fat diets were associated with an increased risk of premature death and adiposity in an adult offspring by a record linkage cohort analysis.[17] Recently, it has become widely recognized that NCDs are the long-term outcome of physiological adaptations to the environment, and the complicated process referred to as "programming". "Programming" refers to the process where by a stimulus at a critical window of development has long-term effects. Epigenetics is the study of chemical changes in DNA and histones that affects how genes are expressed without alterations of DNA sequences. More evidence from epidemiological work based on large cohort studies and animal models that explored epigenetic mechanisms confirmed that malnutrition or over-nutrition during the fetal period alters the epigenetic expression status of metabolic genes in the fetus and that this altered expression can persist and have a profound impact on the development of NCDs in adulthood.[18,19] Epigenetic mechanisms have also determined the transgenerational disease transmission.

Pregnancy as a stress test for future metabolic syndrome

A number of studies have reported women with gestational diabetes mellitus (GDM) have a substantially increased risk for type 2 diabetes in later life. A study conducted showed that women with GDM have a sevenfold increased risk of developing type 2 diabetes in their lifetime.[20] Approximately half of these women develop diabetes in the 1st 5–10 years after the index pregnancy. The ADA in 2015 recommended follow up and screening for women with GDM to detect persistent diabetes at 6–12 weeks postpartum, and women with a history of GDM should have lifelong screening for the development of diabetes or pre-diabetes at least every three years.[21] Women with a history of GDM found to have pre-diabetes should receive lifestyle interventions. In addition, coexisting obesity and progressive weight gain are additive factors for progression to type 2 diabetes. A study by O'Sullivan[22] showed that the incidence of diabetes in participants who had previous transient gestational glucose intolerance was significantly higher for overweight subjects (46.7%) than for those of normal weight (25.6%). He stated that among persons at high risk, like GDM, excess weight also predicted the severity of the subsequent diabetic condition. What is more, women treated for GDM had lower rates of hypertensive disorders of pregnancy, cesarean deliveries, and less weight gain.

Some epidemiologists have commented that preeclampsia is not only a pregnancy disease but also a risk factor for developing diseases later in life. Women who have had preeclampsia seem to be at higher risk of premature death, mortality from ischemic heart disease, and CVDs including ischemic heart disease and hypertension. A case control study showed that patients with hypertensive pregnancies showed an abnormal activation of the endothelium which persists after pregnancy, which may represent an explanation of the increased risk of CVD later in life.[23] Pregnant women with adverse perinatal complications can also risk NCDs in later life.

Early intervention to NCDs

Over the past decade, China has strengthened its primary healthcare system and increased investment in public health interventions. Although China has made good progress in developing and implementing these strategies and policies for NCDs prevention and control, many challenges still remain. Such as, there is insufficient public funding for NCDs care and

management, and NCDs patients are economically burdened due to limited benefit packages covering NCDs treatment offered by health insurance schemes. A life-course approach to reduction of risk of NCDs suggests that early-life interventions may be more effective and improve functional capacity. The major force, which is responsible for the emergence of NCDs, is the rapid increase in high-risk lifestyle behavior like tobacco use, the harmful use of alcohol, physical inactivity, and an unhealthy diet, which are causes of overweight and obesity, raised blood pressure, raised blood glucose and dyslipidemia. Early life development (1000 days, including gestation, and after two years of age) is not only the critical time for development of tissues, organs, and the nervous system, but also increasingly recognized as period of peak susceptibility to nutritional insults. It is pivotal to teach the importance of healthy behavior before and during pregnancy, in early infancy and in childhood, for future well-being. Nutritional guidelines in pregnancy, based on evidence to promote healthy fetal development, should be well established and widely disseminated. Research on the association between early nutrition and adult outcomes showed that a focus on improvements in nutrition in pregnancy and linear growth in the first 2 years of life could lead to substantial reductions in stunting and in improved survival.[24] The Institute of Medicine (IOM) Guidelines in 2011 stated that energy needs are increased only in the second trimester (+15%) and third trimester (+20%); including 20% for total energy, 54% for protein, increased proportions of minerals and trace elements and vitamins, like 50% for iron, 50% for folate, and 46% for vitamin B6. Yang et al[25] suggested an acceptable macronutrient distribution range for carbohydrate (50%−60% of energy), protein (15%−20% of energy), and fat (25%−30% of energy; limit saturated and trans-fats) for GDM patients. Breast milk provides an optimal source of nutrition for infants. Many organizations, including the World Health Organization (WHO), the European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN), and the American Academy of Pediatrics (AAP), recommend that healthy term infants be exclusively breastfed for the first 6 months of life.[26] Breastfeeding appears to have a protective effect on excessive early infant weight gain and later obesity. Strategies and social policies are needed to promote a longer breastfeeding duration and should be integrated with comprehensive efforts to prevent childhood obesity and to reduce the long term burden of chronic diseases. Moreover, pregnant women should also control their weight gain during pregnancy, according to the guidelines of the IOM for weight gain during pregnancy in May 2009, which suggested that recommendations to patients be based on pre-pregnancy BMI. For BMI levels <18.5, 18.5−24.9, 25−29.9, and >30 kg/m^2, weight gain ranges are suggested at 12.7−18.4, 11.3−15.9, 6.8−11.3, and 5.0−9.1 kg, respectively, and the recommended rate of weight gain are 0.450−0.590, 0.363−0.454, 0.227−0.318, and 0.181−0.272 kg/week in the second and third trimester. There is evidence suggesting that weight management interventions in pregnancy are effective for reducing the incidence of obesity, GDM, and preeclampsia, and even more effective for reducing the mortality and morbidity of the fetus.

So it is highlighted that intervention in early life may be able to alter trajectories of later disease risk more cost-efficiently than traditional lifestyle modifications or treatment in later life.

Conclusions

The global burden of NCDs is rising dramatically worldwide and is causing a double poor-health burden in China. Early life influences play an important role in the prevalence of NCDs because maternal lifestyle and nutritional conditions will affect the risk of metabolic disorders in the next generation. Although there is an absence of high-quality cohort data for the long-term outcome of maternal and infant intervention to prevent related NCDs, the current recommendations based on the theory of DOHaD presume that controlling weight and obesity during pre-pregnancy and pregnancy, reducing the incidence of GDM, preeclampsia in pregnancy, 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 NCDs. The DOHaD Society had established affiliated societies in China in 2009, and Chinese doctors could share the achievements of research in our country at the congress of DOHaD. Making knowledge available to develop an understanding of the DOHaD offers the potential to encourage informed diet and lifestyle choices supporting reduction of NCDs risk in current and future generations.

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