RESEARCH ARTICLE

The Mother-Infant Study Cohort (MISC): Methodology, challenges, and baseline characteristics

Hadia Radwan1*, Mona Hashim1, Reyad Shaker Obaid1, Hayder Hasan1, Farah Naja2, Hessa Al Ghazal3, Hamid Jan Jan Mohamed4, Rana Rizk5,6, Marwa Al Hilali1, Rana Rayessa3, Ghamra Izzaldin1

1 Department of Clinical Nutrition and Dietetics, College of Health Sciences, Research Institute of Medical and Health Sciences (RIMHS), University of Sharjah, Sharjah, United Arab Emirates, 2 Department of Nutrition and Food Sciences, American University of Beirut, Beirut, Lebanon, 3 Family Health Promotion Center, Sharjah, United Arab Emirates, 4 Nutrition and Dietetics Program, Universiti Sains Malaysia, Kelantan, Malaysia, 5 Department of Health Services Research, Maastricht University, Maastricht, The Netherlands, 6 Institut National de Sante Publique, d’Épidémiologie Clinique et de Toxicologie (INSPECT-LB), The Lebanese University, Beirut, Lebanon

* hradwan@sharjah.ac.ae

Abstract

Background
The United Arab Emirates (UAE) exhibits alarming high prevalence of Non-Communicable Diseases (NCDs) and their risk factors. Emerging evidence highlighted the role of maternal and early child nutrition in preventing later-onset NCDs. The objectives of this article are to describe the design and methodology of the first Mother and Infant Study Cohort (MISC) in UAE; present the baseline demographic characteristics of the study participants; and discuss the challenges of the cohort and their respective responding strategies.

Methods
The MISC is an ongoing two-year prospective cohort study which recruited Arab pregnant women in their third trimester from prenatal clinics in Dubai, Sharjah and Ajman. Participants will be interviewed six times (once during pregnancy, at delivery, and at 2, 6, 12 and 24 months postpartum). Perinatal information is obtained from hospital records. Collected data include socio-demographic characteristics, lifestyle, dietary intake and anthropometry; infant feeding practices, cognitive development; along with maternal and infant blood profile and breast milk profile.

Results
The preliminary results reported that 256 completed baseline assessment (mean age: 30.5 ±6.0 years; 76.6% multiparous; about 60% were either overweight or obese before pregnancy). The prevalence of gestational diabetes was 19.2%. Upon delivery, 208 women-infant pairs were retained (mean gestational age: 38.5±1.5 weeks; 33.3% caesarean section delivery; 5.3% low birthweight; 5.7% macrosomic deliveries). Besides participant retention,
the main encountered challenges pertained to cultural complexity, underestimation the necessary start-up time, staff, and costs, and biochemical data collection.

Conclusions
Despite numerous methodological, logistical and sociocultural challenges, satisfactory follow-up rates are recorded. Strategies addressing challenges are documented, providing information for planning and implementing future birth cohort studies locally and internationally.

Introduction
Adequate nutrition during “the first 1000 days of life”, i.e. the period extending from conception up to the child’s second year of life, greatly affects fetal growth and birth outcomes, and is essential to ensure health and development of infants and children to their full potential [1–6]. Proper breastfeeding and complimentary feeding practices during this period have a lasting impact on a child’s health [7,8], and can save the life of 800,000 infants each [9]. Consequently, the World Health Organization (WHO) and the United Nations Children’s Fund (UNICEF) recommend that infants be exclusively breastfed for the first six months of life, up to two years of age or beyond [7,10,11].

Furthermore, early-life exposures that influence growth during development, including genetic, epigenetic, nutritional and environmental, may modulate adult disease risk [12]. Recent scientific literature is investigating the period extending from gestation to infancy and early childhood as a window of opportunity for curbing the non-communicable disease (NCD) pandemic through developmental programming [13,14]. In specific, high pre-pregnancy weight and weight gain and mother’s diet during early gestation were associated with an adverse cardio-metabolic profile in the offspring, such as increased risk of childhood body mass index (BMI), body fat and systolic blood pressure [13,15]. Understanding the nature of these exposures might be a key to preventing disease and improving health [16].

Population-based prospective cohort studies are key study designs for investigating life course processes [17]. Pregnancy and birth cohort studies are especially suited for exploring the origins of health and disease that begin as early as in pre-pregnancy, fetal life and infancy. The strength and liability of these longitudinal studies lie in their potential to explore causal relationships whilst requiring less recall than other epidemiological study designs [18,19]. Therefore, well-designed and well-conducted birth cohort studies are particularly valuable for understanding the role of pre- and postnatal environment on immediate and future health [12].

Until recently, conducting cohorts addressing maternal and child nutrition and its impact on health outcomes in developing countries was limited [20–22], especially in the Middle East region [23–25]. Generating birth cohort data from this region is useful for exploring country- and population-specific early-life predictors of health and disease. This is essential especially for countries where the economic transition and subsequent unplanned lifestyle and nutrition transition has had devastating consequences on the population health [26,27]. In particular, the United Arab Emirates (UAE) exhibited in recent years an enormous economic growth, that was paralleled with surging rates of NCDs and their risk factors in adult and pediatric populations [26,27] as well as a dramatically growing probability of premature death [28]. Changes in infant feeding practices were not isolated from the nutrition transition in the country; rather, a decline in exclusive breastfeeding, a high dependence on bottle-
feeding and suboptimal weaning practices are being increasingly reported [29,30]. Taking into consideration the resulting high morbi-mortality and economic losses, designing and implementing appropriate NCD prevention and control programs through translational research are at the top of local and regional agendas [31,32]. To move these agendas forward, the Mother-Infant Study Cohort (MISC) is launched. The MISC aims to longitudinally investigate the effects of nutrition and lifestyle characteristics on birth outcomes, infant nutritional status and cognitive development, as well as early-life cues of NCDs, with a focus on the Emirati setting. Also, the findings of the MISC are planned to be used for a cross-country comparison with other Gulf-based cohorts, such as the ongoing Mother and Infant Nutritional Assessment (MINA) cohort study in Qatar and Lebanon [25]. The ultimate aims of the MISC are to advance scientific research on women’s and children’s health in the UAE and Arab region, to act as a model for generating evidence-based findings, translating them into culturally-specific and targeted practice recommendations, and to advocate for a meaningful change at the policy level.

Although, birth cohorts and life course designs offer opportunities, their implementation is uniquely challenging [33,34]. Being the first birth cohort in the UAE, the MISC faced numerous methodological, logistical, and sociocultural challenges. It is important to present an overview of the methodology, protocol and challenges of the MISC to inform the planning and implementation of future birth cohort studies locally, regionally and internationally. Accordingly, the objectives of this article are to: describe the design and methodology of the MISC; present the baseline demographic characteristics of the study participants; and discuss the challenges of the cohort and their respective responding strategies.

Materials and methods

Study design and overview

MISC is the first prospective cohort study in the UAE to comprehensively investigate maternal and infant factors in relation to child health outcomes, as well as early-life determinants of NCDs, through integration of sociodemographic, dietary, lifestyle, anthropometric and biological and cognitive data. At present, recruitment of study participants is completed; data collection and preliminary analyses are being conducted.

Ethical approval

The study was approved by the Research and Ethics Committee, University of Sharjah (REC/14/01/1505) and by Al Qassimi Clinical Research Centre Ethical Research Committee (REC Reference Number: 215 12015–03), by the Ministry of Health Ethical Research Committee (R02) and by Dubai Health Authority (DSREC-0/2016). The research ethics bodies focused on ensuring adherence to the regulatory requirements for the protection of pregnant women and babies as vulnerable research subjects, throughout all study procedures (consent documentation, data collection including blood withdrawal requirements, and data transfer). It was thus requested by Al Qassimi Clinical Research Centre to prepare a separate consent form to obtain the fathers’ approval on the behalf of the infants, since according to Emirati law, the father is the legal guardian. Moreover, special considerations for blood withdrawal by pediatric-certified phlebotomists were noted.

