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EDITORIAL

Early Life Nutrition during the First 1000 Days from a Malaysian Perspective

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ABSTRAK

Tempoh 1000 hari pertama kehidupan bermula dari kandungan dalam rahim sehinggalah hari jadi anak tahun yang kedua, merupakan fasa penting dalam perkembangan manusia. Kertas ulasan ini menegaskan kepentingan tempoh kritikal ini dalam satu analisis komprehensif demi menerokai kesan pelbagai aspek pemakanan melalui tiga fasa yang berbeza iaitu tempoh kehamilan, tempoh penyusuan susu ibu dan tempoh pengenalan makanan pelengkap. Dalam tempoh kehamilan, indeks jisim badan ibu merupakan faktor penting yang mempengaruhi kesihatan ibu dan anak. Pemakanan yang optimum, termasuk mikronutrien penting seperti asid folik, zat besi, iodin, dan vitamin D, adalah penting untuk mengurangkan risiko seperti kecacatan tiub neural dan gangguan berkaitan yang masih menjadi masalah kesihatan di Malaysia. Penyusuan susu ibu eksklusif dalam enam bulan pertama lepas lahir adalah penting untuk perkembangan kognitif dan sistem imun kanak-kanak. Permulaan makanan pelengkap pada masa yang tepat juga sangat penting untuk mencegah masalah obesiti kanak-kanak dan mengurangkan masalah kekurangan zat makanan. Kertas ulasan ini membincangkan kepentingan dan peranan kritikal nutrisi seimbang dalam tempoh 1000 hari pertama kehidupan. Kertas ini juga mengupas situasi semasa dan menggariskan strategi serta intervensi untuk memastikan kanak-kanak mendapat nutrisi yang mencukupi dalam fasa yang penting ini dalam konteks di Malaysia.

Kata-kunci: *Tempoh 1000 hari pertama kehidupan; tempoh kehamilan; tempoh penyusuan susu ibu; tempoh pengenalan makanan pelengkap*

ABSTRACT

The first 1000 days of life, encompassing the period from conception to a child's second birthday, represents a pivotal phase in human development. This review paper highlighted the importance of this critical window with a comprehensive

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analysis exploring the multifaceted impact of nutrition during the three distinct phases: the pregnancy-intrauterine period, early infancy-breastfeeding period, and early childhood-complementary feeding period. Within the pregnancy-intrauterine period, the maternal body mass index emerges as a crucial factor, directly affecting the well-being of both mother and child. Optimal nutrition, including essential micronutrients such as folic acid, iron, iodine, and vitamin D, are imperative to mitigate the risk of neural tube defects and related disorders, which remain a concern in Malaysia. Exclusive breastfeeding during the initial six months of life is identified as a cornerstone of infant development, nurturing both the child's cognitive abilities and immune system. Timely introduction of complementary foods is equally vital, acting as a safeguard against childhood obesity and undernutrition. This review paper provided an in-depth examination of the importance and critical role of nutrition in the first 1000 days of life. It further outlined the current status, recommended strategies and interventions to improve child nutrition during this crucial phase in the Malaysian context.

Keywords: Early childhood-complementary feeding period; early infancy-breastfeeding period; first 1000 days of life; pregnancy-intrauterine period

INTRODUCTION

The first 1000 days of life, spanning from conception until the child's second birthday (Schwarzenberg et al. 2018), represents a critical period where nutrition profoundly influences both immediate health and long-term development, shaping an individual's susceptibility to chronic diseases in adulthood. During this timeframe, essential nutrients are crucial for rapid growth, organ development, and the establishment of metabolic patterns. Furthermore, it is a pivotal phase for neurodevelopment, given the rapid rate at which cognitive functions develop (Saavedra et al. 2016). Inadequate nutrition during this crucial window can result in permanent alterations in tissue structure and physiological processes (Mandy & Nyirenda 2018). Hence, nutrition during early life stands as a pivotal and adjustable environmental factor. To ensure optimal nutrition during this critical period, it is essential for mothers to maintain a proper maternal diet during pregnancy, exclusively breastfeed for the first six months, introduce appropriate complementary foods after six months, and continue breastfeeding until the child reaches the age of two (Cunha et al. 2015). This comprehensive approach helps to establish the foundation for a lifetime of good health and well-being.

NUTRITION DURING PREGNANCY

Review of Current Recommendations on Energy Intake

Maternal nutrition during the first 1000 days of life is critical, impacting both the mother's and the foetus's well-being. Unfortunately, in many countries, pregnant women's nutritional status often fall below necessary standards, leading to severe complications, including anaemia, pre-eclampsia, haemorrhage, and even maternal mortality. Additionally, inadequate maternal nutrition can have detrimental effects on infants, resulting in outcomes such as stillbirth, low birth weight, impaired growth, and developmental delays (Rocco et al. 2005). On the other hand, the rising prevalence of maternal obesity can influence foetal and neonatal development through a process known as developmental programming, potentially predisposing offspring to obesity and cardiovascular diseases, including hypertension (Inzani & Ozanne 2022).

The concept that long-term chronic disease risk is linked to in-utero nutrition emerged from David Barker's 1980s research, suggesting its role in adult ischemic heart disease (Barker 2007). This idea has expanded into the Developmental Origins of Health and Disease (DOHaD) hypothesis, indicating that foetal and neonatal DNA undergoes epigenetic modifications in response to external environmental factors (Langley-Evans & McMullen 2010). It is now widely accepted that lasting structural and functional changes during gestation contribute to diseases that emerge later in life.

Malaysia, with the highest obesity prevalence in Southeast Asia, reflects a global trend of increasing overweight or obese adults. The National Health and Morbidity Survey (NHMS) in 2019 revealed that one in two adults (50.1%), aged 18 and above was either overweight (30.4%) or obese (19.7%), with a higher prevalence in females and in the Indian population (Shahrir et al. 2021). Globally, the proportion of maternal obesity varies, ranging from 10.1% to 17.9% (Bogaerts et al. 2012; Onubi et al. 2016). This rise in obesity is concerning for women of child-bearing potential as more women will begin their pregnancy with a higher BMI. The 2016 NHMS report revealed that maternal obesity had reached a prevalence of 14.6%, with mothers of advanced age, in the 45-49 age group exhibited the highest prevalence of obesity at a staggering 69.2%. Malays have the highest prevalence of 16.8%, followed by Indians at 15.6%, and Chinese at 5.8%. In 2021, 28.6% of pregnant women were overweight, with an additional 22.6% were classified as obese, a significant increase from 2016, where only 14.6% were categorised as such (Shahrir et al. 2021). The close relationship between obesity and impaired glucose tolerance increases the risk of gestational diabetes mellitus (Catalano 2010). Maternal obesity is linked to a 3.6 times higher likelihood of macrosomia in infants (Shahrir et al. 2021), who are at risk of obesity and metabolic disorders in later life. High birth weight is also associated with a slightly increased risk of type 1 diabetes, though the precise mechanisms are unclear (Savona-Ventura & Chircop 2003).

Energy needs during pregnancy vary and depend on factors like pre-pregnancy weight, body mass index (BMI), maternal age, gestational stage, energy expenditure, and basal metabolic rate (Blumfield et al. 2012). Although there are variations in guidelines, it is generally acknowledged that the extra energy requirements are relatively small. According to International Federation of Gynecology and Obstetrics (FIGO) recommendations, the increase in dietary energy intake during pregnancy should be moderate, with a suggested range of 340-450 kcal per day during the second and third trimesters. Simultaneously, they advocate for moderate exercise of 30 minutes per day while advising against engaging in hard physical labour during the later stages of pregnancy (Hanson et al. 2015). Moreover, RCOG recommends a modest increase in energy requirements during the third trimester, approximately 200 kcal per day, roughly a 10% rise from the recommended daily intake of 1940 kcal/day in a non-pregnant adult woman (Ho et al. 2016).

Recommended Nutrient Intake (RNI) guidelines in Malaysia advise pregnant women to increase their daily calorie intake by around 280 kcal and 470 kcal during the second and third trimesters (National Coordinating Committee on Food and Nutrition, Ministry of Health Malaysia 2017). Despite these recommendations, a meta-analysis of well-nourished women found that the average increase in daily energy intake during pregnancy was only about 140 kJ/day (Blumfield et al. 2012). This shift in energy requirements may be due to reduced physical activity, a sedentary lifestyle, and a rising prevalence of higher pre-pregnancy BMI. Excessive energy intake can lead to excessive gestational weight gain and adverse pregnancy outcomes. As pregnancy advances, women experience reductions in energy expenditure through less physically strenuous activities and increased sedentary time (Löf at al. 2011). These adaptations are essential for facilitating weight gain during pregnancy.

