UNIVERSITI PUTRA MALAYSIA

EFFECT OF MICRONUTRIENT SUPPLEMENTS ON NUTRITIONAL STATUS OF INFANTS IN GAZA STRIP, PALESTINe

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By

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EFFECT OF MICRONUTRIENT SUPPLEMENTS ON NUTRITIONAL STATUS OF INFANTS IN GAZA STRIP, PALESTINE

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February 2018

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Faculty : Medicine and Health Sciences

Growth faltering is a common form of undernutrition in developing countries. Micronutrients deficiency including vitamin A, vitamin D, iron, and zinc has been associated with growth retardation in young children. This study aims to determine the impact of micronutrient powder supplementation on the nutritional status of infants in Gaza Strip, Palestine. The study was conducted in two phases. In phase one, a retrospective cohort study involving 2650 children from five primary health clinics was carried out to assess the growth patterns from birth to 24 months as to provide support for timing of micronutrient supplementation for phase two. In phase two, a prospective parallel randomized controlled trial was conducted with 200 infants aged six months being randomly selected from two United Nations Relief and Works Agency (UNRWA) clinics. The infants were randomly assigned into two groups: control (received National Micronutrient Supplement) and experimental (received Micronutrients powder for 12 months with National Micronutrient Supplement). The primary outcomes measured were weight, length, circumferences of head, waist and mid upper arm, triceps and subscapular skinfolds and hemoglobin of children, while the secondary outcomes included children' dietary intakes and child feeding practices of mothers. Analysis in phase one was based on descriptive statistics, whereas Student's t-test and General Linear Model (GLM) for repeated measures were used in phase two (based on a per protocol analysis). In the process of phase two, 18 and 12 participants dropped out of the experimental and control groups, respectively. The results of phase one indicated that faltering in length was more pronounced than weight faltering. From 6 to 24 months, while the prevalence of underweight was relatively stable (~ 5%), there was a decreasing trend in the prevalence of wasting (10 – 2.8%) but an increasing trend for stunting prevalence (9 – 20.4%). At the end of the study, the experimental group had a significant increase in all anthropometric measures except length-for-age and triceps skinfold-for-age z scores. Whereas, the control group showed a significant increase in weight, length, circumferences of head, waist, and mid upper arm-for-age, and subscapular skinfold-for-age z scores only. In both groups, a significant increase was observed in most nutrients (except fat and iron intakes), but a significant decrease in hemoglobin. The overall group effect was observed in hemoglobin, vitamin D intake, and all anthropometric measures except body mass index-for-age, head circumference-for-age, and subscapular skinfold-for-age z scores with higher mean in the experimental group as compared to the control group. The changes in hemoglobin, carbohydrate, protein, and vitamin D intakes, and most of anthropometric measures (except head circumference-for-age, waist circumference-for-age, mid upper arm circumference-for-age, and subscapular skinfold-for-age z scores) showed a significant group by time interaction with a higher increment in the experimental group as compared with the control group (except triceps skinfold-for-age z score and protein intake). Moreover, the reduction in hemoglobin was significantly lower in the experimental group than that in the control group. At the end of the study, the experimental group had significantly lower proportions of anemia (11.4% vs. 52.3%, $p < 0.001$) and stunting (1.2% vs. 18.3%, $p < 0.05$) than the control group. In conclusion, micronutrient powder was found to have beneficial effects on anthropometric and biochemical measures of under-two children in this study. However, more studies are needed to better understand the contribution of micronutrient powder supplementation to energy and nutrient intakes. The findings also suggested that the addition of micronutrient powder supplements to the Ministry of Health supplementation protocol could improve the nutritional status of young children.

Abstrak tesis yang dibentangkan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