Study setting and population

Participants were recruited from antenatal clinics in three main public governmental hospitals, and seven Primary Health Care (PHC) clinics and Mother and Child Centers (MCH) in the
Emirates of Sharjah, Dubai and Ajman. The research team visited the pre-specified clinics, screened eligibility criteria of pregnant women attending the clinics, informed them of the objectives, conduct and timeline of the study and invited them to participate. The study followed a convenient sampling and did not adopt a special advertisement for recruitment. Eligible women were asked, along with the fathers, to provide signed consent to participate in the study, and were given a copy of it. The participants were chosen according to the following criteria.

**Inclusion criteria**

- Pregnant women:
  - Emirati or Arab expatriate
  - Age: 19–40 years
  - Singleton pregnancy
  - Within the third trimester of pregnancy (27–42 weeks of gestation)
  - Free of chronic diseases (diabetes, hypertension, kidney disease, cancer, or other chronic diseases), autoimmune disorders, or infections with the human immunodeficiency virus, or hepatitis in preconception
  - Receiving antenatal care in any of the above-mentioned clinics and expected to give birth in a participating public hospital
  - Not planning to permanently leave the UAE during the timeline of the study.
- Infants:
  - Early term (37 weeks of gestation) or full term (between 39 weeks 0 days, and 40 weeks 6 days of gestation) live birth infants
  - Free of major illnesses (congenital diseases or any health condition that could deter breastfeeding, such as cleft lip or cleft palate), i.e. apparently healthy infants.

**Exclusion criteria**

- Pregnant women:
  - Multiple pregnancy (pregnant with two or more fetuses)
  - High risk pregnancy or pre-eclampsia
  - History of chronic diseases.
- Infants:
  - Preterm (<37 weeks of gestation) or late term (>42 weeks of gestation) infants
  - Congenital diseases or any health condition that could deter breastfeeding.

Bearing in mind that loss to follow-up might be “not at random” and lead to biased estimates [35], different strategies were put place to increase participation and retention in the cohort: sharing the biomedical results with the study participants at 7-month postpartum; providing gift vouchers and toiletries for attendance to each time-point, ensuring transportation coverage, if needed. In an attempt to increase retention, text messages will be sent to each participant at each time-point. Recruitment was completed during June 2016.
Sample size and power analysis

As mentioned above, one of the main purposes of the MISC is to explore the relationship between maternal characteristics and infant outcomes. When the assessed variables are both continuous, we often resort to Pearson’s correlation coefficient ($r$), enabling the assessment of a linear dependence (correlation) between the variables, as well as the strength and direction of this correlation. The absolute value of $r$ ranges between 0 and 1, and its increasing magnitude indicates a stronger association. Taken the limited data on the above-mentioned associations, $r = 0.2$ was chosen, as it yields the largest sample size. An $r < |0.2|$ indicates a weak correlation - usually considered too small to be clinically significant. Using the Power Analysis and Sample Size System (PASS) software version 11, the sample size needed to detect a correlation as small as $|0.2|$, at 80% power and 5% type I error, is determined at 193 (rounded-up at 200). Another way of assessing the relationship between maternal and infant-related factors is through regression analysis, where an outcome variable is regressed on a number of explanatory variables (predictors). Based on the rationale of considering 10–15 observations per predictor, the sample size of 200 would be sufficient to conduct regression analyses on up-to 15 predictors. Since it is not expected to exceed this number of independent variables per regression model, we considered the sample size of 200 as adequate. Considering that previous birth cohorts showed a retention rate of 85% [36], it was anticipated that around 15% of the participants will be lost after the first visit. Furthermore, we expected to lose an additional 10% due to preterm delivery and another 10% due to still birth. As such, the original sample size was inflated by 35% and the target sample size was determined at 270 pregnant women. We expect to retain around 65% of the participants at two years postpartum.

Study protocol

Assessments for this cohort were planned over six time-points, extending from late pregnancy till two years postpartum. The postpartum time-points were chosen in parallel with the immunization schedule in the UAE, when mothers are expected to visit the PHCs/MCHs to vaccinate their infants. The cohort assessments and timeline are detailed in Table 1. Data were collected via interviewer-administered questionnaires, anthropometric measurements, dietary records, bio-specimens (blood and breast milk) analyses and review of hospital electronic medical records. Data collection tools and methods are detailed below.

Questionnaires

Multi-component questionnaires used for this study were adapted from the MINA cohort study [25]. These are content-validated, culturally-adapted and pilot-tested questionnaires that were revised for use in this study among Emirati pregnant women. The Arabic version of the questionnaires were administered by trained research nutritionists.

Maternal sociodemographic characteristics and lifestyle: sociodemographic factors include age, nationality, place of residence, occupation, education, parity, and income. Lifestyle practices include physical activity, cigarette and shisha (narghile/water pipe) smoking. Physical activity was assessed using the Pregnancy Physical Activity Questionnaire (PPAQ) [37] during the third trimester of pregnancy, and the short International Physical Activity Questionnaire (IPAQ) [38] during postpartum. Metabolic equivalents (METs) were computed, and physical activity levels were classified as low, moderate or high-intensity. Maternal cigarette smoking dose will be assessed according to Bachir and Chaaya [39], maternal shisha smoking dose will be assessed according to Tamim et al. [40]. These questions were extended with one question inquiring about other smokers living in the same house.
Maternal dietary intake: maternal intake was evaluated using a culture-specific food frequency questionnaire (FFQ) and multiple-pass 24-hour dietary recalls. The used FFQ is a semi-quantitative questionnaire consisting of 89 items, grouped into 24 food categories comprehensively representing the Gulf and Middle Eastern cuisine. The 24-hour recalls were assessed using the United States Department of Agriculture’s Multiple Pass Food Recall (MPR), which attenuates recall bias [41,42]. For the FFQs and 24-hour recalls, participants were assisted with the reference portions of the two-dimensional food portion visual (Millen and Morgan, Nutrition Consulting Enterprises, Framingham, Massachusetts, United States).
as well as supplementary visual aids about portion sizes of common items in the traditional Gulf and Middle Eastern cuisine meals [43], to help estimating ingested quantities. Daily energy and nutrient intakes will be calculated using the food composition tables provided by the NUTRIONIST PRO™ diet analysis software (Axxya Systems LLC., USA, version 5.1.0, 2014, First Fata Bank, Nutritionist Pro, San Bruno, CA) and the food composition table of Middle Eastern foods for local and traditional dishes [44]. Supplement use were assessed via questions on the type, dose and frequency of used vitamins, minerals, herbal or other products.

**Infant feeding practices and dietary intake**: breastfeeding and complementary feeding practices will be assessed based on WHO indicators [45], and categorized as exclusive breastfeeding, predominant breastfeeding, or complementary feeding. In order to assess the infant’s complementary feeding, mothers will be asked about the timing of introduction and type of solid, semi-solid and soft foods. Minimum dietary diversity, minimum meal frequency, minimum acceptable diet, and consumption of iron-rich or iron-fortified foods will be assessed.

**Infant cognitive development**: assessed using the 12 and 24-month Ages and Stages Questionnaire (ASQ). The ASQ system is originally a parent-completed questionnaire but may also be completed by a professional interacting with the infant and the parent. The ASQ is a developmental screening tool, widely used in pediatric populations. It exhibits high measures of sensitivity, specificity, and reliability [46]. Total scores will be computed for communication, gross motor, fine motor, problem solving and personal-social areas, and assessed based on the cut-off values suggested by Squires and Bricker [47]. The Arabic versions provided by the publisher will be used.