In summary, the clinical implications of providing dietary advice during pregnancy are significant. They call for a shift in focus from merely increasing food intake to enhancing dietary quality and micronutrient composition, along with recommending appropriate supplement use. Reforms in dietitian advice during antenatal care may be necessary to avoid excessive weight gain with potential adverse consequences for maternal and neonatal health.

Selecting Micronutrient Intake Recommendations and Special Considerations for at Risk Populations

(i) Folate

Adequate intake of folate, a water-soluble essential B vitamin (B9), is essential for various bodily functions, including the formation of red and white blood cells, energy production, and cell growth (Abbasi et al. 2018). Moreover, folate plays a significant role in preventing neural tube defects (NTDs), which are birth abnormalities occurring between days 18 and 28 after conception when the neural tube fails to close properly (Greene & Copp

2014).

To reduce the risk of NTDs, all pregnant women are recommended to take a daily supplement of 400 µg of folic acid starting one month before conception and continuing until the 12th week of pregnancy. Individuals at a higher risk of NTDs are advised to take a higher daily dose of 4-5 mg of folic acid (Dwyer et al. 2022). Unfortunately, inadequate folic acid intake persists among many women of child-bearing age. Factors contributing to this include a high prevalence of unplanned pregnancies, limited knowledge, challenges in translating knowledge into behavioural changes, and barriers to supplement utilisation, such as cost, accessibility, and compliance issues (Australian Institute of Health and Welfare 2016).

Obesity in women doubles the risk of NTDs due to inadequate folate absorption, even with recommended supplementation (Huang et al. 2017). Blood folate concentrations often remain deficient even with recommended folate supplementation (Koren & Kaplan 2021). Additionally, they are at 5-10 times higher risk of having a baby with spina bifida (Zhang et al 2021). Weight loss in obese women has shown to increase folate levels even without change in folate intake (Ortega et al. 2009). Therefore, weight loss may be a key strategy to reduce folate deficiency in obese women.

Diabetic women face a 2-4 times increased risk of giving birth to a baby with birth defects (Correa et al. 2012). Excess glucose can decrease the expression of the Pax3 gene required for neural tube closure, elevating the risk of NTDs (Loeken 2005). To mitigate this risk, the American Diabetes Association recommends 400 mcg of folic acid daily in nonpregnant women with pre-existing diabetes and 600 mcg daily for women who are pregnant or who plan to become pregnant (Kitzmiller et al. 2008). Pregnant women should follow a low-carb diet that contains folate-rich foods to reduce risk of NTDs.

The use of antiepileptics, such as valproic acid and carbamazepine, can significantly increase the risk of NTDs in newborns, effectively doubles this risk (Yerby 2003). In cases where switching medications is not an option, a strategy involves substantially increasing folate intake by 10-fold through supplementation. This typically involves supplementing with 4 mg of folic acid daily before and during pregnancy (American Academy of Pediatrics 2017).

The impact of folic acid supplementation in preventing NTDs has been well-documented. In the United Kingdom, daily consumption of 4 mg of folic acid during the periconceptual period led to a remarkable 70% reduction in the recurrence of NTDs among women with a history of NTD-affected pregnancies (MRC Vitamin Study Research Group 1991). Similarly, in China, daily consumption of 400 µg of folic acid reduced the risk of NTD-affected pregnancies by 79%, in Hebei province, where the incidence of NTD was high at 50-60 per 10,000 (Berry et al. 1999). In Australia, mandatory folic acid fortification in bread has successfully increased folic acid consumption among women of childbearing age, reducing the occurrence of NTDs (Australian Institute of Health and Welfare 2016).

In Malaysia, the estimated NTD rate is 10 per 10,000 births and the median of folic acid intake is approximately 202 µg which amounts to 50.6% of the Malaysian Recommended Nutrient Intakes level. Alarmingly, around 15% of them exhibited plasma folate deficiency, while 9% of them were deficient in red blood cell (RBC) folate. The prevalence of deficiency was the highest among the Indian population which is 21.5 (Khor et al. 2006). Based on the 2019 NHMS, one out of every five Malaysians, or 21.3% of the population, suffer from anaemia. Of particular concern is the prevalence among women of reproductive ages, with nearly three out of ten, or 29.9%, between 15- and 49-years old suffering from anaemia (Ministry of Health Malaysia 2019). Recognising the gravity of this issue, the Malaysian Cabinet has approved a proposal by the Health Ministry to make it mandatory for manufacturers to fortify 25 kg wheat flour packages with both folic acid and iron (New Straits Times 2022). Once implemented following amendments to the Food Regulations of 1985, every 100 grams of wheat flour will contain 6.0 mg of iron and 260 µg of folic acid. This initiative aligns with global efforts to address anaemia, as seen in the FDA's mandate for fortification of all grain cereal products with folic acid in 1998 (United States Food and Drug Administration 1996).

(ii) Iron

Iron is essential during pregnancy to meet the increased demands of both the developing foetus and the placenta, as well as to support the expansion of maternal red blood cell mass. Iron deficiency during pregnancy can lead to adverse outcomes, including maternal anaemia, which is associated with risks of low birth weight, preterm birth, and susceptibility to infectious diseases (Peña-Rosas et al. 2015). Iron is crucial for cognitive development, particularly in infants, as it plays key roles in various neurological processes. This includes synaptogenesis, myelination, energy metabolism, and neurotransmitter production, all critical for brain development. Preterm infants are at higher risk of iron deficiency due to their increased iron requirements and potential disruptions in maternal iron supply (German & Juul 2021).

In regions with a high prevalence of conditions like thalassemia, concerns may arise regarding iron overload during universal iron supplementation. However, research suggests that recommended iron doses do not lead to iron overload in thalassaemic individuals (Sinlapamongkolkul et al. 2023). Iron deficiency anaemia (IDA) is a significant concern during pregnancy, accounting for a substantial portion, ranging from 75% to 95% of anaemia cases (Halimi et al. 2011). Pregnant women often begin with insufficient iron stores, making dietary measures alone is inadequate (Milman 2015).

In Malaysia, the mean dietary iron intake is typically around 10 mg per day. Therefore, the need for iron prophylaxis becomes inevitable to prevent IDA as dietary measures alone is often inadequate in this context. The daily diet should ideally contain at least 27 mg of iron with 25% bioavailability, but drastic dietary changes can be challenging for many women (Milman 2015). The prevalence of anaemia in Malaysia during pregnancy varies between 19.3% and 57.4%, while the occurrence of iron deficiency ranged from 31.6% to 34.6%, with factors like age, delayed antenatal care initiation, non-adherence to iron supplements, ethnicity, education, income, and employment influencing the occurrence of anaemia (Abd Rahman et al. 2022).

The consequences of maternal iron deficiency extend beyond the mother, affecting the developing foetus and newborn. The iron status of the newborn may depend on the mother's iron status as research indicates a significant correlation between maternal and foetal serum ferritin levels (Milman et al. 1991). Research indicates that early childhood iron deficiency, even when treated with iron, can have long-lasting effects on cognitive development and recognition. Animal experiments have highlighted a critical time window in early pregnancy when iron deficiency can impair brain development in a way that cannot be fully reversed by later intervention with iron treatment. In Chile, IDA in early childhood, even when sufficiently treated with iron, was associated with compromised recognition and memory at both 4 and 10 years of age (Congdon et al. 2012).

In Malaysia, alarming statistics show a high prevalence of anaemia in infants and children. In the NSM 2023 congress, the Iron Strong Study results reported that more than 1 in 3 (34.5%) infants 6-12 months old in Malaysia are at the greatest risk of anaemia, characterised by haemoglobin levels of less than 12 g/dL. This alarming trend is further corroborated by the NHMS 2022 report, indicating that nearly half (46.5%) of children under the age of 5 in the country are anaemic (NutraIngredients-Asia 2023).