KESAN SUPLEMEN MIKRONUTRIEN KE ATAS STATUS PEMAKANAN BAYI DI SEMENANJUNG GAZA, PALESTIN

Oleh

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Penurunan kadar pertumbuhan adalah keadaan biasa bagi masalah kekurangan zat makanan di negara-negara membangun. Kekurangan mikronutrien termasuk vitamin A, vitamin D, zat besi dan zink dikaitkan dengan pertumbuhan terbantut dalam kalangan kanak-kanak. Kajian ini bertujuan untuk mengenal pasti kesan pemberian serbuk mikronutrien terhadap status pemakanan kanak-kanak di Gaza, Palestin. Kajian ini dijalankan dalam dua fasa. Pada fasa pertama, kajian kohort retrospektif melibatkan 2650 kanak-kanak dari lima klinik kesihatan utama telah dijalankan untuk menilai corak pertumbuhan dari kelahiran hingga 24 bulan untuk menyokong masa pemberian suplemen mikronutrien pada fasa kedua. Pada fasa kedua, kajian rawak terkawal prospektif selari telah dijalankan terhadap 200 bayi berumur enam bulan yang dipilih secara rawak dari klinik-klinik United Nations Relief and Works Agency (UNRWA). Bayi-bayi itu telah diasingkan kepada dua kumpulan secara rawak: kumpulan kawalan (menerima Suplemen Mikronutrien Kebangsaan) dan kumpulan eksperimen (menerima serbuk Mikronutrien selama 12 bulan bersama Suplemen Mikronutrien Kebangsaan). Hasil utama yang dinilai ialah berat, panjang, ukur lilit kepala, pinggang dan bahagian atas lengan, trisep dan lapisan kulit subskapular dan hemoglobin kanak- kanak, sementara hasil sampingan termasuk pengambilan makanan kanak-kanak dan amalan pemberian makan oleh ibu kepada kanak-kanak. Analisis pada fasa pertama berdasarkan statistik diskriptif, sementara Student's t-test dan General Linear Model (GLM) untuk ukuran berulang digunakan untuk fasa kedua (berdasarkan analisis pada protokol). Dalam proses fasa kedua, terdapat 18 dan 12 peserta masing-masing telah keluar daripada kumpulan eksperimen dan kawalan. Keputusan fasa satu menunjukkan penurunan pada ukuran panjang lebih ketara berbanding penurunan berat. Dari 6 hingga 24 bulan, sementara prevalens kekurangan berat badan adalah stabil (~5 %), terdapat penurunan pada prevalens kesusutan berat badan (10 – 2.8%), tetapi, terdapat peningkatan pada prevalens terbantut (9 – 20.4%). Pada akhir kajian, terdapat peningkatan signifikan pada kumpulan eksperimen dalam semua ukuran antropometri kecuali skor z panjang-untuk-umur dan lipatan kulit trisep-untuk-umur. Sedangkan, kumpulan kawalan menunjukkan peningkatan signifikan pada ukuran berat, panjang, ukur lilit kepala, pinggang dan bahagian atas lengan-untuk-umur, dan skor z lipatan kulit subskapular-untuk-umur sahaja. Pada kedua-dua kumpulan, didapati terdapat peningkatan signifikan pada kebanyakan nutrien (kecuali pengambilan lemak dan zat besi), tetapi terdapat penurunan signifikan pada hemoglobin. Kesan pada keseluruhan kumpulan didapati pada hemoglobin, pengambilan vitamin D, dan semua ukuran antropometri kecuali skor z indeks jisim badan-untuk-umur, ukur lilit kepala-untuk-umur, dan lipatan kulit subskapular-untuk-umur dengan min lebih tinggi pada kumpulan eksperimen berbanding kumpulan kawalan. Perubahan pada hemoglobin, pengambilan karbohidrat, protein, vitamin D dan kebanyakan ukuran antropometri (kecuali skor z ukur lilit kepala-untuk-umur, ukur lilit pinggang-untuk-umur, ukur lilit bahagian atas lengan-untuk-umur dan lipatan kulit subskapular-untuk-umur) menunjukkan kumpulan signifikan melalui interaksi masa dengan peningkatan yang lebih pada kumpulan eksperimen berbanding kumpulan kawalan (kecuali skor z lipatan kulit trisep-untuk-umur dan pengambilan protein). Lebih-lebih lagi, penurunan hemoglobin adalah lebih rendah secara signifikan pada kumpulan eksperimen berbanding kumpulan kawalan. Pada akhir kajian, kumpulan eksperimen didapati mempunyai kadar anemia yang lebih rendah secara signifikan (11.4% vs. 52.3%, $p < 0.001$) dan terbantut (1,2% vs, 18.3%, $p < 0,05$) berbanding kumpulan kawalan. Sebagai kesimpulan, serbuk mikronutrien didapati mengandungi kesan yang bermanfaat pada ukuran antropometri dan biokimia kanak-kanak berumur dua tahun ke bawah dalam kajian ini. Walaubagaimanapun, lebih banyak kajian diperlukan untuk lebih memahami kesan pengambilan serbuk mikronutrien terhadap pengambilan tenaga dan nutrien. Hasil kajian juga mencadangkan bahawa penambahan serbuk mikronutrien di dalam protokol suplemen Kementerian Kesihatan boleh meningkatkan status pemakanan kanak-kanak kecil.