**Anthropometry**

**Maternal anthropometric assessment**: height, weight, waist circumference and blood pressure were measured following standard techniques. Pre-pregnancy and post-partum weights were evaluated according to WHO classification criteria for BMI [48]. The rate of pregnancy weight gain was assessed according to the Institute of Medicine BMI criteria for pregnant women [49]. Waist circumference will be classified according to the International Diabetes Federation’s cut-off for abdominal obesity in females of Middle Eastern origin (≥80 cm) [50]. Percent body fat will be measured by bioelectrical impedance (Tanita WB 100A digital scale); values >32% will be classified as high [51]. Blood pressure will be evaluated according to the National Heart, Lung, and Blood Institute of the National Institute of Health criteria [52]; values of systolic (SBP) >140 mmHg or diastolic blood pressure (DBP) >90 mmHg indicate hypertension.

**Gestational Diabetes Mellitus (GDM)**: GDM was diagnosed according to the National Institute for Health and Care Excellence (NICE) Diabetes in Pregnancy [53] guidelines. Blood glucose was measured and analyzed at the PHC/MCHs. All participants did a 2-hour 75 g Oral Glucose Tolerance Test (OGTT) to test for GDM. The latter was defined as a 2-hour plasma glucose level ≥7.8 mmol/L (140 mg/dl). The results were obtained from the mothers’ medical record.

**Infant anthropometric assessment**: measurements of head circumference, length, weight and mid-upper arm circumference (MUAC) will be performed following standard techniques by nurses at the hospitals, PHCs/MCHs. Weight and length measurements will be used to assess stunting, wasting, underweight, overweight, and obesity, following WHO criteria on child growth standards [54]. The MUAC will be used to assess the infant’s nutritional status, following WHO and UNICEF criteria [55]; values <11.5 cm indicate severe under-nutrition.
(wasting), 11.5–12.5 cm indicate moderate under-nutrition, and >12.5 cm indicate that the infant is well nourished.

Biochemical assessments

**Blood profile**: maternal and infant biochemical assessments include fasting serum lipid profile (triglyceride, total cholesterol, high density lipoprotein (HDL) and low density lipoprotein (LDL)-cholesterol), glucose, insulin, high molecular weight (HMW) adiponectin, high-sensitivity C-reactive protein (hs-CRP), Tumor necrosis factor (TNF)-α and interleukin (IL)-6 and vitamin D. Following the delivery, maternal blood samples (10 mL) were collected by certified phlebotomists in appropriate test tubes, centrifuged and temporarily stored, within 30 minutes of collection, in hospital freezers (-80°C). Stored samples were transported monthly in an icebox from the hospitals to the University of Sharjah, Sharjah Institute for Medical Research (SIMR) Laboratories, for storage (-80°C) and analysis. During postpartum, at the 6th month-visit, maternal (10 mL) and infant (5 mL) blood samples will be collected, processed and aliquoted in PHCs/MCHs’ laboratories and transported directly to the SIMR laboratories in an icebox for storage and analysis.

**Breast milk profile**: the assessment includes proximate analysis, fatty acid, oligosaccharides, HMW adiponectin, hs-CRP, TNF-α, IL-6 and insulin and vitamin D. Breast milk samples (10 mL) will be collected, upon delivery and during 6 months postpartum, using commercially available electrical breast pumps by the mother or the nurse, and placed in sterile polypropylene tubes, which ensures the collection of fore, mid, and hind milk within each sample. The samples will be directly transported to the SIMR laboratories for storage (-80°C) and analysis.

Perinatal information

Perinatal information was obtained from the mother’s medical records at the hospital in which the delivery took place. These include occurrence of complications and GDM during pregnancy and delivery, delivery method, gestational age, date of delivery, sex, weight, length, and head circumference of infants.

Quality assurance procedures

Several quality control measures are undertaken to ensure validity and reliability of collected data. Prior to data collection, collectors followed extensive training on study procedures, standardization of data collection and minimization of interviewer bias, and were provided with a comprehensive operation manual. This training was done in collaboration with experts from the Department of Nutrition and Food Sciences at the American University of Beirut (AUB). Manuals describing data collection procedures were developed and administered to participating centers. Data collection instruments were identical in all sites and were calibrated. Quality checks are routinely conducted for entered data by trained research assistants and one statistician. Finally, since birth cohorts often face planning and implementation challenges [56,57], the MISC research team sought to document encountered challenges and addresses them in a systematic manner. The challenges were noted through weekly meetings with the research assistants, and discussions with the participants and the nurses in the PHCs/MCHs, and responding strategies were planned based on researchers’ experiences and implemented after discussions within the research team, consultations with key scholars and support by relevant literature.
Statistical analysis

Collected data are entered and analyzed using the Statistical Package for the Social Sciences (SPSS) software version 21.0. Six categories of variables are planned to be generated: maternal factors, pregnancy complications, birth outcomes, dietary intake, feeding practices and infant factors. The normality of data for all variables will be examined using Shapiro-Wilk test. For normally distributed continuous variables, means and standard deviations will be presented, and Student’s t test will be used. For skewed data, medians and interquartile ranges will be generated and Mann-Whitney U test will be performed. For categorical variables, frequencies will be presented, and Pearson Chi-square and Fisher’s Exact tests will be used, as appropriate. The associations between the variables will be examined using multiple linear regressions when the outcome of interest is continuous, and logistic regressions when the outcome considered is categorical. As a first step, the outcome variables will be cross-tabulated against potential confounders; those with p-values <0.2 will be entered into the model. A p-value <0.05 indicates statistical significance.

Finally, a comparative analysis is planned for baseline sociodemographic characteristics and exposures of participants who remained in the cohort and those who were lost to follow-up. If both groups are found to be similar, it is highly plausible that participants who finished the study and based on whom the conclusions will be generated are representative of the population who enrolled in the cohort. If significant differences are found with respect to main assessed factors, minimum requirements for addressing attrition will be reported [58] and alternative analytical approaches will be used to handle missing values of participants who were lost to follow-up [59].

Results

Participants’ characteristics

420 pregnant women in their third trimester were invited to participate, and 266 accepted to enroll (63.3%). As reasons for non-enrolment, our record showed that 36% (55/154) were not interested, 27% (42/154) declined due to the long duration of the cohort, and 20% (31/154) refused to enrol due to husband disapproval, while the remaining 17% (26/154) did not enrol because of blood collection. Ten mothers, who initially agreed to enroll, had to be excluded, since they had to leave before completing the baseline questionnaire due to time constraints. They did not differ in their characteristics from the other participants. Only 256 mothers completed the baseline questionnaire. Their baseline characteristics are shown in Tables 2 and 3. The mean age of the participants was 30.5±6.0 years, more than half of them were non-Emirati and the majority were university graduates and not employed. The majority of our starting sample was multiparous (76.6%) and up to 60% were either overweight or obese before they were pregnant. All except 7 were non-smokers (97.2%); however, 105 (40.5%) were subject to passive smoking. The prevalence of GDM was 19.2%. Between inclusion and delivery, 48 women were lost to follow-up, resulting in 208 women-infant pairs (dropout rate: 18.7%). The mean gestational age at delivery was 38.7±1.5 weeks. One-third of the infants were delivered by caesarean section, and about half of the newborns were boys. Finally, 5.3% and 5.7% of pregnancies resulted in low birthweight and macrosomia, respectively (Table 4).

Challenges and responding strategies

First, we underestimated the number of required staff and we faced a high turnover of trained research assistants that could not be easily replaced. This resulted in supplementary training sessions for newly recruited agents, time delays, and additional costs. Furthermore, data
collection used interviewer-administered questionnaires, which is resource-intensive, in terms of human capital, cost and time. Second, the recruitment was limited by the participants’ concerns of study duration or lack of interest. Also, some mothers were reluctant to enroll before obtaining their husband’s approval. To develop and maintain confidence and familiarity between the participants and research team, we established a nurse-liaison in each participating center, where a key nurse acted as a facilitator between involved parties (research assistants, PHCs/MCHs administration, and participants). Third, data collection at delivery was extremely challenging. Same-day discharge and shortened post-delivery hospital stays offered limited time to collect information and samples from mothers and neonates at the hospital. In response, we adopted a daily tracking of participants approaching their due dates. Despite this, some women were missed at delivery or discharge. Participant retention was also critical. Common reasons for attrition were the inability to locate participants usually due to disconnected communication, lack of interest of some participants and husbands’ disapprovals. Several actions were taken to enhance retention, such as offering incentives (e.g. gift vouchers, infant toiletries...), obtaining other contact detail information for participants who consistently did not answer phone calls, and maintaining communication with the participants through phone calls or text messages. Moreover, we highlight the importance of discussing and negotiating the research details with the husbands in order to enhance their understanding of the study’s significance, and their approval to their wives’ participation.