These numbers reveal critical gaps in healthcare practices, especially in maternal health and early childhood nutrition. Several areas need improvement, including screening for iron deficiency in pre-school children, iron supplementation for breastfed infants, and the underutilisation of Delayed Cord Clamping. It is important to note that breast milk contains relatively low iron levels, and while infants have a remarkable capacity to absorb iron from breast milk, supplementation during early infancy has shown benefits in cognitive development (Friel et al. 2003). The American Academy of Pediatrics (AAP) recommends iron drops at a dose of 1 mg/kg/day for exclusively breastfed infants starting at 4 months and universal screening for iron deficiency at 12 months (Baker et al. 2010). Earlier iron supplementation may start in the first month of age for infants born under circumstances involving pregnancy or birth complications, such as diabetes, low birth weight, prematurity, or those classified as small for gestational age and consuming breast milk. Infant will also receive iron from sources such as meats, iron-fortified cereals, and green vegetables upon the commencement of complementary solid foods (Baker et al. 2010).

To ensure an effective public health approach, screening infants at 4 months and monitoring parameters like ferritin levels, haemoglobin concentrations, MCV, dietary intake, and maternal risk factors are crucial.

(iii) Iodine

Iodine deficiency is a global concern, recognised as the leading cause of brain damage worldwide. Maternal iodine deficiency is associated with various adverse outcomes, including the increased risk of lower birth weight and infant mortality, hearing impairment, impaired motor skills, and neurological dysfunction. The World Health Organisation (WHO) defines the optimal level of iodine intake, as measured by the median urinary iodine (UI) concentration, within the range of 100 to 199 microg/L (Niwattisaiwong et al. 2017).

WHO recommends 250 mcg of iodine supplementation daily for pregnant women in countries where less than 20% of households have access to iodised salt (World Health Organisation, United Nations Children's Fund, & International Council for the Control of Iodine Deficiency Disorders 2007). Iodine deficiency is the most prevalent in regions with iodine-deficient soils, which are commonly found in inland areas, mountainous regions, and flood-prone areas. Moreover, coastal regions can experience iodine deficiency due to leaching effects from snow, water, and heavy rainfall, which removes iodine from the soil.

In Malaysia, one such region grappling with this issue is Sarawak, where endemic iodine deficiency disorders (IDD) are well-documented, with goitre prevalence ranging from 40% to over 90%. In some villages, congenital iodine deficiency syndrome has been observed. To combat this public health challenge, Sarawak has implemented mandatory universal salt iodisation (USI) since 2008. The Ministry of Health extended this initiative to the entire nation, making it mandatory from September 30, 2020, to add iodine to all refined salt or salt weighing 20 kg or less before sale in Malaysia, with iodine content ranging from 20-40 mg/kg.

Despite seven years of universal salt iodisation implementation, the median urinary iodine concentration (UIC) among pregnant women was measured at 105.6 µg/L, suggesting iodine deficiency in this population. Furthermore, 65.0% of pregnant women had a UIC of less than 150 micrograms per liter (µg/L) (Kuay 2018). A recent study conducted in Sarawak, Malaysia, had revealed a concerning trend in iodine deficiency among pregnant women, despite a decade of universal salt iodisation (USI) efforts in the region. Pregnant women continue to exhibit iodine deficiency, while school-aged children demonstrate adequate iodine status (Kuay et al. 2021). This underscores the persistence of this critical public health issue, given that iodine requirements increase by at least 50% during pregnancy. Maternal iodine deficiency can have dire consequences, impairing fetal neurological development and even reducing mean IQ scores by as much as 12-13.5 points, with the most severe form leading to cretinism. Iodine supplementation has shown promise in cases of moderate to severe deficiency, improving birth weight, reducing mortality, and enhancing developmental scores by 10-20%. Universal salt iodisation remains the most cost-effective means of delivering iodine to improve maternal and infant health (Zimmermann 2012). However, challenges exist, such as a growing health-conscious trend that reduces salt intake and medical conditions that requiring salt restriction.

(iv) Vitamin D

Vitamin D, a fat-soluble vitamin, plays a crucial role in promoting calcium absorption from the gut and supporting normal bone mineralisation and growth. During pregnancy, the demand for vitamin D increases significantly, as the foetus relies entirely on maternal vitamin D for its development and growth. Maternal vitamin D deficiency is associated with various adverse pregnancy outcomes, including gestational diabetes, pre-eclampsia, preterm birth, low birth weight, and caesarean section (De-Regil et al. 2016). Beyond its role in calcium regulation, vitamin D is involved in other vital functions, such as immune modulation in activated B and T lymphocytes and regulation of insulin and thyroid hormones.

As of 2012, the World Health Organisation (WHO) did not recommend routine vitamin D supplementation for pregnant women. However, supplementation of 200 International Units (IU) per day could be considered if deficiency was identified, as evidence regarding the safety of vitamin D supplementation during pregnancy was limited. It was also noted that dosages up to 4000 IU per day should be safe during both pregnancy and lactation (Institute of Medicine of the National Academies (US) 2010). Certain individuals are at a higher risk of vitamin D deficiency, including vegetarians, individuals with darker skin tones, those with limited sun exposure, and those who extensively cover their skin with clothing or sunscreen.

A study by Lee et al. (2017) to evaluate relationship between vitamin D and pregnancy outcomes revealed that a substantial 71.7% of the participants displayed vitamin D deficiency, emphasising the prevalence of this nutritional concern. Additionally, 21.0% of the participants had vitamin D insufficiency, with only 7.3% having adequate levels of 25-hydroxyvitamin D (25-OH-vit D), exceeding the recommended threshold of 30 ng/mL (Lee et al. 2017).

In the study that was done in Malaysia in examining the association of vitamin D deficiency and pregnant women, approximately 43% of the participants were found to be deficient in vitamin D, with an average daily intake of 8.7 $\pm$ 6.7 µg (equivalent to 360 International Units). Notably, 75% of the participants fell below the Recommended Nutrient Intake (RNI) of 15 µg or 600 International Units, indicating a widespread shortfall in vitamin D intake. Pregnant women with higher vitamin D intake were less likely to experience deficiency, and non-Malays showed an 87% reduction in the odds of vitamin D deficiency (Woon et al. 2019).

When it comes to vitamin D intake, dietary sources often fall short, particularly when maternal dairy consumption is limited. The primary natural source of vitamin D is sunlight interacting with the skin, but cultural practices and sun protection measures have inadvertently contributed to the resurgence of vitamin D deficiency (Nimitphong & Holick 2013). Breast milk typically contains low concentrations of vitamin D, further complicating the issue (Hollis et al. 2015). Several risk factors for vitamin D deficiency in infants include exclusive breastfeeding without supplementation, delayed introduction of complementary foods, and preterm or small-for-gestational-age status (Tan et al. 2020).

A global consensus supports the administration of a daily dose of 400 international units of vitamin D in infants, particularly in high-risk groups, to enhance bone health and prevent rickets. This supplementation is well-tolerated and lacks toxicity concerns. However, it's important to note that higher doses do not offer additional benefits and may lead to elevated blood levels of vitamin D and hypercalcemia. Therefore, it is strongly recommended to implement universal vitamin D supplementation shortly after birth, regardless of the mode of feeding, and continue until the age of 12 months. After this age, vitamin D supplementation is advised exclusively for children in at-risk groups (Jullien 2021).

INFANT NUTRITION

Exclusive Breast Feeding, Breastmilk Feeding and Human Milk Diet

Breast milk is often considered the gold standard for infant nutrition, with the World Health Organisation (WHO) recommends exclusive breastfeeding for the first six months, followed by the introduction of complementary liquids and solid foods. Furthermore, WHO advises continued breastfeeding for at least two years or longer (World Health Organisation 2009).

During pregnancy, the mother's diet plays a crucial role in the cognitive and visual development of infants in their first year of life. Breast milk provides essential fatty acids, including arachidonic acid (AA), long-chain polyunsaturated fatty acids (LC-PUFAs), docosahexaenoic acid (DHA), linoleic acid (LA), and alpha-linolenic acid (ALA). DHA and AA, found in the brain and retina membrane lipids, are critical for infant visual and neuronal functions (Yuhas et al. 2006). These fatty acids' profile varies with the maternal diet of ALA, LA, and DHA (Birch et al. 2005).

Observational studies highlight the impact of early nutrition on short-term and long-term health outcomes. Infants who are formula-fed are at a higher risk of various health concerns, including a greater likelihood of becoming overweight, more infections within the first year, and lower cognitive scores.

The composition of infant formula has shifted since the mid-20th century, with vegetable oils replacing milk fat, which lacks essential components found in dairy fat, such as the Milk Fat Globule Membrane (MFGM) (Brink & Lönnerdal 2020).