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Doctor of Philosophy. The members of the Supervisory Committee were as follows:

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LIST OF ABBREVIATIONS

AEs	: Adverse Event(s)
AGA	: Appropriate for Gestational Age
ANOVA	: Analysis of Variance
BAZ	: Body Mass Index-for-Age z score
BMI	: Body Mass Index
CDC	: Centers for Disease Control
CHD	: Congenital Hip Dislocation
CI	: Confidence Interval
Cm	: Centimeter
CRF	: Case Report Form
d/L	: Deciliter
DRI	: Dietary Reference Intakes
FAO	: Food and Agriculture Organization of the United Nations
g	: Gram
GLM	: General Linear Model
HAZ	: Height-for-Age z scores
HB	: Hemoglobin
HC/A	: Head circumference for age
HC	: Head Circumference
HCZ	: Head Circumference-for-Age z score
ID	: Iron Deficiency
IDA	: Iron Deficiency Anemia
IDD	: Iodine Deficiency Disorders
IQR	: Inter Quartile Range
IU	: International Unit
IZiNCG	: International Zinc Nutrition Consultative Group
JKEUPM	: Ethics Committee for Research Involving Human Subjects
Kcal	: Kilocalorie
Kg	: Kilogram
L/A	: Length for age

LAZ	: Length-for-Age z score
LBW	: Low Birth Weight
LGA	: Large for Gestational Age
Mcg	: Microgram
MD	: Micronutrient deficiency
Mg	: Milligram
mm	: Millimeter
MMN	: Multiple Micronutrient
MNP	: Micronutrients Powder
MOH	: Ministry of Health
MUAC/A	: Mid-upper arm circumference for age
MUAC	: Mid Upper Arm Circumference
MUACZ	: Mid-upper arm circumference for age z score
NMS	: National Micronutrient supplements
NNSS	: National Nutrition Surveillance System
NUGAG	: Nutrition Guidance Expert Advisory Group
OR	: Odds Ratio
PAPFAM	: Pan-Arab Project for Family Health
PCBS	: Palestinian Central Bureau of Statistics
PHC	: Primary Health Care
PhD	: Philosophy of Doctorate
PMS	: Palestinian micronutrient survey
RAE	: Retinol Activity Equivalents
RDA	: Recommended Dietary Allowance
RNI	: Reference Nutrient Intake
RR	: Relative Risk
SD	: Standard Deviation
SGA	: Small for Gestational Age
SMD	: Standardized Mean Difference
SPSS	: Statistical Package for Social Science
SSF/A	: Sub scapular skinfold for age
SSF	: Subscapular Skinfold

SSFZ	: Sub scapular skinfold for age z score
TSF/A	: Triceps skinfold for age
TSF	: Triceps Skinfold
TSFZ	: Triceps skinfold for age z score
UNFPA	: UNICEF and United Nations Population Funds
UNICEF	: United Nations Children's Fund
UNRWA	: United Nations Relief and Works Agency for Palestine Refugees in the Near East
VAD	: Vitamin A deficiency
VAD	: Vitamin A Deficiency
VDD	: Vitamin D deficiency
W/A	: Weight for age
WAZ	: Weight-for-Age z score
WC/A	: Waist circumference for age
WC	: Waist Circumference
WCZ	: Waist Circumference for age z score
WHO	: World Health Organization
WLZ	: Weight-for-Length z score

CHAPTER 1

INTRODUCTION

1.1 Background

Micronutrients are minerals and vitamins that are essential in small amounts, vital for life and needed for a broad range of body functions. Micronutrient deficiencies are documented as a global public health and clinical problem affecting 2 billion people in the developed and developing countries (Tulchinsky, 2010). Deficiencies of minerals and vitamins affect people of all ages and genders, as well as certain at-risk groups. They not only cause specific diseases but also act as exacerbating factors in chronic diseases, greatly impacting morbidity, mortality, and quality of life (Tulchinsky, 2010). Throughout the world, the four most widespread forms of micronutrient deficits are vitamin A, iron, zinc, and iodine deficiencies (Ahmed et al., 2012). Deficiencies occur when people do not consume foods such as vegetables, fruits, fortified foods and meat as they are very expensive and locally they are not available (WHO, 2007a).

Vitamin A Deficiency (VAD) is recognized in developing countries as a public health problem. Globally, VAD affects the lives of about 190 million children of preschool age (WHO, 2013a). In Palestine, the prevalence of VAD among children aged 1 to 5 years was 22% (WHO, 2008c). However, in 2013, the Palestinian micronutrient survey (PMS) reported that vitamin A status was sufficient among 27% of under-five children only, and severe deficiency was more prevalent (36.8%) among Gaza Strip children (Palestinian MOH, 2014). Insufficient dietary intake, poor absorption and socio-economic constraints leading to depleted vitamin A stores in the body are potential determinants of VAD in developing countries (Akhtar et al., 2013). Intense VAD leads to xerophthalmia, the most common cause of preventable blindness among children (WHO, 2009c). The World Health Organization (WHO) reported that about 250,000 - 500,000 children turn blind each year by VAD (WHO, 2013b). VAD does not only harm the eyes but also increases childhood mortality (Kennedy et al., 2003).