Blood collection, especially from infants, was our biggest anticipated challenge. It was sometimes surrounded by technical difficulties and parents’ refusals. When needed,

| Table 2. Baseline sociodemographic characteristics of study participants. |
|-----------------------------|------------------|------------------|
| Sociodemographic characteristics of pregnant women (n = 256) | N(%) |
| **Nationality** | |
| Arab Emirati | 105(41.0) |
| Arab non-Emirati | 151(59.0) |
| **Age of women (years)** | |
| <25 | 57(22.3) |
| 25–29.9 | 62(24.2) |
| ≥30 | 137(53.5) |
| **Education level** | |
| Intermediate or less | 35(13.7) |
| High school/Technical Diploma | 140(54.7) |
| University | 81(31.6) |
| **Family monthly income (AED)** | |
| <5,000 | 18(7.0) |
| 5,000–10,000 | 72(28.1) |
| >10,000 | 103(40.2) |
| Does not know/Refused to answer | 63(24.6) |
| **Employment status** | |
| Housewife | 211(82.4) |
| Employee | 45(17.6) |
| **Maternity leave** | |
| 1 month | 14(5.5) |
| 2 months | 18(7.0) |
| 3 months | 9(3.5) |
| Does not know | 4(1.5) |

https://doi.org/10.1371/journal.pone.0198278.t002
specialized pediatric nurses were hired to perform blood withdrawal. Finally, maintaining the quality of collected data is an ongoing challenge, requiring a rigorous information system, periodic data tracking and quality check, and unanimous adaptation of pre-specified data collection and management protocols (Table 5).

**Discussion**

This article described the details of the methodology and the challenges as well the baseline characteristics of the participants in the MISC cohort study. The MISC is the first effort in the UAE, and among the very first research projects in the Arab world, to prospectively address key questions related to women and children’s health. Being a longitudinal study, the MISC runs the advantage of providing descriptive, as well as etiological information. Accordingly, it is anticipated to generate results that overcome available evidence in the UAE, which is mostly focused on adults and limited by its cross-sectional nature.

Existing and planned birth cohort studies are urged to encourage implementation experience and data sharing to leverage the initial investment required to establish these cohorts and

---

**Table 3. Baseline clinical characteristics and practices during pregnancy of study participants.**

| Maternal clinical characteristics (n = 256) | N(%) or Mean±SD |
|-------------------------------------------|-----------------|
| **Parity**                                |                 |
| Primiparous                               | 60(23.4)        |
| Multiparous                               | 196(76.6)       |
| **Pre-gestational BMI (Kg/m²)**           |                 |
| Underweight                               | 11(4.3)         |
| Normal Weight                             | 93(36.3)        |
| Overweight                                | 76(29.7)        |
| Obese                                     | 76(29.7)        |
| **Blood pressure (mm Hg)**                |                 |
| Systolic blood pressure                   | 113.7±10.5      |
| Diastolic blood pressure                  | 66.1±8.5        |
| **GDM**                                   |                 |
| Yes                                       | 49(19.2)        |
| No                                        | 207(80.8)       |
| **Practices during pregnancy (n = 259)**  |                 |
| Smoking                                   |                 |
| Non-smoker                                | 249(97.3)       |
| Smoker                                    | 7(2.7)          |
| Smoking among family members              |                 |
| Husband                                   | 94(36.7)        |
| Other family member                       | 11(4.3)         |
| **Physical activity (METs)**              |                 |
| Low intensity activity                    | 137(53.5)       |
| Moderate intensity activity               | 59(23.1)        |
| High intensity activity                   | 31(12.1)        |
| No physical activity                      | 29(11.3)        |
| **Vitamin/mineral supplements**           |                 |
| Yes                                       | 218(85.2)       |
| No                                        | 38(14.8)        |

BMI: body mass index; GDM: gestational diabetes mellitus; MET: metabolic equivalents

https://doi.org/10.1371/journal.pone.0198278.t003
enable cross-comparisons. This contributes to the efforts aiming to advance scientific knowledge and practice from a local to global levels. The MISC joins regional and international birth cohort studies endeavors investigating early metabolic programming of lifelong health. Specifically, a comparison of country-specific results within the Arab region is planned with the Mother and Infant Nutritional Assessment (MINA) cohort study [25]. Moreover, the MISC will collaborate with ongoing international birth cohorts through networking, data sharing and pooling, by being part of the Birth Cohort Consortium of Asia (BiCCA) (http://www.bicca.org/).

Our findings are expected to critically inform the design of sustainable, effective and cost-effective interventions aiming to promote infant health. The MISC goes hand in hand with the governmental vision and national efforts aiming to promote and enforce the implementation of international guidelines on infant and young children feeding in the UAE, in particular the WHO and UNICEF Baby Friendly Hospital initiative (WHO/UNICEF BFHI) [60] and Infant and Young Child Feeding (IYCF) [61]. Within this scope, the findings of the project are also much needed to advocate for the implementation of supportive policies for women during lactation and early childhood, such as adequate maternity leave, breastfeeding breaks and flexibility. Finally, the MISC intends to generate information that could eventually be used to curb the NCD epidemic in future generations, thus reduce pertaining preventable morbi-mortality burden. This is in line with global [62], regional [31], and national [32] agendas.

The preliminary results reveal that our sample is skewed towards housewives, multiparous, well educated, from economically well-off households, and vaginally delivering women. All of which are documented predictors of the duration and exclusivity of breastfeeding in the UAE [30]. Furthermore, our preliminary results showed that 29.7% were overweight and 29.7% were obese before pregnancy. These percentages are below previous estimates among adult Emirati females (overweight: 31.4% and obesity: 34.2%) [27]. It is arduous to compare our sample with those of the general population of Arab women of childbearing age and their

| Table 4. Baseline delivery and infant characteristics. |
|------------------------------------------------------|
| **Delivery characteristics (n = 208)** * | N(%) or Mean±SD |
| **Complications during pregnancy** | |
| No | 164(78.8) |
| Yes | 44(21.2) |
| **Type of delivery** | |
| Normal | 139(66.8) |
| Caesarean section | 69(33.2) |
| **Gestational age at delivery (weeks)** | 38.7±1.5 |
| **Infant characteristics (n = 208)** * | N(%) or Mean±SD |
| **Sex** | |
| Male | 117(56.3) |
| Female | 91(43.7) |
| **Birth head circumference (cm)** | 34.2±1.3 |
| **Birth length (cm)** | 50.1±2.3 |
| **Birth weight** | |
| Low weight (<2.5 Kg) | 11(5.3) |
| Normal weight (2.5–4.0 Kg) | 185(89.0) |
| Macrosomia (>4.0 Kg) | 12(5.7) |

*Date of running analysis: There were 208 delivered women out of 256 pregnant women
offspring in the country, mostly due to the lack of pertaining published data. The prevalence of GDM among participants (18.9%) falls within global estimates (<1%-28%) [63], and within those reported from the UAE (7.9%-24.9%) [64]. This prevalence is however different than rates reported from other countries, i.e. 24% in Saudi Arabia [65] and 16.3% in Qatar [66]. Benchmarking against other studies is challenging, taking the diversity of definitions used to diagnose GDM [67]. While we acknowledge these limitations, we do not expect them to hinder the interpretation of our data, since we aim in this cohort to longitudinally investigate