Milk fat globules consist of a double-layered phospholipid membrane that envelops them, playing vital roles in supporting infant nutrition and development, including synaptogenesis and myelin formation (Tanaka et al. 2013). The MFGM also possesses immunological and antimicrobial properties, as studies show a reduced occurrence of ear infections and enhanced cognitive development with MFGM supplementation or breastfeeding (Ambrożej et al. 2021).

Shifting the focus to carbohydrate content in breast milk, Human Milk Oligosaccharides (HMOs) are complex carbohydrates found in breast milk that play crucial roles in infant nutrition, immune system development, and gut microbiome. HMOs are most abundant in colostrum, with approximately 20-25 grams per litre (Thurl et al. 2017). Structurally diverse HMOs contain Sialic acid and have been linked to cognitive development. Breast-fed preterm infants have superior developmental scores at 18 months of age and even higher IQ levels by the age of 7 (Lucas et al. 1992). Indirect evidence further substantiates these findings, illustrating that brain development and cognition are partially dependent on Sialic acid-containing gangliosides and poly-Sialic acid-containing glycoproteins (Wang 2009). Sialic acid concentrations in the brain, peaking at over twice the normal levels a few months prior to birth through the age of 2 years accentuate the significance of this compound (Svennerholm et al. 1989). Moreover, research has shown that post-mortem brains of breast-fed infants had significantly higher ganglioside-bound and protein-bound sialic acid concentrations compared to formula-fed infants (Wang et al. 2003).

HMOs also support a healthier gut microbiota by promoting growth of beneficial bacteria like Bifidobacterium longum and Bifidobacterium breve and inhibiting pathogenic bacteria like GBS (Walsh et al. 2020). HMOs have been shown to significantly hinder the growth of Group B Streptococcus (GBS) by up to 89% and inhibit the adhesion of Acinetobacter baumannii by up to 11% (Ackerman et al. 2018; Spicer et al. 2021).

Breast milk, rich in human milk oligosaccharides (HMOs), can reduce the risk of necrotising enterocolitis (NEC) which is a serious threat to premature infants. Recent research examined 200 very low birthweight infants primarily fed human milk and found that NEC cases had lower levels of a specific HMO, disialyllacto-N-tetraose (DSLNT). Importantly, DSLNT levels fluctuated in individual milk samples, but a consistent pattern emerged when averaged over multiple days. These findings suggest that low DSLNT in a mother's milk could serve as a non-invasive marker to identify NEC risk. This may influence clinical practice by guiding the choice of donor milk and fortifiers. Additionally, DSLNT might inspire the development of new

NEC prevention therapies (Autran et al. 2018). Emerging evidence also suggests that necrotising enterocolitis (NEC) in premature infants may be preceded by enteric dysbiosis, marked by an abundance of Gram-negative bacteria (Fundora et al. 2020).

Promoting breastfeeding and the use of human milk in Neonatal Intensive Care Units (NICUs) can result in significant cost savings for healthcare systems. For example, in the UK, NHS could save millions annually through reduced incidents of necrotising enterocolitis, sepsis, and infant mortality (Mahon et al. 2016). The maternal microbiome and its transfer during the perinatal period and through breastfeeding influences infant health, by programming the infant microbiome and the onset of various diseases, including conditions such as allergies, asthma, type I diabetes, epilepsy, and autism (Amir et al. 2020; Liu et al. 2023; Saurman et al. 2020). Factors that modulate the microbiome profile are determined by maternal health, gestational age, mode of delivery, breastfeeding and the practices of Kangaroo Mother Care which could impact infant well-being.

Human milk banks are recommended to ensure infants receive the nutritional benefits of human breast milk when the biological mother cannot breastfeed. In countries with a Muslim-majority population, the establishment of human milk banks poses unique challenges, primarily due to cultural considerations related to the concept of milk kinship. To address this issue, it is advisable to implement human milk banks while incorporating additional safeguards designed to prevent potential conflicts arising from milk kinship among newborns in these cultural contexts (Seah & Cheah 2017).

However, it is worth noting that despite these challenges, there have been notable instances of successful implementation. For instance, Singapore achieved a significant milestone on August 17, 2017, by officially launching its first human milk bank (HMB) at KK Women's and Children's Hospital. Particularly noteworthy is that this initiative received endorsement from the Islamic Religious Council of Singapore. Their endorsement was based on the understanding that, under medical guidance, it is permissible for Muslim premature infants to receive donor human milk (Seah & Cheah 2017). The pasteurisation process may remove some bioactive components but still offers benefits such as reducing the incidence of necrotising enterocolitis (NEC) (Boyd et al. 2007; McGuire & Anthony 2003). Furthermore, the Exclusive Human Milk Diet (EHMD) has garnered attention for its potential benefits in premature infant care, with varying results in different studies. Implementing EHMD programs requires a collaborative team effort and can lead to reduced comorbidities and cost savings (Swanson et al. 2023). The EHMD concept holds promise and large multi-centre trials are awaited to show it is beneficial in practice and cost-effective.

An innovative alternative to human milk banking is Biomilq, a pioneering start-up in the USA that is at the forefront of a ground-breaking endeavour to replicate breast milk outside of the human body. Their pioneering approach involves the cultivation of lab-grown 'human milk,' a promising development that may come to fruition within just three years. To accomplish this remarkable feat, Biomilq relies on donated human breast tissue and milk. The intricate process involves nurturing these cells in specialised flasks, providing them with essential nutrients, and then placing them within a state-of-the-art bioreactor which is meticulously designed to simulate the natural breast environment. Within the confines of this bioreactor, the cells efficiently assimilate nutrients and exude the vital components of breast milk (CNN Business 2022).

Rapid weight gain in infancy, particularly during the first 2 years of life, has been identified as a predictor of an increased risk of obesity in childhood and adulthood. Breastfeeding, with its lower protein content, is associated with reduced weight gain velocity in infancy and a lower risk of obesity. Reducing protein content in breast milk substitutes to align them more closely with breast milk may help to prevent childhood obesity (Koletzko et al. 2013). Notably, faster linear growth shortly after reaching term age was linked to improved cognition among preterm infants, but if this growth spurt continued, it was also associated with a higher risk of overweight and obesity in later years. Furthermore, BMI gain over the 18 months following term gestation was correlated with an increased risk of later overweight and obesity, with less apparent benefit for IQ (Belfort et al. 2013).

Preterm infant growth can be optimised with appropriate nutritional practices, reducing the risk of non-communicable diseases. Implementing Quality Improvement practices in neonatal care, including early parenteral nutrition, structured feeding protocols, and a multidisciplinary nutrition team, can help to ensure premature infants receive the essential nutrients that they need to thrive. Fortification of breast milk and care should be aimed to deliver nutrient intakes in line with internationally recognised recommendations, with a mean protein intake of 3.7 g/kg/day during the first 2 weeks of life (Andrews et al. 2019). Ensuring optimal growth trajectories with proper nutrition and monitoring will mitigate the double burden of malnutrition that could impact later health.

Complementary Feeding

As infants grow and become more active beyond their initial 6 months of life, the inadequacy of exclusive breastfeeding in meeting their nutritional needs becomes evident. This nutritional gap widens as infants and young children age (Dewey 2001; World Health Organisation & United Nations Children's Fund 2003). Complementary feeding plays a vital role in addressing this gap. However, inadequate complementary feeding practices can lead to adverse effects on the growth of infants and young children, resulting in delayed motor and cognitive development, nutrient deficiencies, and malnutrition (Bhutta et al. 2013).

Complementary feeding is the process that begins when breast milk or infant formula alone can no longer meet the nutritional requirements of infants, necessitating the introduction of other foods and liquids alongside breast milk or a suitable breast-milk substitute (World Health Organisation 2002). The World Health Organisation (WHO) recommends exclusive breastfeeding until the age of 6 months, after which breastfeeding should continue alongside the timely introduction of appropriate complementary foods (World Health Organisation 2002). Delaying the introduction of complementary feeding increases the risk of energy and nutrient deficiencies and does not prevent allergies. Conversely, introducing them too early can risk overnutrition and nutrient imbalances (Muraro et al. 2014).

In 2020, malnutrition remained a significant global issue among children under the age of 5, characterised by a dual burden, with 22% experienced stunting, and 6.7% faced wasting (Food and Agriculture Organisation 2022). According to the National Health and Morbidity Survey 2022, Malaysia has seen a concerning increase in rates of child malnutrition, with all three categories experiencing a rise. Stunting now affects 21.8% of children, compared to 17.7% in 2015; wasting has increased to 9.4% from 8.1% in 2015; and underweight has risen to 14.1% from 12.4% in 2015. In reviewing the hospital records over a span of two years (2019 and 2020) at the Hospital Canselor Tuanku Muhriz , it was observed that children attending the paediatric clinics exhibited high prevalence rates for wasting, underweight, and stunting, standing at 33.2%, 20.9%, and 15.6%, respectively. Notably, children born preterm or with low birth weight faced an even greater risk. Childhood overnutrition, on the other hand, characterised by overweight or obesity, surged from 4.2% in 1990 to 6.7% in 2010 worldwide (Ng et al. 2014).