Iron deficiency is the most common and widespread nutritional disorder in the world. The WHO reported that iron deficiency anemia (IDA) affecting 42% of children aged 6 – 59 months worldwide (WHO, 2015b). In Palestine, the overall occurrence of anemia amongst preschool children in Gaza Strip was 59.7%, and the prevalence of mild and moderate anemia were 46.5%, and 13.5%, respectively (El Kishawi et al., 2015). Sirdah et al. (2014) found that the prevalence of iron deficiency anemia in Gaza Strip was 33.5% among preschool children. IDA is more prevalent in young children and infants and may result from insufficient intake and absorption of iron, increased requirements of iron during growth, or unnecessary iron losses (Chaparro, 2008). IDA is related with impaired cognitive function, chronic fatigue and diminishing well-being (Jimenez et al., 2015).

Iodine is another nutrient which is vital due to its role as a constituent of thyroid hormones, and it must be obtained via dietary or exogenous sources (Rohner et al., 2014). Globally, 240.9 million people have insufficient iodine intake, and 29.8% of them are young children (Andersson et al., 2012). A national survey in Turkey reported that 27.8% of young children had severe and moderate deficiency of iodine (Erdoğan et al., 2009). In Egypt, despite mandatory household salt iodization, 25% of children had a clinical goiter (Mirmiran et al., 2012). Whereas, it has been observed in Palestine that the annual mortality rate from iodine deficiency decreased by 73.9% since 1990 (Health Grove by Graphiq, 2016), and 15% of Palestinian children were affected by goiter (Bakhiet & Lynn, 2015). The leading cause of iodine deficiency disorders (IDD) is low dietary intake of iodine (Pearce et al., 2013). IDD consists of a group of disorders that vary from hypothyroidism to simple goiter, decreased intelligent quotient, impaired psychosomatic performance and typical cretinism (Zimmermann et al., 2008).

Zinc (Zn) is essential for cell growth, immune response and contributes to the production of enzymes which are necessary for the synthesis of RNA and DNA (Webster-Gandy et al., 2011). It has been projected that zinc deficiency affects about one-third of the world's population (WHO, 2012b). Wessells and Brown (2012) estimated that the prevalence of inadequate zinc intake ranged from 7.5% in high-income regions to 30% in low-income regions. In Palestine, Zakout et al., (2010) reported that the prevalence of zinc deficiency among stunted children aged 1 to 3 years in Gaza Strip was 74.5%. Zinc deficiency has serious wide-ranging health consequences and is thought to be one of the most prevalent micronutrient deficits in the globe. Globally, about 800,000 deaths amongst children below 5 years of age occur yearly due to pneumonia (406,000), diarrhea (176,000) and malaria (207,000). High mortality rate amongst children resulting from these infections has been reported to be associated with inadequate zinc intake (Black et al., 2008). Major contributors to zinc deficiency are dietary factors such as low consumption of animal source foods, high intake of plant foods containing phytate (Roohani et al., 2013) and lack of dietary diversity (Gebremedhin et al., 2011). Adverse health outcomes of zinc deficiency include impaired immune function, short stature and disorders such as malaria, diarrheal diseases and respiratory infections (Bhowmik & Chiranjib, 2010; Walker et al., 2013).

Micronutrient deficiency is common during the period of dietary transition in infancy when complementary food is added to milk feeding (Dewey, 2013). After six months of age, the nutrient concentration in human milk declines as a micronutrient source in relation to the requirements for growth and a greater demand is placed on the complementary food as source of nutrients (Vossenaar & Solomons, 2012). However, complementary foods are commonly deficient in several micronutrients particularly iron, zinc, calcium, and B vitamins (Gibson et al., 2010), which may adversely affect growth and cognitive function (Walker et al., 2011). The use of family foods with adequate micronutrient density and provision of fortified complementary foods given at home could improve the nutritional status of the children (Harris & Jack, 2011; Raine et al., 2010; WHO, 2011c).

1.2 Problem Statement

Undernutrition (growth retardation and micronutrient deficiency) prevail at moderate to high levels among under-five children, particularly from low-income families in developing countries (Black et al., 2008). One in three children who are under five in these countries are malnourished, and 61% are anemic (WHO, 2015b). Poor dietary habits and inadequate nutrient intakes are major factors associated with undernutrition, and often include low micronutrient intake (Rah et al., 2010; Roman Viñas et al., 2011). Therefore, micronutrient deficiencies should be of great concern to health authorities.

Studies on the effect of micronutrient supplementation on growth status have produced inconsistent findings. The positive effects of micronutrient supplementation on growth were reported in a systematic review of randomized controlled trials involving children below the age of two and five years from low-income families (Ramakrishnan et al., 2004). However, the findings from two systematic reviews of randomized controlled trials, quasi-experimental and before-after studies, and observational studies (cohort and case-control) aimed to identify the impact of food fortification with single, multiple micronutrients, or micronutrients powder supplement (MNP) on growth of children including under-two and preschool children (ages 2 to 5 years) did not show positive effects on growth, although they showed positive trends (De-Regil et al., 2013; Jai Das et al., 2013). Lack of effect can be due to the short duration (< 12 months) of the involvement to show actual long-term effect of micronutrient on a growth pattern, using of a single rather than multiple micronutrient supplements, or poor adherence and compliance to the supplementation programs.