### Table 5. The MISC: Challenges and responding strategies.

| Challenges                                      | Responding strategies                                                                 |
|-------------------------------------------------|----------------------------------------------------------------------------------------|
| Launching the cohort                            |                                                                                       |
| Underestimating number of staff required         | Ongoing hiring and training                                                            |
| High turnover of research assistants             | Supplementary training (time/cost implications)                                        |
| Participant recruitment                         |                                                                                       |
| Concerns of study duration                       | Establishing nurse-liaison (maintain confidence and familiarity between involved parties) |
| Lack of interest                                 |                                                                                       |
| Reluctance to enroll before obtaining husband’s approval |                                                                                   |
| Data collection                                  |                                                                                       |
| Notification of delivery often overlooked         | Daily tracking of participants approaching due dates                                  |
| Same-day discharge, shortened post-delivery stays (limited time to collect information and samples at the hospital) | Providing the mothers with necessary supplies and instructions on sample collection at home and arranging a pick-up the next day |
| Milk supply is not fully developed               |                                                                                       |
| Difficulty to provide milk with a pump           |                                                                                       |
| Blood collection (especially from infants)       | Recruiting specialized pediatric nurses                                               |
| Technical difficulties/Parental refusal          |                                                                                       |
| Quality assurance                                | Rigorous information system infrastructure                                           |
|                                                                                           | Periodic data tracking and quality check                                               |
|                                                                                           | Unanimous adaptation of pre-specified data collection and management protocols         |
| Data collection using interviewer-administered questionnaire (resource-intensive) | Relocate additional cost                                                               |
| Participant retention                           |                                                                                       |
| Participant fatigue                              | Maximize participant convenience:                                                    |
|                                                                                           | Efficiency in data collection (challenging with multi-component questionnaires)         |
|                                                                                           | Flexibility of data collectors to commute between study sites at convenient times for participants |
| Missed appointments and late arrivals            | Reminders through direct communication at each data collection time-point               |
| Lack of interest                                 | Maintaining communication (phone calls/messages)                                       |
| Husbands’ reluctance                            | Offering incentives                                                                  |
|                                                                                           | Involve the husbands in research details and raise their awareness                   |
| Repeatedly missed appointments                   | Obtaining other contact detail information                                             |
|                                                                                           | Repeated efforts for restoring communication                                           |
|                                                                                           | Rescheduling the infant vaccination appointment to increase convenience to the mothers (within acceptable dates for vaccinations) |
| Exclusion                                        |                                                                                       |
| Methodological considerations                    |                                                                                       |
| Potential unequal distribution of confounders and inherent dissimilarities between-groups | Collecting data relating to numerous potential confounders                             |
|                                                                                           | Careful control through statistical analyses                                           |
| Potential differential loss to follow-up         | Comparative analysis of baseline and last-observation characteristics between attired/retained participants |
| Limited ability to generalize the results to non-Arab residents                            | Priority of obtaining ethnic-specific data due to current lack of evidence             |

https://doi.org/10.1371/journal.pone.0198278.t005
determinants of infant health and early-life cues of NCDs, rather than generating national prevalence of breastfeeding, NCDs or their risk factors.

Strength and limitations

The MISC is a longitudinal study integrated within the healthcare system, rather than operating in the idealized experimental environment, consequently allowing the generation of “real life” data [68] in an ethical and practical fashion. The study entails comprehensive and systematic prospective quantitative assessments of mothers and children. It provides an all-inclusive analysis of the determinants of pregnancy, birth, mothers and children’s hard and proxy outcomes, without recurring to participant recall, and allows the suggestion of a clear temporal sequence between exposures and outcomes. Another strength of this study is the adoption of culturally-adapted data collection tools. Furthermore, the interviewer-administered questionnaires used in this study are expected to provide consistency and clarity in the administration and understanding of questions, unlike self-administered questionnaires.

The MISC aims to explore new perspectives in “fetal programming” and management of NCDs. Specifically, the MISC is first to explore the effect of early-life exposures on the cognitive development of young Arab children and is expected to enrich existing international evidence [69–71]. In addition, the MISC addresses numerous novel biomarkers, and pioneers in exploring these biomarkers specifically in children, by correlating maternal milk and blood biomarkers with infant blood biomarkers and immediate outcomes, in people with Arab ethnicity. Accordingly, results from the MISC complement the international evidence on the association between maternal and infant biomarkers and their effects on infant physiology [72–74]. In particular, the MISC will evaluate the specific short-term effects of lactation on maternal body composition (adiposity), as well as maternal and child cardio-metabolic homeostasis, and anti- and pro-inflammatory biomarkers. If lactation is found to exert beneficial metabolic and cognitive effects, then the translation of the findings from the MISC may have a significant public health impact. Lactation promotion is expected to be a low-cost, feasible strategy for the prevention of NCDs and promotion of intergenerational health [75,76].

The findings of MISC may be applicable to other country members of the Gulf Cooperation Council, exhibiting similar cultural, social and economic characteristics, and are similarly struggling to contain and mitigate the NCDs epidemic. Finally, the MISC design and measurements are consistent with those of other regional and international birth cohorts. This is expected to facilitate comparisons across-studies and improve the power to identify predictors of health and disease among infants.

As for the limitations, first, since mothers were not randomly assigned to different exposure groups, unequal distribution of confounders between-groups of comparison, and inherent dissimilarities relating to the mothers’ choice of specific behaviors might lead for possible biases. Therefore, we collected data relating to numerous potential confounders, and we planned to control for them through statistical analyses. This shall minimize bias from reverse causation or unmeasured confounding and might provide a robust alternative to the randomization of mothers which is unlikely to be feasible or ethical. Second, we could not collect information about non-enrollees because they did not consent to participate in the study. It would have been interesting to compare their characteristics with the participants to identify potential biases in recruitment. However, we do not expect to have major differences regarding their characteristics that could influence our results. Future cohorts could benefit from our experience in this regard, and not oversee this limitation. Furthermore, differential loss to follow-up could introduce bias. Subsequently, we planned for a comparative analysis of baseline and last-observation characteristics between women (and their children, where applicable) who attrited.
and those who completed the cohort. Finally, the exclusion of non-Arab women limits our ability to generalize our results to the population residing in the UAE. However, we only included Arab women to avoid any ethnic variability in the evaluation of adiponectin, as well as its relationship with other biomarkers [77–80]. We prioritized this issue over the possibility of generalizing our findings, taken the lack of available evidence related to adiponectin.

Finally, the implementation of this cohort was subject to many logistical, methodological and sociocultural challenges that required tailored remedial strategies. Many of these challenges are common to birth cohorts [56,81,82]. At this stage, we recommend that the complex ethical issues involved in conducting a birth cohort, must be carefully considered. Moreover, the necessary start-up time, staff, and costs must not be underestimated and funding of extra costs relating to logistical complexity and added expenses must be accounted for. Moreover, it is recommended that future cohort studies actively include the father as a participant, and examine the paternal factors that contribute to NCDs in infants. This is suggested to strengthen the study scientifically and logistically.

**Conclusion**

The present article details the design and methodology of one of the first birth cohorts in the Arab region. It is also the first documentation of practical strategies used to conduct a birth cohort in the UAE. Since “new birth cohort studies are a resource for the present as well as the future” [83], the MISC is intended to enhance our understanding of predictors of infant health and early-life cues of NCDs. It is also intended to be the backbone for the development of country-specific nutritional guidelines during gestation and childhood, and a basis for the implementation of public health initiatives aiming to promote maternal and infant health and curb the NCDs epidemic. The MISC attempts to be a model for future cohort studies in the region in terms of design, conduct, reporting and public health advocacy.