A UNICEF review highlighted the pressing need for changes and adjustments in complementary feeding practices. Several issues are shaping the nutritional landscape for infants and young children (United Nations Children's Fund 2020). Notably, there is increasing evidence about the importance of the first 1,000 days of life, where factors like the gut microbiome are influenced by diet and the type and timing of introducing complementary feeding play a crucial role (United Nations Children's Fund 2019). Impact of climate change on food production and the potential risks associated with the increased consumption of highly processed, nutrient-poor foods raise further concerns. Moreover, ultra-processed foods are often high in calories but lacking in essential nutrients for children (Binns & Low 2019; Popkin et al. 2020).

Another worrisome trend highlighted by the review is the rising rate of obesity in the Asia Pacific Region. In Malaysia, obesity rates among children have reached alarming levels at 14.8% (Ministry of Health Malaysia 2019). The review also shed light on the increasing rate of food allergies, influenced by factors like antibiotic use, C-section deliveries, and reliance on formula feeds (Feehley et al. 2019; Sicherer et al. 2017). Importantly, the review emphasised that delaying the introduction of complementary foods does not prevent allergies and points to a concerning loss of interest in preserving food culture, with the allure of commercial infant and baby food (Binns et al. 2020).

The insight provided by the Asia Pacific Academic Consortium for Public Health (APACPH), Public Health Nutrition Group highlights prevalent micronutrient deficiencies in Southeast Asia and their significant impact on public health. Strategies to address these deficiencies include, having meat in infant diet, iodine fortification program through the distribution of iodised salt, and promoting dietary diversity to ensure adequate intake of vitamins A and D, and calcium. Dietary diversity, achieved by including at least four out of seven food groups, plays a crucial role in complementary feeding. These groups encompass grains, legumes, dairy products, flesh foods, eggs, vitamin A-rich fruits and vegetables, and other fruits and vegetables. Promoting dietary diversity not only leads to a balanced nutrient intake but also helps to reduce exposure to toxins and lower the risk of allergies (Binns et al. 2020).

Iron and iodine deficiencies are prominent public health challenges, and numerous studies have been conducted to investigate screening and supplementation strategies for these essential micronutrients. Anaemia, primarily caused by iron deficiency, remains a significant concern. To address this issue, the AAP in 2010 recommended universal screening for anaemia by assessing haemoglobin (Hb) concentration at around one year of age (Baker et al. 2010). However, the UK National Screening Committee (UK NSC) in 2017 did not propose specific guidelines for the supplementation or screening of iron deficiency anaemia in children under five years old (UK National Screening Committee 2017). In terms of iron supplementation, AAP's 2010 guidelines suggest commencing iron supplementation at a dosage of 1 mg/kg per day in breastfed infants at four months of age, continuing until iron-rich complementary foods are incorporated into the diet. Alternatively, the World Health Organisation (WHO) in 2016 advises daily supplementation of 10-12.5 mg of elemental iron in infants and young children aged six to twenty-three months in regions where anaemia prevalence exceeds 40% (World Health Organisation 2016).

Moving on to iodine, the WHO in 2007 outlined recommendations for iodine supplementation in children under two years of age. In areas with consistent salt iodisation programs, additional iodine supplementation is unnecessary. However, in regions with uneven distribution of iodised salt, specific guidelines are provided based on age groups. For infants aged 0-6 months, WHO recommends daily iodine supplementation of 250 mcg for lactating mothers who are exclusively breastfeeding infants. For infants aged 7-24 months, daily iodine supplementation of 250 mcg for lactating mothers who continue to breastfeed, along with the inclusion of iodine-fortified complementary foods, is advised (World Health Organisation 2014).

The APACPH Public Health Nutrition Group identifies significant barriers to achieving appropriate infant and young child nutrition in Southeast Asia. Challenges include issues of marketing and promotion of breast milk substitutes, the rather relentless promotion of commercial infant foods with high levels of salt and sugar and yet lacking in diversity of tastes and textures, the popularity of unhealthy squeeze-pack foods and sugar-sweetened beverages, concerns about food contamination, nonresponsive feeding practices, inappropriate misleading advice from family and friends, and a lack of correct professional support (Binns et al. 2020).

CONCLUSION

In conclusion, the first 1000 days of life, spanning from conception to a child's second birthday, represents a crucial developmental phase that forms the basis for lifelong health and well-being. The significance of this period cannot be emphasised enough, and as discussed in this review, some fundamental best practice guidelines when implemented, may potentially modulate the outcomes for the infants and even the mothers themselves.

To enhance maternal nutrition, review of current guidelines should be considered for best practices, especially in recommended maternal energy consumption during pregnancy. Additionally, other than just implementing, effective folic acid- and iron-fortified wheat flour also may address micronutrition deficiencies in pregnant mothers. To combat iron deficiency issues, measures include, (i) delayed cord clamping should be implemented as the standard of practice for all uncomplicated deliveries nationwide; (ii) initiate iron supplementation for healthy term fully breastfed infants at 4 months, and/or conduct infant population screening for anaemia. Furthermore, vitamin D supplementation of 400 IU for fully breastfed infants is recommended. A comprehensive review of the universal salt iodisation programme, especially in regions like Sarawak, with a reference to maternal iodine supplementation, to address any loopholes and bridge the gaps.

When it comes to complementary feeding, introduction of solids may need to be advanced earlier at four months, especially in exclusively breastfeeding infants in a population with a high rate of iron deficiency anaemia in early childhood. Dietary advice at maternal child health and paediatric clinics should include suggested menu preparations on a diverse selection of four commonly available food groups, which are also culturally acceptable in our local population.

Promoting breast milk feeding must be continued and further enhanced, particularly in feeding the preterm and low birth weight infants. Initiatives like the EHMD and the establishment of local human milk banks will significantly improve infant nutrition and outcomes. Additionally, personalised nutrition interventions and the fortification of breast milk may help to tailor growth optimisation to the unique requirements of the individual infant, and possibly even in catering for gender-specific nutritional considerations. Future large multi-centre trials are needed to confirm if nutritional recommendations need to tailor to an individualised and gender-specific approach.

The commitment, engagement, and regulation of industries play pivotal roles in ensuring optimal nutrition delivery in the first 1000 days. Ensuring responsibility in knowledge sharing is vital for promoting a "nutrition-savvy" community. Supermarkets and groceries should feature recommended foods for pregnancy, lactation, and complementary feeding, with the regular monitoring by the Ministry of Health's nutrition division or any authorised bodies. Implementing measures with clear labelling, such as "This particular food is not recommended if you are pregnant," and advisory statements like "Breast milk is best; consume this formula only as a substitute if prescribed or medically indicated," can be effective. Furthermore, the way breast milk substitutes are marketed should be closely monitored, with every claim meticulously vetted by a special media regulatory body. The addition of more nutrients, which are not yet recommended as the standard of care, should not justify a premium status that demands higher pricing for these substitutes. "Growing up formula" should be rebranded for special indications and not positioned as a replacement for complementary feeding.

Finally, it is hoped that all the stakeholders involved in the maternal and child nutrition may work together to significantly contribute to the health and well-being of both mother and infant pairs during this critical 1000-day period for a better future generation of this nation.

REFERENCES

Abbasi, I.H.R., Abbasi, F., Wang, L., Abd El Hack, M. E., Swelum, A.A., Hao, R., Yao, J., Cao, Y. 2018. Folate promotes S-adenosyl methionine reactions and the microbial methylation cycle and boosts ruminants production and reproduction. *AMB Express* **8**: 65.

Abd Rahman, R., Idris, I.B., Isa, Z.M., Rahman, R.A., Mahdy, Z.A. 2022. The prevalence and risk factors of iron deficiency anemia among pregnant women in Malaysia: A systematic review. *Front Nutr* **9**: 847693.

Ackerman, D.L., Craft, K.M., Doster, R.S., Weitkamp, J.H., Aronoff, D.M., Gaddy, J.A., Townsend, S.D. 2018. Antimicrobial and antibiofilm activity of human milk oligosaccharides against *Streptococcus agalactiae, Staphylococcus aureus,* and *Acinetobacter baumannii. ACS Infect Dis* **4**(3): 315-24.