Several studies have reported that micronutrient supplementation significantly improved micronutrient status of children under five years (Allen et al., 2009; Cardoso et al., 2016; Christian et al., 2012; S. Kounnavong et al., 2011). A systematic review of randomized clinical trials and program evaluations including children aged from 6 to 18 months suggested that home feeding with MNP is an effective intervention as iron supplementation in treating anemia with better acceptance due to reduced side effects (Dewey et al., 2009). Moreover, Suchdev et al. (2012) from Kenya reported that MNP reduced the rate of iron and vitamin A deficiency effectively and raised the recovery rate of anemia in young children. In a double-blind, placebo-controlled trial undertaken to test the efficacy of MNP included low dose of iron and zinc (each 2.5 mg/day), Troesch et al. (2011) showed that MNP decreased the prevalence of iron and zinc deficiency among children with low iron status.

The Nutrition Guidance Expert Advisory Group strongly recommends home fortification of foods with micronutrients to improve the nutritional status of children under-five (WHO, 2011c). In recent years, fortification of home-made food with micronutrients provided in powdered form, crushable tablets, and lipid-based spreads has been recognized as a possible strategy to prevent micronutrient deficiencies in vulnerable groups, such as young children who cannot swallow tablets. It has been reported that micronutrient supplements in syrups or drops are less effective due to poor compliance. A possible explanation is the side effects of iron in the micronutrient drops or syrups such as constipation, nausea, vomiting and diarrhea (Driscoll et al., 2010; Galloway & McGuire, 1994; Hyder et al., 2002). Iron drops, which are usually more concentrated, require careful monitoring as to prevent the risk of overdose (Mora, 2002). Also, iron in drop or syrup form could produce metallic aftertaste and dark stain on the teeth which could further reduce compliance to the micronutrient supplementation (Galloway & McGuire, 1994; Schauer & Zlotkin, 2003; Yip & Ray, 1994). In the other hand, micronutrient powder contains lipid-encapsulated coating which does not allow iron to dissolve into food; consequently, it does not change the color or taste of food or produce iron related side effects (Zlotkin et al., 2005).

The connection between micronutrient deficiency and growth faltering is closely entwined. A high prevalence of co-existing micronutrient deficiencies including iron, zinc, and vitamin A has been reported among stunted children (Anderson, Jack, et al., 2008). Further, impaired linear growth is a prominent feature of zinc deficiency among young children in both developed and developing countries (Brown et al., 2002). Indeed, the International Zinc Nutrition Consultative Group suggests that the prevalence of stunting can be used as an indirect indicator for the risk of zinc deficiency (Hotz & Brown, 2004). On the other hand, zinc is known to be essential for intra-and intercellular transport of vitamin A and its absorption (Ahn & Koo, 1995). As well as a significant linear relations have been identified between iron and zinc statuses (Yokoi et al., 2007), and low iron status is a risk factor for reduced serum retinol (Thurlow et al., 2006). Certainly, there is abundant evidence that stunted children are likely to be zinc deficient and are also at high risk to nutritional iron deficiency anemia because the nutritional factors associated with zinc deficiency are similar to those for iron deficiency (Hotz & Brown, 2004).

In Palestine, efforts have been implemented to improve micronutrient deficiencies among children. Since 2001, supplementation program was undertaken to treat deficiency of iron, vitamin A, and vitamin D among under-two children using iron, vitamin A, and vitamin D drops (MOH, 2005b). However, high prevalence of iron deficiency anemia, subclinical vitamin A and D, and zinc deficiencies continue to exist (MARAM, 2004; Mohammed Khalil Abu Jami, 2013; Sirdah et al., 2014; Taha, 2011). Further, official reports (PCBS, 2011) indicated that Palestinian children less than five had a higher risk for nutritional deficiencies than other population groups. Radi et al. (2009) revealed that 72% of children under two in Gaza city were anemic, and the prevalence of wasting, stunting, and underweight were 34.3%, 31.4%, and 31.45%, respectively. These findings suggest a risk of micronutrient deficiencies and that the effectiveness and coverage of the supplementation program seems to be insufficient. To this date, no micronutrient powder supplementation study has been conducted on children who are under two years in Gaza Strip of Palestine or neighboring countries. Therefore, the current study aimed at filling the gap on information regarding the prevalence of undernutrition and effectiveness of the supplementary programs on under-two children.

1.3 Objectives

A. Phase one (Growth study)

i. General objective:

1. To assess growth in the first 24 months of life of Palestinian children in the Gaza Strip.

ii. Specific objectives:

1. To identify the prevalence of underweight, stunting and wasting at 6, 9, 12, 15, 18 and 24 months old.
2. To identify the timing and pattern of growth faltering (underweight, stunting, and wasting).