**Acknowledgments**

We are extremely grateful to the participants involved in the MISC cohort for their time and dedication. We are thankful to the research team and research assistants especially, Noor Chehayber, Shaima Hachem, and Rana Al Al Alami for their sincere work and enthusiasm in recruitment and data collection. We deeply appreciate the support and help of the directors, nurses, phlebotomists, and clerks in the Al Baraha, Al Qassimi, Khalifa Ajman hospitals, MCH and PHC clinics in Sharjah, Dubai, and Ajman. We thank Ms. Nada Adra for her technical and statistical assistance. We are gratitude to Medala for their support and help and a very special thanks to the Sharjah Baby Friendly Office director and staff for their support to the MISC research project.

**Author Contributions**

**Conceptualization:** Hadia Radwan, Mona Hashim, Reyad Shaker Obaid, Hayder Hasan, Farah Naja, Hessa Al Ghazal, Hamid Jan Jan Mohamed.

**Data curation:** Hadia Radwan, Mona Hashim, Reyad Shaker Obaid, Hayder Hasan, Farah Naja, Hessa Al Ghazal, Hamid Jan Jan Mohamed, Rana Rizk, Marwa Al Hilali, Rana Rayess, Ghamra Izzaldin.

**Formal analysis:** Hadia Radwan, Mona Hashim, Hayder Hasan.

**Funding acquisition:** Hadia Radwan.
Investigation: Hadia Radwan, Reyad Shaker Obaid, Farah Naja, Hessa Al Ghazal, Marwa Al Hilali, Rana Rayess, Ghamra Izzaldin.

Methodology: Hadia Radwan, Mona Hashim, Reyad Shaker Obaid, Hayder Hasan, Hamid Jan Jan Mohamed.

Project administration: Hadia Radwan.

Resources: Hadia Radwan, Reyad Shaker Obaid, Hessa Al Ghazal, Hamid Jan Jan Mohamed, Marwa Al Hilali, Rana Rayess, Ghamra Izzaldin.

Software: Hayder Hasan, Rana Rizk.

Supervision: Hadia Radwan.

Validation: Hadia Radwan.

Writing – original draft: Hadia Radwan, Mona Hashim, Rana Rizk.

Writing – review & editing: Hadia Radwan, Mona Hashim, Reyad Shaker Obaid, Hayder Hasan, Farah Naja, Hessa Al Ghazal, Hamid Jan Jan Mohamed, Rana Rizk.

References

1. Beckhaus AA, Garcia-Marcos L, Forno E, Pacheco-Gonzalez RM, Celedon JC, Castro-Rodriguez JA. Maternal nutrition during pregnancy and risk of asthma, wheeze, and atopic diseases during childhood: a systematic review and meta-analysis. Allergy. 2015; 70: 1588–1604. https://doi.org/10.1111/all.12729 PMID: 26296633

2. Blake-Lamb TL, Locks LM, Perkins ME, Woo Baidal JA, Cheng ER, Taveras EM. Interventions for childhood obesity in the first 1,000 days a systematic review. Am J Prev Med. 2016; 50: 780–789. https://doi.org/10.1016/j.amepre.2015.11.010 PMID: 26916260

3. WHO Regional Office for Europe. Good Maternal Nutrition The best start in life. Copenhagen: World Health Organization; 2016.

4. Ramakrishnan U, Grant F, Goldenberg R, Zongrone A, Martorell R. Effect of women’s nutrition before and during early pregnancy on maternal and infant outcomes: A systematic review: Periconceptual nutrition and maternal and infant outcomes. Paediatr Perinat Epidemiol. 2012; 26: 285–301.

5. Siega-Riz AM, Viswanathan M, Moos MK, Deierlein A, Mumford S, Knaack J, et al. A systematic review of outcomes of maternal weight gain according to the Institute of Medicine recommendations: birthweight, fetal growth, and postpartum weight retention. Am J Obstet Gynecol. 2009; 201: 339.e1–339.e14.

6. Zhou W, Hong Q, Sun X, Yang S, Hao Y. The independent and joint associations of maternal pre-pregnancy body mass index and gestational weight gain with macrosomia: systematic review and meta-analysis. Int J Clin Exp Med. 2016; 9: 22931–22947.

7. Horta BL, Victora CG. Long-term effects of breastfeeding—a systematic review. World Health Organization. 2013. http://biblio.sztataszert.hu/long-term_effects_of_breastfeeding_who_2013

8. Woo Baidal JA, Locks LM, Cheng ER, Blake-Lamb TL, Perkins ME, Taveras EM. Risk factors for childhood obesity in the first 1,000 days. Am J Prev Med. 2016; 50: 761–779. https://doi.org/10.1016/j.amepre.2015.11.012 PMID: 26916261

9. Victora CG, Bahl R, Barros AJD, Franca GVA, Horton S, Krarup J, et al. Breastfeeding in the 21st century: Epidemiology, mechanisms, and lifelong effect. Lancet. 2016; 387: 475–490. https://doi.org/10.1016/S0140-6736(15)01024-7 PMID: 26689575

10. Chivers P, Hands B, Parker H, Buisara M, Beilin LJ, Kendall GE, et al. Body mass index, adiposity rebound and early feeding in a longitudinal cohort (Raine Study). Int J Obes. 2010; 34: 1169–1176.

11. World Health Organization. Exclusive breastfeeding. World Health Organization. 2017. http://www.who.int/nutrition/topics/exclusive_breastfeeding/en/

12. Koletzko B, Brands B, Chourdakis M, Cramer S, Grote V, Hellmuth C et al. The power of programming and the early nutrition project: Opportunities for health promotion by nutrition during the first thousand days of life and beyond. Ann Nutr Metab. 2014; 64: 187–196.
13. Gaillard R, Steegers EAP, Franco OH, Hofman A, Jaddoe VWV. Maternal weight gain in different periods of pregnancy and childhood cardio-metabolic outcomes. The Generation R Study. Int J Obes. 2015; 39: 677–685.

14. Barker DJP. The developmental origins of adult disease. J Am Coll Nutr. 2004; 23(Suppl 6): 588S–595S.

15. Gluckman PD, Hanson MA, Buklijas T. A conceptual framework for the developmental origins of health and disease. J Dev Orig Health Dis. 2010; 1: 6–18. https://doi.org/10.1017/S2040174409990171 PMID: 25142928

16. Langley-Evans SC. Developmental programming of health and disease. Proc Nutr Soc. 2006; 65: 97–105. PMID: 16441949

17. Manolio TA, Bailey-Wilson JE, Collins FS. Genes, environment and the value of prospective cohort studies. Nature Rev Genet. 2006; 7: 812–820. https://doi.org/10.1038/nrg1919 PMID: 16983377

18. Goldberg J, Jones R, Bruner MN, Pronczuk J. Why carry out a longitudinal birth survey? Paediatr Perinat Epidemiol. 2009; 23: 1–14. https://doi.org/10.1111/j.1365-3016.2008.01009.x PMID: 19490440

19. Knox SS, Echeverria D. Methodological issues related to longitudinal epidemiological assessment of developmental trajectories in children. J Epidemiol Community Health. 2009; 63(Suppl 1): i1–i3.

20. Campbell A, Rudan I. Systematic review of birth cohort studies in Africa. J Global Health. 2011; 1: 46–51.

21. Loy SL, Hamid Jan JM. The Universiti Sains Malaysia Pregnancy Cohort Study: Maternal-infant adiposity development until the first year of life. Health Environ J. 2014; 5: 50–64.