Ambrożej, D., Dumycz, K., Dziechciarz, P., Ruszczy ski, M. 2021. Milk fat globule membrane supplementation in children: \ Systematic review with meta-analysis. Nutrients **13**(3): 714.

American Academy of Pediatrics. 2017. *Guidelines for perinatal care*.

Amir, M., Brown, J.A., Rager, S.L., Sanidad, K. Z., Ananthanarayanan, A., Zeng, M.Y. 2020. Maternal microbiome and infections in pregnancy. *Microorganisms* **8**(12): 1996.

Andrews, E.T., Ashton, J.J., Pearson, F., Beattie, R.M., Johnson, M.J. 2019. Early postnatal growth failure in preterm infants is not inevitable. *Arch Dis Child Fetal Neonatal Ed* **104**(3): F23541.

Australian Institute of Health and Welfare. 2016. Monitoring health impacts of mandatory folic acid fortification: Summary. AIHW. https://www.aihw.gov.au/reports/food-nutrition/monitoring-health-impacts-of-mandatory-folic-acid/summary [5 November 2023].

Autran, C.A., Kellman, B.P., Kim, J.H., Asztalos, E., Blood, A.B., Spence, E.C.H., Patel, A.L., Hou, J., Lewis, N.E., Bode, L. 2018. Human milk oligosaccharide composition predicts risk of necrotising enterocolitis in preterm infants. Gut, **67**(6): 1064-70.

Baker, R.D., Greer, F.R., Committee on Nutrition, American Academy of Pediatrics. 2010. Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0-3 years of age). *Pediatrics* **126**(5): 1040-50.

Barker, D.J. 2007. The origins of the developmental origins theory. *J Intern Med* **261**(5): 412-7.

Belfort, M.B., Gillman, M.W., Buka, S.L., Casey, P. H., McCormick, M.C. 2013. Preterm infant linear growth and adiposity gain: Trade-offs for later weight status and intelligence quotient. *J Pediatr* **163**(6): 1564-9.e2.

Berry, R.J., Li, Z., Erickson, J.D., Li, S., Moore, C.A., Wang, H., Mulinare, J., Zhao, P., Wong, L.Y.C., Gindler, J., Hong, S.X., Gunter, E., Correa, A. 1999. Prevention of neural-tube defects with folic acid in China. *N Engl J Med* **341**(20): 1485-90.

Bhutta, Z.A., Das, J.K., Rizvi, A., Gaffey, M.F., Walker, N., Horton, S., Webb, P., Lartey, A., Black, R.E. 2013. Evidence-based interventions for improvement of maternal and child nutrition: What can be done and at what cost? *Lancet* **382**: 452-77.

Binns, C., Low, W.Y. 2019. Time to get on with it: Climate change needs public health action now. *Asia Pac J Public Health* **31:** 581-3.

Binns, C., Lee, M.K., Yun Low, W., Baker, P., Bulgiba, A., Dahlui, M., Thuy Duong, D.T., Guldan, G., Hairi, N., Hokama, T., Kagawa, M., Karunathilake, I., Abdul Majid, H., Maycock, B., Nanishi, K., Qiu, L., Raheem, R.A., Scott, J., Tang, L. 2020. Guidelines for complementary feeding of infants in the Asia Pacific Region: APACPH public health nutrition group. *Asia Pac J Public Health* **32**(4): 179-87.

Birch, E.E., Castañeda, Y.S., Wheaton, D.H., Birch, D.G., Uauy, R.D., Hoffman, D.R. 2005. Visual maturation of term infants fed long-chain polyunsaturated fatty acid–supplemented or control formula for 12 mo. *Am J Clin Nutr* **81**(4): 871-9.

Blumfield, M.L., Hure, A.J., Macdonald-Wicks, L., Smith, R., Collins, C.E. 2012. Systematic review and meta-analysis of energy and macronutrient intakes during pregnancy in developed countries. *Nutr Rev* **70**(6): 322-36.

Bogaerts, A., Van den Bergh, B., Nuyts, E., Martens, E., Witters, I., Devlieger, R, 2012. Socio-demographic and obstetrical correlates of pre-pregnancy body mass index and gestational weight gain. *Clin Obes* **2**(5-6): 150-9.

Boyd, C.A., Quigley, M.A., Brocklehurst, P. 2007. Donor breast milk versus infant formula for preterm infants: A systematic review and meta-analysis. *Arch Dis Child Fetal Neonatal Ed* **92**(3): F169-F175.

Brink, L.R., Lönnerdal, B. 2020. Milk fat globule membrane: The role of its various components in infant health and development. *J Nutr Biochem* **85**: 108465.

Catalano, P.M. 2010. The impact of gestational diabetes and maternal obesity on the mother and her offspring. *J Dev Orig Health Dis* **1**(4): 208-15.

CNN Business. 2022. BIOMILQ is creating 'human milk' for babies in a lab. https://edition.cnn.com/2022/05/03/business/lab-grown-human-milk-biomilq-health-climate-hnk-spc-intl/index.html [5 November 2023].

Congdon, E.L., Westerlund, A., Algarin, C.R., Peirano, P. D., Gregas, M., Lozoff, B., Nelson, C.A. 2012. Iron deficiency in infancy is associated with altered neural correlates of recognition memory at 10 years. *J Pediatr* **160**(6): 1027-33.

Correa, A., Gilboa, S.M., Botto, L.D., Moore, C.A., Hobbs, C.A., Cleves, M.A., Riehle-Colarusso, T.J., Waller, D.K., Reece, E.A.; National Birth Defects Prevention Study. 2012. Lack of periconceptional vitamins or supplements that contain folic acid and diabetes mellitus–associated birth defects. *Am J Obstet Gynecol* **206**(3): 218.e1-13.

Cunha, A.J., Leite, Á.J., Almeida, I.S. 2015. The pediatrician's role in the first thousand days of the child: The pursuit of healthy nutrition and development. J Pediatr **91**(6 Suppl 1): 44-51.

De-Regil, L.M., Palacios, C., Lombardo, L.K., Peña-Rosas, J.P. 2016. Vitamin D supplementation for women during pregnancy. *Cochrane Database of Syst Rev* 2016(1): CD00887.

Dewey, K.G. 2001. Nutrition, growth, and complementary feeding of breastfed infants. *Pediatr Clin North Am* **48**(1): 87-104.

Dwyer, E.R., Filion, K.B., MacFarlane, A.J., Platt, R.W., Mehrabadi, A. 2022. Who should consume high-dose folic acid supplements before and during early pregnancy for the prevention of neural tube defects? *BMJ* **377**: e067728.

Feehley, T., Plunkett, C.H., Bao, R.Y., Choi Hong, S.M., Culleen, E., Belda-Ferre, P., Campbell, E., Aitoro, R., Nocerino, R., Paparo, L., Andrade, J., Antonopoulos, D.A., Berni Canani, R., Nagler, C.R. 2019. Healthy infants harbor intestinal bacteria that protect against food allergy. *Nat Med* 25(3): 448-53.

Food and Agriculture Organization (FAO). 2022. Global nutrition targets: Trends in childhood stunting and overweight. https://www.fao.org/3/cc0639en/online/sofi-2022/global-nutrition-targets-trends.html [5 November 2023].

Friel, J.K., Aziz, K., Andrews, W.L., Harding, S.V., Courage, M.L., Adams, R.J. 2003. A double-masked, randomized control trial of iron supplementation in early infancy in healthy term breast-fed infants. *J Pediatr* **143**(5): 582-6.

Fundora, J.B., Guha, P., Shores, D.R., Pammi, M., Maheshwari, A. 2020. Intestinal dysbiosis and necrotizing enterocolitis: Assessment for causality using bradford-hill criteria. *Pediatr Res* **87**(2): 235-48.

German, K.R., Juul, S.E. 2021. Iron and neurodevelopment in preterm infants: A narrative review. *Nutrients* **13**(11): 3737.

Greene, N.D.E., Copp, A.J. 2014. Neural tube defects. *Ann Rev Neurosci* **37**(1): 221-42.

Halimi, S., Halimi, S.M.A., Shoaib, M. 2011. Oral versus parenteral iron therapy for correction of iron deficiency anaemia in pregnancy. *Gomal J Med Sci* **9**(1): 3-5.