B. Phase two (Micronutrients supplementation study)

i. General objectives:

1. To evaluate the effectiveness of micronutrient supplementation intervention for 12 months on nutritional status of infants aged six months.

ii. Specific objectives:

1. To compare anthropometric measures, biochemical measures, and dietary factors between experimental and control groups before the intervention in relation to:
    a. Length for age (L/A), weight for age (W/A), weight for length (W/L), and BMI for age.
    b. Head circumference for age (HC/A), Waist circumference for age (WC/A), mid-upper arm circumference for age (MUAC/A).
    c. Triceps skin fold for age (TSF/A) and sub scapular skin fold for age (SSF/A).
    d. Hemoglobin (Hb)
    e. Dietary intakes (e.g., energy, carbohydrates, fat, protein, iron, vitamin A and D).

2. To determine changes in anthropometric measures, biochemical measures, and dietary factors within experimental and control group (before and after intervention) in relation to:
    a. Length for age (L/A), weight for age (W/A), weight for length (W/L), and BMI for age.
    b. Head circumference for age (HC/A), Waist circumference for age (WC/A), mid-upper arm circumference for age (MUAC/A).

c. Triceps skin fold for age (TSF/A) and sub scapular skin fold for age (SSF/A).
d. Hemoglobin (Hb)
e. Dietary intakes (e.g., energy, carbohydrates, fat, protein, iron, vitamin A and D).

3. To compare changes (before and after intervention) in anthropometric measures, biochemical measures, and dietary factors between experimental and control groups in relation to:
   a. Length for age (L/A), weight for age (W/A), weight for length (W/L), and BMI for age.
   b. Head circumference for age (HC/A), Waist circumference for age (WC/A), mid-upper arm circumference for age (MUAC/A).
   c. Triceps skin fold for age (TSF/A) and sub scapular skin fold for age (SSF/A).
   d. Hemoglobin (Hb).
   e. Dietary intakes (e.g., energy, carbohydrates, fat, protein, iron, vitamin A and D).

1.4 Study Hypothesis

Phase two (Micronutrients supplementation study)

1. Anthropometric measures (i.e. length for age (L/A), weight for age (W/A), weight for length (W/L), BMI for age, head circumference for age (HC/A), waist circumference for age (WC/A), mid-upper arm circumference for age (MUAC/A), triceps skin fold for age (TSF/A), and sub scapular skin fold for age (SSF/A)) will be improved significantly in children receiving the MNP with the NMS compared to children receiving the NMS only.
2. Biochemical measures (blood level of hemoglobin) will be improved significantly in children receiving the MNP with the NMS compared to children receiving the NMS only.
3. Dietary intakes (i.e. energy, carbohydrate, fat, protein, iron, vitamin A, and vitamin D intakes) will be improved significantly in children receiving the MNP with the NMS compared to children receiving the NMS only.

1.5 Research Questions

A. Phase one (Growth study)

1. What is the prevalence of underweight, stunting, and wasting at 6, 9, 12, 15, 18, and 24 months old among children living in Gaza Strip?
2. Does the prevalence of underweight, stunting, and wasting among boys is higher than girls?
3. What is the onset point of growth faltering among under-two children?

B. Phase two (Micronutrients supplementation study)

1. Is there an effect of MNP on the anthropometric measures (i.e. length for age (L/A), weight for age (W/A), weight for length (W/L), BMI for age, head circumference for age (HC/A), waist circumference for age (WC/A), mid-upper arm circumference for age (MUAC/A), triceps skin fold for age (TSF/A), and sub scapular skin fold for age (SSF/A))?
2. Is there an effect of MNP on the biochemical measures (blood level of hemoglobin)?
3. Is there an effect of MNP on dietary intakes (i.e. energy, carbohydrate, fat, protein, iron, vitamin A, and vitamin D intakes)?

1.6 Research Framework

The research framework is presented in Figure 1.1. The first phase (growth study) of this research assessed the prevalence and trend of growth faltering amongst children from birth to two years old. The findings of the first phase study would provide support for appropriate age group micronutrient supplementation (Adu-Afarwuah et al., 2007; Giovannini et al., 2006; Jack et al., 2012). The second phase of this research was a micronutrient supplementation trial for 12 months that evaluated the effectiveness of MNP on nutritional status of infants (6 months old). Children in the experimental group received three sachets of MNP per week plus the National Micronutrient Supplements (NMS); children in the control group, on the other hand, received NMS only. The effects of MNP with NMS and NMS on the anthropometric measures (e.g. weight, length, head circumference, waist circumference, mid upper arm circumference, triceps skinfold, subscapular skinfold), biochemical measures (e.g. blood hemoglobin), and dietary factors (e.g. calories, carbohydrate, fat, protein, iron, vitamin A, and vitamin D) were evaluated. The socio-demographic, dietary, genetic, and child factors were examined as possible covariates.