22. Victora CG, Hallal PC, Araujo CL, Menezes AM, Wells JC, & Barros FC. Cohort Profile: The 1993 Pelotas (Brazil) Birth Cohort Study. Int. J. Epidemiol. 2008; 37(4):704–709. https://doi.org/10.1093/ije/dyn177 PMID: 17646051

23. AlSeaidan M, Al Wotayan R, Christophi CA, Al-Makhseed M, Abu Awad Y, Nassan F, et al. Birth Outcomes in a Prospective Pregnancy–Birth Cohort Study of Environmental Risk Factors in Kuwait: The TRACER Study. Paediatr Perinat Epidemiol. 2016; 30: 408–417. https://doi.org/10.1111/ppe.12296. PMID: 27193754

24. AlNaja F, Nasreddine L, Al Thani AA, Yunis K, Clinton M, Nassar A, et al. Study protocol: Mother and Infant Nutritional Assessment (MINA) cohort study in Qatar and Lebanon. BMC Pregnancy Childbirth. 2016; 16: 98. https://doi.org/10.1186/s12884-016-0864-5. PMID: 27146913

25. AlNaja F, Nasreddine L, Al Thani AA, Yunis K, Clinton M, Nassar A, et al. Study protocol: Mother and Infant Nutritional Assessment (MINA) cohort study in Qatar and Lebanon. BMC Pregnancy Childbirth. 2016; 16: 98. https://doi.org/10.1186/s12884-016-0864-5. PMID: 27146913

26. Ng SW, Zaghloul S, Ali H, Harrison G, Yeatts K, El Sadig M, et al. Nutrition transition in the United Arab Emirates. Eur J Clin Nutr. 2011; 65: 1328–1337. https://doi.org/10.1038/ejcn.2011.135 PMID: 21772317

27. WHO Regional Office for the Eastern Mediterranean. Plan of action for the prevention and control of noncommunicable diseases in the Eastern Mediterranean Region. Cairo: World Health Organization. 2011.

28. World Health Organization. Noncommunicable Diseases (NCD) Country Profiles, 2014. United Arab Emirates. World Health Organization. Retrieved 12 May 2017, from http://www.who.int/nmh/countries/uae_en.pdf.

29. Al Tajir GK, Sulieman H, Badrinath P. Intragroup Differences in Risk Factors for Breastfeeding Outcomes in a Multicultural Community. J Hum Lact. 2006; 22: 39–47. https://doi.org/10.1177/08903344050283626. PMID: 16467286

30. Radwan H. Patterns and determinants of breastfeeding and complementary feeding practices of Emirati Mothers in the United Arab Emirates. BMC Public Health. 2013; 13: 171. https://doi.org/10.1186/1471-2458-13-171 PMID: 23442221

31. WHO Regional Office for the Eastern Mediterranean. Plan of action for the prevention and control of noncommunicable diseases in the Eastern Mediterranean Region. Cairo: World Health Organization. 2011.

32. UAE Vision. World-Class Healthcare | UAE Vision 2021. Vision2021.ae. 2017. Retrieved 12 May 2017, from https://www.vision2021.ae/en/national-priority-areas/world-class-healthcare

33. Ben-Shlomo Y, Kuh D. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges, and interdisciplinary perspectives. Int. J. Epidemiol.2002; 31: 285–293. PMID: 11980781

34. Ng J W, Barrett L M, Wong A, Kuh D, Smith G D, Relton C L. The role of longitudinal cohort studies in epigenetic epidemiology: challenges and opportunities. Genome Biology. 2012; 13: 246. PMID: 22747587
35. Kristman V, Manno M, Côté P. Loss to Follow-Up in Cohort Studies: How Much is Too Much? Eur. J. Epidemiol. 2003; 19: 751–760. https://doi.org/10.1023/B:EJEP.0000036668.02655.f8

36. Gracie SK, Lyon AW, Kehler HL, Pennell CE, Dolan SM, McNeil DA, et al. All Our Babies Cohort Study: recruitment of a cohort to predict women at risk of preterm birth through the examination of gene expression profiles and the environment. BMC Pregnancy Childbirth. 2010; 10: 87. https://doi.org/10.1186/1471-2393-10-87 PMID: 21192811

37. Chasan-Taber L, Schmidt MD, Roberts DE, Hosmer D, Markenson G, Freedson PS. Development and Validation of a Pregnancy Physical Activity Questionnaire: Medicine & Science in Sports & Exercise. 2004; 36: 1750–1760. https://doi.org/10.1249/01.MSS.0000142303.49306.0D

38. The IPAQ Group. Downloadable questionnaires—International Physical Activity Questionnaire. 2014. Sites.google.com. Retrieved 12 May 2017, from https://sites.google.com/site/theipaq/questionnaire_links

39. Bachir R, Chaaya M. Maternal Smoking: Determinants and Associated Morbidity in Two Areas in Lebanon. Matern Child Health J. 2008; 12: 298–307. https://doi.org/10.1007/s10995-007-0242-z PMID: 17587161

40. Tamim H, Yunis K, Chemaitelly H, Alameh M, Nassar A, National Collaborative Perinatal Neonatal Network Beirut, Lebanon. Effect of narghile and cigarette smoking on newborn birthweight. BJOG: An International Journal of Obstetrics & Gynaecology. 2007; 115: 91–97. https://doi.org/10.1111/j.1471-0528.2007.01568.x

41. Moshfegh AJ, Rhodes DG, Baer DJ, Murayi T, Clemens JC, Rumpler WV, et al. The US Department of Agriculture Automated Multiple-Pass Method reduces bias in the collection of energy intakes. Am J Clin Nutr. 2008; 88: 324–332. https://doi.org/10.1093/ajcn/88.2.324 PMID: 18669367

42. Raper N, Perluff B, Ingwersen L, Steinfeldt L, Anand J. An overview of USDA’s Dietary Intake Data System. J. Food Comp. Anal. 2004; 17: 545–555. https://doi.org/10.1016/j.jfca.2004.02.013.

43. Abu Dhabi Food Control Authority. A Photographic Atlas of Food Portions for the Emirate of Abu Dhabi. User’s Guide. Abu Dhabi: 2014. Abu Dhabi Food Control Authority.

44. Nasreddine L, Hwalla N, Sibai A, Hamze M, Parent-Massin D. Food consumption patterns in an adult urban population in Beirut, Lebanon. Public Health Nutr. 2006; 9: 194–203. https://doi.org/10.1079/PHN2005855. PMID: 16571173

45. World Health Organization. Indicators for assessing infant and young child feeding practices: part 1: definitions: conclusions of a consensus meeting held 6–8 November 2007 in Washington DC, USA.2008. Retrieved from http://apps.who.int/iris/handle/10665/43895

46. Velikonja T, Edbrooke-Chil ds J, Calderon A, Sleed M, Brown A, Deighton J. The psychometric properties of the Ages & Stages Questionnaires for ages 2–2.5: a systematic review: ASQ-3 TM and ASQ: SE systematic review. Child Care Health and Dev. 2017; 3: 1–17. https://doi.org/10.1111/cch.12397

47. Squires J, Bricker D. Ages & Stages Questionnaires[R], Third Edition (ASQ-3TM): A Parent-Completed Child-Monitoring System. Brookes Publishing Company; 2009.

48. World Health Organization. Obesity: Preventing and Managing the Global Epidemic. 2000 ( 1st ed.). Geneva.

49. Institute of Medicine. Weight Gain During Pregnancy: Reexamining the Guidelines. Washington, DC: The National Academies Press. 2009.