Hanson, M.A., Bardsley, A., De-Regil, L.M., Moore, S.E., Oken, E., Poston, L., Ma, R.C., McAuliffe, F.M., Maleta, K., Purandare, C.N., Yajnik, C.S., Rushwan, H., Morris, J.L. 2015. The international federation of gynaecology and obstetrics (FIGO) recommendations on adolescent, preconception, and maternal nutrition: "Think Nutrition First." I*nt J Gynaecol Obstet* **131**(S4): S213-253.

Ho, A., Flynn, A.C., Pasupathy, D. 2016. Nutrition in pregnancy. Obstet Gynaecol Reprod Med **26**(9): 259-64.

Hollis, B.W., Wagner, C.L., Howard, C.R., Ebeling, M., Shary, J.R., Smith, P.G., Taylor, S.N., Morella, K., Lawrence, R.A., Hulsey, T.C. 2015. Maternal versus infant vitamin d supplementation during lactation: A randomized controlled trial. *Pediatrics* **136**(4): 625-34.

Huang, H.Y., Chen, H.L., Feng, L.P. 2017. Maternal obesity and the risk of neural tube defects in offspring: A meta-analysis. *Obes Res Clin Pract* **11**(2): 188-97.

Institute of Medicine of the National Academies (US). 2010. *Dietary reference intakes for calcium and vitamin D.* National Academy Press.

Inzani, I., Ozanne, S.E. 2022. Programming by maternal obesity-A pathway to poor cardiometabolic health in the offspring. *Proc Nutr Soc* **81**((3): 227-42.

Jullien, S. 2021. Vitamin D prophylaxis in infancy. *BMC Pediatr* **21**(Suppl 1): 319.

Khor, G.L., Duraisamy, G., Loh, S.P., Green, T. 2006. Dietary and blood folate status of Malaysian women of childbearing age. *Asia Pac J Clin Nutr* **15**(3): 341-9.

Kitzmiller, J.L., Block, J.M., Brown, F.M., Catalano, P.M., Conway, D.L., Coustan, D.R., Gunderson, E.P., Herman, W.H., Hoffman, L.D., Inturrisi, M., Jovanovic, L.B., Kjos, S.I., Knopp, R.H., Montoro, M.N., Ogata, E.S., Paramsothy, P., Reader, D.M., Rosenn, B.M., Thomas, A.M., Kirkman, M.S. 2008. Managing preexisting diabetes for pregnancy: Summary of evidence and consensus recommendations for care. *Diabetes Care* **31**(5): 1060-79.

Koletzko, B., Beyer, J., Brands, B., Demmelmair, H., Grote, V., Haile, G., Gruszfeld, D., Rzehak, P., Socha, P., Weber, M., European Childhood Obesity Trial Study Group. 2013. Early influences of nutrition on postnatal growth. *Nestle Nutr Inst Workshop Ser* **71**: 11-27.

Koren, G., Kaplan, Y.C. 2021. Obesity, neural tube defects and folic acid: A complex relationship. *Clin Exp Obstetr Gynecol* 48: 223-7.

Kuay, L.K. 2018. Iodine deficiency disorders among pregnant women in Sarawak, Malaysia. *Int J Public Health Res* **8**(2): Article 2.

Kuay, L.K., Chin, T.B., Ying, C.Y., Hussain, H., Mahmud, N.A., Kassim, M.S.A., Harith, A.A., Man, C.S., Salleh, R., Aris, T. 2021. Pregnant women are iodine deficient while school-aged children demonstrate adequate iodine status in Sarawak, Malaysia. *Food Nutr Bull* 42(3), 406-13.

Langley-Evans, S.C., McMullen, S. 2010. Developmental origins of adult disease. *Med Princ Pract* **19**(2): 87-98.

Lee, C.L., Ng, B.K., Wu, L.L., Cheah, F.C., Othman, H., Ismail, N.A.M. 2017. Vitamin D deficiency in pregnancy at term: Risk factors and pregnancy outcomes. Horm Mol Biol Clin Investig **31**(3): 20170005.

Löf, M. Physical activity pattern and activity energy expenditure in healthy pregnant and non-pregnant Swedish women. *Eur J Clin Nutr* **65**(12): 1295-301.

Loeken, M.R. 2005. Current perspectives on the causes of neural tube defects resulting from diabetic pregnancy. *Am J Med Genet C Semin Med Genet* 135C(1): 77-87.

Lucas, A., Morley, R., Cole, T.J., Lister, G., Leeson-Payne, C. 1992. Breast milk and subsequent intelligence quotient in children born preterm. *Lancet* **339**(8788): 261-4.

Liu, T., Jia, F., Guo, Y., Wang, Q., Zhang, X., Chang, F., Xie, Y. 2023. Altered intestinal microbiota composition with epilepsy and concomitant diarrhea and potential indicator biomarkers in infants. *Front Microbiol* **13:** 1081591.

Mahon, J., Claxton, L., Wood, H. 2016. Modelling the cost-effectiveness of human milk and breastfeeding in preterm infants in the United Kingdom. *Health Econ Rev* **6**(1): 54.

Mandy, M., Nyirenda, M. 2018. Developmental origins of health and disease: The relevance to developing nations. *Int Health* **10**: 66-70.

McGuire, W., Anthony, M.Y. 2003. Donor human milk versus formula for preventing necrotising enterocolitis in preterm infants: Systematic review. Arch Dis Child Fetal Neonatal Ed 88(1); F11-4.

Milman, N. 2015. Iron deficiency and anaemia in pregnant women in malaysia? Still a significant and challenging health problem. *J Preg Child*

Health **02**: 168.
Milman, N., Agger, O.A., Nielsen, O.J. 1991. Iron supplementation during pregnancy: Effect on iron status markers, serum erythropoietin, and human placental lactogen. A placebo-controlled study in 207 Danish women. *Danish Med Bull* **38**: 471-6.
Ministry of Health Malaysia. 2019. *Report on the National Health and Morbidity Survey 2019: Non-Communicable Diseases (NCDs).*
MRC Vitamin Study Research Group. Prevention of neural tube defects: Results of the medical research council vitamin study. 1991. *Lancet* **338**(8760): 131-7.
Muraro, A., Halken, S., Arshad, S.H., Beyer, K., Dubois, A.E., Du Toit, G., Eigenmann, P.A., Grimshaw, K.E., Hoest, A., Lack, G., O'Mahony, L., Papadopoulos, N.G., Panesar, S., Prescott, S., Roberts, G., de Silva, D., Venter, C., Verhasselt, V., Akdis, A.C., Sheikh, A. EAACI Food Allergy and Anaphylaxis Guidelines Group. 2014. EAACI food allergy and anaphylaxis guidelines. Primary prevention of food allergy. *Allergy* **69**: 590-601.
National Coordinating Committee on Food and Nutrition, Ministry of Health Malaysia. 2017. RNI: Recommended Nutrient Intakes for Malaysia. Putrajaya, Malaysia: National Coordinating Committee on Food and Nutrition (NCCFN). https://hq.moh.gov.my/nutrition/wp-content/uploads/2017/05/FA-Buku-RNI.pdf [5 November 2023].
New Straits Time. 2022. MOH to Implement Mandatory Iron and Folic Acid Fortification of Wheat Flour. https://www.nst.com.my/news/nation/2022/04/791939/moh-implement-mandatory-iron-and-folic-acid-fortification-wheat-flour [5 November 2023].
Ng, M., Fleming, T., Robinson, M., et al. 2014. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: A systematic analysis for the global burden of disease study 2013. *Lancet* **384**(9945): 766-81.
Nimitphong, H., Holick, M.F. 2013. Vitamin D status and sun exposure in southeast Asia. *Dermatoendocrinol* **5**(1): 34-7.
Niwattisaiwong, S., Burman, K.D., Li-Ng, M. 2017. Iodine deficiency: Clinical implications.I **84**: 236-44.
NutraIngredients-Asia. 2023. Danone for iron: Firm to step up iron deficiency anaemia research in SEA and the case for supplementation. https://www.nutraingredients-asia.com/Article/2023/07/25/Danone-to-step-up-iron-deficiency-anaemia-research-in-SEA [5 November 2023].
Onubi, O.J., Marais, D., Aucott, L., Okonofua, F., Poobalan, A.S. 2016. Maternal obesity in Africa: A systematic review and meta-analysis. *J Public Health* **38**(3): e218-31.
Ortega, R.M., López-Sobaler, A. M., Andrés, P., Rodríguez-Rodríguez, E., Aparicio, A., Perea, J.M. 2009. Folate status in young overweight and obese women: Changes associated with weight reduction and increased folate intake. J Nutr Sci Vitaminol **55**(2): 149-55.
Peña-Rosas, J.P., De-Regil, L.M., Garcia-Casal, M.N., Dowswell, T. 2015. Daily oral iron supplementation during pregnancy. *Cochrane Database of Syst Rev* **2015**(7): CD004736.
Popkin, B.M., Corvalan, C., Grummer-Strawn, L. M. 2020. Dynamics of the double burden of malnutrition and the changing nutrition reality. *Lancet* **395**: 65-74.
Rocco, P. L., Orbitello, B., Perini, L., Pera, V., Ciano, R.P., Balestrieri, M. 2005. Effects of pregnancy on eating attitudes and disorders: A prospective study. *J Psychosom Res* **59**(3): 175-9.
Saavedra, J.M., Dattilo, A.M. 2016. Nutrition in the first 1000 days of life: Society's greatest opportunity. In Saavedra JM, Dattilo AM (Eds.), Early nutrition and long-term health: Mechanisms, consequences, and opportunities. United Kingdom. Woodhead Publishing, Elsevier.
Saurman, V., Margolis, K.G., Luna, R.A. 2020. Autism spectrum disorder as a brain-gut-microbiome axis disorder. *Dig Dis Sci* **65**(3): 818-28.
Savona-Ventura, C., Chircop, M. 2003. Birth weight influence on the subsequent development of gestational diabetes mellitus. *Acta Diabetologica* 40(2): 101-4.
Schwarzenberg, S.J., Georgieff, M.K. 2018. Advocacy for improving nutrition in the first 1000 days to support childhood development and adult health. *Pediatrics* **141**(2): e20173716.
Seah, S.S.Y., Cheah, F.C. 2017. Empowering mothers of preterm infants for continuous breastfeeding in Malaysia. *Perinatology* **18**(3): 81-9.
Shahrir, N.F., Abdul Jalil, R., Jeganathan, J.R., Devi Karalasingam, S., Mohd Nordin, N., Abdullah, M.F., Sa'at, N. 2021. Maternal obesity and its associated factors and outcomes in Klang Valley, Malaysia: Findings from national obstetric registry. *Malays Fam Physician* **16**(3): 56-67.
Sicherer, S.H., Allen, K., Lack, G., Taylor, S.L., Donovan, S.M., Oria, M. 2017. Critical issues in food allergy: A National Academies consensus report. *Pediatrics* **140**: e20170194.
Sinlapamongkolkul, P., Surapolchai, P., Viprakasit, V. 2023. Justification of universal iron supplementation for infants 6-12 months in regions with a high prevalence of thalassemia: Iron supplementation for infants 6-12 months in regions with a high prevalence of thalassemia. *Mediterr J Hematol Infect Dis* **15**(1): e2023056.
Spicer, S.K., Moore, R.E., Lu, J., Guevara, M.A.,