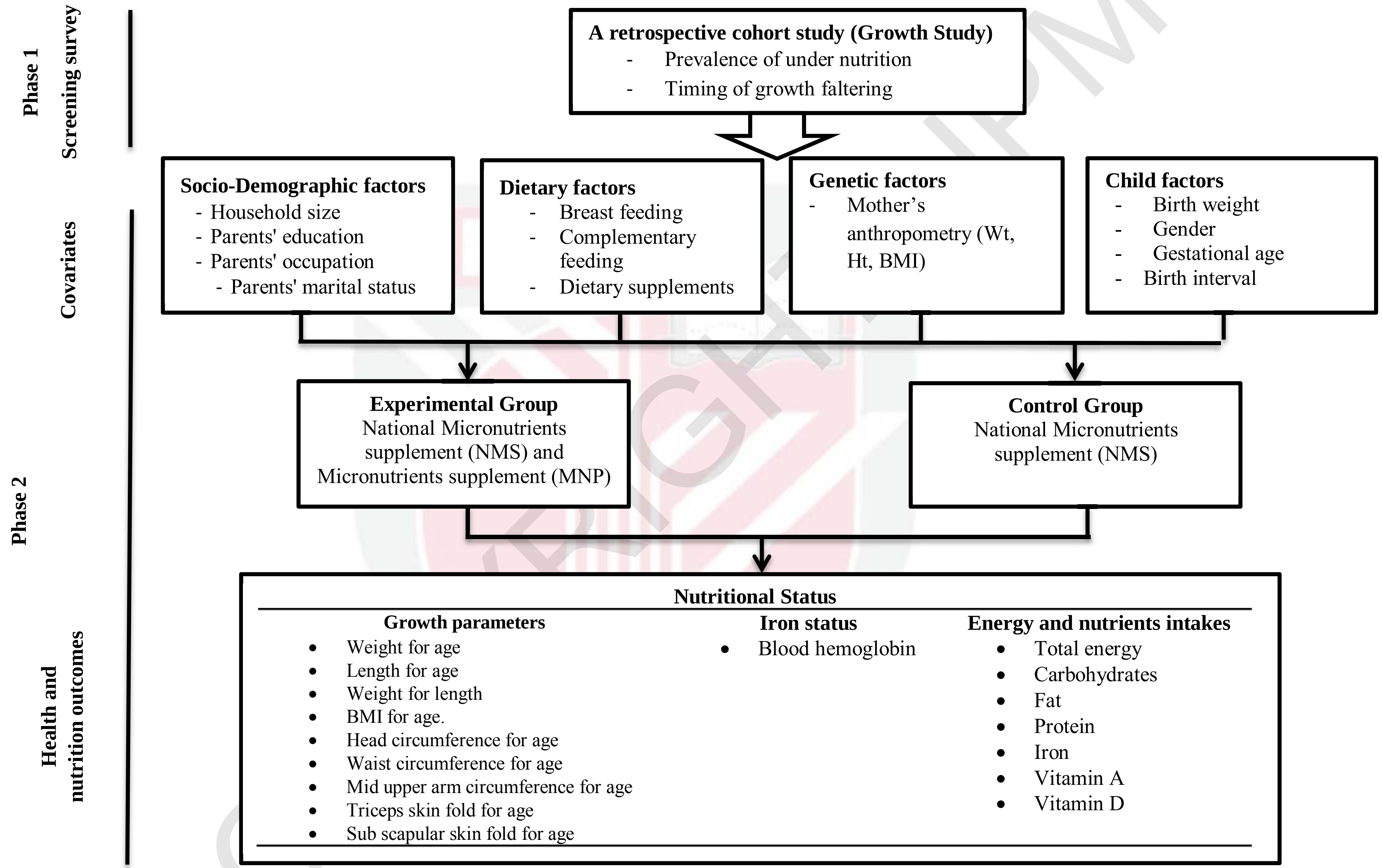

Figure 1.1 : Research Framework

1.7 Significance of Study

The period from birth to 24 months of age is one of the most critical periods for linear growth. It is too the time of peak growth retardation prevalence, particularly stunting, in developing countries due to high demand of nutrients and limited quality and quantity of complementary foods. It has been reported that growth retardation is largely irreversible after about two years of age and there is only a narrow window of opportunity in early life. Therefore, micronutrient supplementation in the first two years after birth is imperative to prevent irreversible consequences of undernutrition.

In Palestine, the persistence of high prevalence of undernutrition among children under five is a serious public health issue, despite improvements in other health indicators such as immunization and infant mortality. Since 2001, the Palestinian Ministry of Health (MOH) has implemented the National Micronutrient Supplementation program to improve the nutritional status of infants using drops of iron, vitamin A, and D supplements (single micronutrient). In spite of these efforts, the prevalence of anemia and growth retardation is still high, where about one-fifth of Palestinian children under five were anemic and the prevalence of chronic undernutrition was 11%. Hence, the present study would provide an alternative to the current effort of the Palestinian Ministry of Health to address micronutrient deficiencies and growth retardation in Palestinian children.