50. Grundy SM. Diagnosis and Management of the Metabolic Syndrome: An American Heart Association/ National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 2005; 112: 2735–2752. https://doi.org/10.1161/CIRCULATIONAHA.105.169404 PMID: 16157765

51. Lohman TG, Roche AF, Martorell R. Anthropometric standardization reference manual. Human Kinetics Books.1988. Retrieved from http://agris.fao.org/agris-search/search.do?recordID=US201300646503

52. NHLBI, NIH. High Blood Pressure in Pregnancy. Nhlbi.nih.gov.2017. Retrieved 12 May 2017, from https://www.nhlbi.nih.gov/health/resources/heart/hbp-pregnancy

53. The National Institute for Health and Care Excellence. Diabetes in pregnancy: management from pre-conception to the postnatal period. Guidance and guidelines. 2015. Nice.org.uk. Retrieved 12 May 2017, from https://www.nice.org.uk/guidance/ng3

54. World Health Organization. Training course on child growth assessment. Geneva: World Health Organization. 2008a.

55. World Health Organization, & UNICEF. WHO child growth standards and the identification of severe acute malnutrition in infants and children: a joint statement by the World Health Organization and the United Nations Children's Fund.2009. Retrieved from http://www.ncbi.nlm.nih.gov/books/NBK200775/

56. Eskenazi B, Gladstone EA, Berkowitz GS, Drew CH, Faustman EM, Holland NT, et al. Methodologic and Logistic Issues in Conducting Longitudinal Birth Cohort Studies: Lessons Learned from the Centers
for Children’s Environmental Health and Disease Prevention Research. Environmental Health Perspectives. 2005; 113(10): 1419–1429. https://doi.org/10.1289/ehp.7670. PMID: 16685053

57. Martin LJ, Woo JG, Geraghty SR, Altaye M, Davidson BS, Banach W, et al. Adiponec tin is present in human milk and is associated with maternal factors. Am J Clin Nutr. 2006; 83: 1106–1111. https://doi.org/10.1093/ajcn/83.5.1106 PMID: 1685053

58. Fewtrell MS, Kennedy K, Singhal A, Martin RM, Ness A, Hadders-Algra M, et al. How much loss to follow-up is acceptable in long-term randomised trials and prospective studies? Arch. Dis. Child. 2008; 93: 458–461. https://doi.org/10.1136/adc.2007.127316 PMID: 1849509

59. Geng EH, Glidden DV, Bangsberg DR, Bwana MB, Musinguzi N, Nash D, et al. A Causal Framework for Understanding the Effect of Losses to Follow-up on Epidemiologic Analyses in Clinic-based Cohorts: The Case of HIV-infected Patients on Antiretroviral Therapy in Africa. Am J Epidemiol. 2012; 175: 1080–1087. https://doi.org/10.1093/aje/kwr444 PMID: 22306557

60. World Health Organization. Baby-friendly Hospital Initiative.WHO.2017a. Retrieved 12 May 2017, from http://www.who.int/nutrition/topics/bfhi/en/

61. World Health Organization. Planning Guide for national implementation of the Global Strategy for Infant and Young Child Feeding. Geneva: World Health Organization.2007a.

62. World Health Organization. Global action plan for the prevention and control of noncommunicable diseases: 2013–2020. 2013. Retrieved from http://apps.who.int/iris/bitstream/10665/94384/1/9789241506236_eng.pdf

63. Jiwani A, Marseille E, Lohse N, Damm P, Kahn J G. Gestational diabetes mellitus: results from a survey of country prevalence and practices. J Matern Fetal Neonatal Med. 2012; 25: 600–610. https://doi.org/10.3109/14767058.2011.587921 PMID: 21762003

64. Agarwal M M, Dhatt G S, Punnose J, Koster G. Gestational diabetes: dilemma caused by multiple international diagnostic criteria. Diabet Med. 2005; 22: 1731–1736. https://doi.org/10.1111/j.1464-5491.2005.01706.x PMID: 16401320

65. Wahabi H, Fayed A, Esmaeil H, Mamdouh H, Kotb R. Prevalence and Complications of Pregestational and Gestational Diabetes in Saudi Women: Analysis from Riyadh Mother and Baby Cohort Study (RAHMA). BioMed Research International. 2017; 1–9. https://doi.org/10.1155/2017/6878263

66. Bener A. Prevalence of gestational diabetes and associated maternal and neonatal complications in a fast-developing community: global comparisons. Int J Womens Health. 2011; 3: 367–373. https://doi.org/10.2147/IJWH.S26094. PMID: 22140323

67. Agarwal M M, Dhatt G S, Shah S M. Gestational Diabetes Mellitus: Simplifying the International Association of Diabetes and Pregnancy diagnostic algorithm using fasting plasma glucose. Diabetes Care. 2010; 3: 2018–2020. https://doi.org/10.2337/dc10-0572.

68. Annemans L, Aristides M, Kubin M. Real-Life Data: A Growing Need. ISPOR.org.2007. Retrieved 12 May 2017, from https://www.ispor.org/news/articles/oct07/rld.asp

69. Innis SM. Impact of maternal diet on human milk composition and neurological development of infants. Am J Clin Nutr. 2014; 99: 734S–741S. https://doi.org/10.3945/ajcn.113.072595 PMID: 24500153

70. Kramer MS, Aboud F, Mironova E, Vanilovich I, Platt R W, Matush L, et al. Breastfeeding and child cognitive development: new evidence from a large randomized trial. Arch. Gen. Psychiatry. 2008; 65: 578–584. https://doi.org/10.1001/archpsyc.65.5.578 PMID: 18458209

71. Zeisel SH. Is maternal diet supplementation beneficial? Optimal development of infant depends on mother’s diet. Am J Clin Nutr.2009; 89: 685S–687S. https://doi.org/10.3945/ajcn.2008.26811F. PMID: 19116319

72. Anderson J, McKinley K, Onugha J, Duazo P, Chernoff M, Quinn EA. Lower levels of human milk adiponectin predict offspring weight for age: a study in a lean population of Filipinos: Human milk adiponectin and child growth in a lean population. Matern Child Nutr. 2016; 12: 790–800. https://doi.org/10.1111/mcn.12216

73. Savino F, Benetti S, Ligouri SA, Sorrenti M, Cordero Di Montezemolo L. Advances on human milk hormones and protection against obesity. Cell Mol Biol (Noisy-Le-Grand). 2013; 59: 89–98.

74. Savino F, Lupica M, Benetti S, Petrucci E, Ligouri S, Cordero Di Montezemolo L. Adiponectin in breast milk: relation to serum adiponectin concentration in lactating mothers and their infants: Adiponectin in mothers, breast milk and infants. Acta Paediatrica. 2012; 101: 1058–1062. https://doi.org/10.1111/j.1651-2227.2012.02744.x

75. Bhutta ZA, Das JK, Rizvi A, Gaffey MF, Walker N, Horton S, et al. Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? The Lancet.2013; 382: 452–477.

76. Pugh LC, Milligan RA, Frick KD, Spatz D, Bronner Y. Breastfeeding duration, costs, and benefits of a support program for low-income breastfeeding women. Birth. 2002; 29: 95–100 PMID: 12000411
77. Abu-Farha M, Behbehani K, Elkum N. High adiponectin levels in lean Arab women compared to Asian women. Biomarker Research. 2015; 3: 7. https://doi.org/10.1186/s40364-015-0032-5 PMID: 25905020

78. Ferris WF, Naran NH, Crowther NJ, Rheeder P, van der Merwe L, Chetty N. The Relationship between Insulin Sensitivity and Serum Adiponectin Levels in Three Population Groups. Horm Metab Res. 2005; 37: 695–701. https://doi.org/10.1055/s-2005-870580 PMID: 16308839

79. Hulver MW, Saleh O, MacDonald KG, Pories WJ, Barakat HA. Ethnic differences in adiponectin levels. Metabolism. 2004; 53: 1–3. https://doi.org/10.1016/j.metabol.2003.07.002 PMID: 14681833

80. Khoo CM, Sairazi S, Taslim S, Gardner D, Wu Y, Lee J, et al. Ethnicity Modifies the Relationships of Insulin Resistance, Inflammation, and Adiponectin With Obesity in a Multiethnic Asian Population. Diabetes Care. 2011; 34: 1120–1126. https://doi.org/10.2337/dc10-2097 PMID: 21464462

81. Lawrance M, Sayers SM, Singh GR. Challenges and strategies for cohort retention and data collection in an indigenous population: Australian Aboriginal Birth Cohort. BMC Med Res Methodol. 2014; 14: 31. http://doi.org/10.1186/1471-2288-14-31 PMID: 24568142

82. White E, Hunt JR, Casso D. Exposure measurement in cohort studies: the challenges of prospective data collection. Epidemiologic Review. 1998; 20: 43–56.

83. Lawlor DA. Intrauterine growth and intelligence within sibling pairs: findings from the Mater-University study of pregnancy and its outcomes. J Epidemiol Community Health. 2005; 59: 279–282. https://doi.org/10.1136/jech.2004.025262. PMID: 15767380