Marshall, D.R., Manning, S.D., Damo, S.M., Townsend, S.D., Gaddy, J.A. 2021. Anti-biofilm activity of human milk oligosaccharides against multi-drug resistant and susceptible isolates of *Acinetobacter baumannii*. *ACS Infect Dis* **7**(12): 3254-63.

Svennerholm, L., Boström, K., Fredman, P., Månsson, J.E., Rosengren, B., Rynmark, B.M. 1989. Human brain gangliosides: Developmental changes from early fetal stage to advanced age. *Biochimica et Biophysica Acta* **1005**(2), 109-17.

Swanson, J.R., Becker, A., Fox, J., Horgan, M., Moores, R., Pardalos, J., Pinheiro, J., Stewart, D., Robinson, T. 2023. Implementing an exclusive human milk diet for preterm infants: Real-world experience in diverse NICUs. *BMC Pediatrics* **23**(1): 237.

Tan, M.L., Abrams, S.A., Osborn, D.A. 2020. Vitamin D supplementation for term breastfed infants to prevent vitamin D deficiency and improve bone health. *Cochrane Database of Syst Rev* **2020**(12): CD013046.

Tanaka, K., Hosozawa, M., Kudo, N., Yoshikawa, N., Hisata, K., Shoji, H., Shinohara, K., Shimizu, T. 2013. The pilot study: Sphingomyelin-fortified milk has a positive association with the neurobehavioural development of very low birth weight infants during infancy, randomized control trial. *Brain Dev* **35**(1): 45-52.

Thurl, S., Munzert, M., Boehm, G., Matthews, C., Stahl, B. 2017. Systematic review of the concentrations of oligosaccharides in human milk. *Nutr Rev* **75**(11): 920-33.

UK National Screening Committee. 2017. UK NSC recommendation on screening for iron deficiency anaemia (IDA) in children under 5 years. https://view-health-screening-recommendations.service.gov.uk/iron-deficiency-anaemia/#:~:text=A%20national%20screening%20programme%20for,a%20slower%20rate%20than%20expected [5 November 2023].

United Nations Children's Fund. 2020. Improving young children's diets during the complementary feeding period: UNICEF programming guidance. https://www.unicef.org/media/93981/file/Complementary-Feeding-Guidance-2020.pdf [5 November 2023].

United Nations Children's Fund. 2019. The first 1000 days. http://1000days.unicef.ph/ [5 November 2023].

United States Food and Drug Administration. 1996. Food standards: Amendments of standards of identity for enriched grain products to require addition of folic acid. *Federal Register* 61: 8781-97.

Wang, B. 2009. Sialic acid is an essential nutrient for brain development and cognition. *Ann Rev Nutr* **29**: 177-222.

Wang, B., McVeagh, P., Petocz, P., Brand-Miller, J. 2003. Brain ganglioside and glycoprotein sialic acid in breastfed compared with formula-fed infants. *Am J Clin Nutr* **78**(5): 1024-9.

Walsh, C., Lane, J.A., van Sinderen, D., Hickey, R.M. 2020. Human milk oligosaccharides: Shaping the infant gut microbiota and supporting health. *J Funct Foods* **72:** 104074.

Woon, F.C., Chin, Y.S., Ismail, I.H., Batterham, M., Abdul Latiff, A.H., Gan, W.Y., Appannah, G., Mohammed Hussien, S.H., Edi, M., Tan, M.L., Chan, Y.M. 2019. Vitamin D deficiency during pregnancy and its associated factors among third trimester Malaysian pregnant women. *PLoS ONE* **14**(6): e0216439.

World Health Organization, United Nations Children's Fund, & International Council for the Control of Iodine Deficiency Disorders. 2007. Assessment of iodine deficiency disorders and monitoring their elimination (3rd ed.). Geneva, Switzerland: WHO. https://iris.who.int/bitstream/handle/10665/43781/9789241595827_eng.pdf?sequence=1 [5 November 2023].

World Health Organization. 2009. Infant and young child feeding: model chapter for textbooks for medical students and allied health professionals. Geneva: WHO.

World Health Organization & United Nations Children's Fund. 2003. Global Strategy for Infant and Young Child Feeding. WHO Press.

World Health Organization. 2002. Complementary Feeding: Report of the Global Consultation Geneva, Switzerland, 2002. https://iris.who.int/bitstream/handle/10665/42739/924154614X.pdf?sequence=1 [5 November 2023].

World Health Organization. 2016. Guideline: daily iron supplementation in infants and children. https://iris.who.int/bitstream/handle/10665/204712/9789241549523_eng.pdf?sequence=1 [5 November 2023].

World Health Organization. 2014. Reaching Optimal Iodine Nutrition in Pregnant and Lactating Women and Young Children. http://www.who.int/nutrition/publications/WHOStatement__IDD_pregnancy.pdf [5 November 2023].

Yerby, M.S. 2003. Clinical care of pregnant women with epilepsy: neural tube defects and folic acid supplementation. *Epilepsia* **44**(Suppl 3): 33-40.

Yuhas, R., Pramuk, K., Lien, E.L. 2006. Human milk fatty acid composition from nine countries varies most in DHA. *Lipids* **41**(9): 851-8.

Zhang, L., Zhang, Y., Li, Z., Ren, A., Liu, J., Ye, R. 2021. Maternal periconceptional body mass index and risk for neural tube defects: Results from a large cohort study in China. *J Matern Fetal Neonatal Med* 34(2): 274-80.

Zimmermann, M.B. 2012. The effects of iodine deficiency in pregnancy and infancy. *Paediatr Perinat Epidemiol* **26**(Suppl 1): 108-17.