In the Gaza Strip, Palestine, the closure of borders and restriction of internal and external movement due to Israeli siege since 2007 have led to high rate of unemployment and elevated inflation as the economy collapsed. As poverty is prevalent, families are not able to provide healthy and balanced diet for their children and subsequently have to rely on aids from local and international organizations. Whereby, complementary foods in Gaza Strip are frequently based on cereals, and such foods are often accompanied by major deficits in iron, iodine, zinc and vitamin A. Therefore, the present study aimed to provide cost-effective supplements (0.80 $ for 30 x 1 gram sachets) to mend the major deficits of micronutrients to improve the nutritional status of children under two.

In Gaza Strip, several studies examined growth status and identified the prevalence and risk factors of malnutrition, but there were no studies about the effect of micronutrient supplements or food fortification programs on the nutritional status of under-two children. Thus, the findings of the present study will fill the information gap on the effectiveness of the micronutrient supplementation interventions on young children. The findings also will help the Ministry of Health, other ministries, and all other stakeholders to identify the most vulnerable population, contribute to formulate interventions and targeting mechanisms, and serve as a baseline that can be compared with subsequent data collection. Additionally, these findings can be an inspiring factor for future studies locally and in the neighbouring countries.

Since the beginning of the National Micronutrient Supplementation program, a lot of money and time have been spent on vitamin A, vitamin D, and Iron supplementation program implemented by Ministry of Health in Palestine to maintain the nutritional status of under-two children. Despite that, no nation-wide study has been undertaken to evaluate the effectiveness of this program. This could be due to financial constraints as such evaluation is expensive to conduct. Therefore, this study can indirectly evaluate the effectiveness of the National Micronutrient Supplementation program and suggest the need to integrate the current study protocol into the government program for implementation at a much larger scale.

1.8 Operational Definition

Undernutrition: the outcome of insufficient food intake, which involves being underweight for child's age, too short for child's age (stunted), thin for child's length (wasted) and deficient in vitamins and minerals (UNICEF, 2009b).

Underweight: low weight-for-age which presented by two categories; moderate underweight ($-2.99 < x < -2$ of 2006 WHO standards mean for weight-for-age) and severe underweight (< -3 SD of 2006 WHO standards mean for weight –for- age) (WHO, 2006).

Stunting: low length-for-age which presented by two categories; moderate stunted ($-2.99 < x < -2$ of 2006 WHO standards mean for length-for-age) and severe stunted (< -3 SD of 2006 WHO standards mean for length-for-age) (WHO, 2006).

Wasting: low weight-for-length which presented by two categories; moderate wasted ($-2.99 < x < -2$ of 2006 WHO standards mean for weight-for-length) and severe wasted (< -3 SD of 2006 WHO standards mean for weight-for-length) (WHO, 2006).

Thinness: low BMI for age which presented by two categories; moderate thinned ($-2.99 < x < -2$ of 2006 WHO standards mean for BMI for age) and severely thinned (< -3 SD of 2006 WHO standards mean for BMI for age) (WHO, 2006).

Micronutrients: nutrients needed by humans and other organisms in their life-time in small amounts to compose a number of physiological functions (Canadian UNICEF Committee, 2006).

National micronutrients supplements (NMS): supplements which have dispensed by the Palestinian MOH since 2001 including vitamin A, vitamin D, and iron, to maintain the nutritional status of Palestinian children less than two years old (MOH, 2009).

Micronutrients supplement powder (MNP): Mixme^{TM} sachets weighed 1 gram, with a mixture powder micronutrients effortlessly sprinkled onto semi-solid foods (World food Programme (WFP) & The UN refugees Agency, 2009). Mixme^{TM} is manufactured by DSM Nutritional Products Europe, Switzerland. It consists of 10 vitamins (A, D, E, B1, B2, B6, niacin, B9, B12 and C) and 5 minerals (zinc, copper, iodine, iron and selenium) (DSM, 2016).

Anemia: The condition of having lower than 100g per litre of blood haemoglobin using a spectrophotometric method.

Dietary pattern: frameworks that people tend to follow when making choices about what to eat. Type and portion size of consumed foods were obtained by asking about the type and amount of consumed food items over the past day using 24-hour diet recall method.

Complementary foods: Any nutritive liquids or non-breast milk foods that are given to young children aged six months are defined as complementary foods and complementary feeding which is the process of introducing these foods (UNICEF, 1998).

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Released Articles:

Albelbeisi, A., Shariff, Z., Mun, C., Abdul Rahman, H., & Abed, Y. (2017). Use of Micronutrient Powder in At-Home Foods for Young Children (6-18 Months): A Feasibility Study. Pakistan Journal of Nutrition, 16(5), 372-377.

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