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Mutaba'ah: Mother and Child Health Study - Protocol for a prospective cohort study in Al Ain, United Arab Emirates

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ABSTRACT

Introduction: Early-life exposures, particularly environmental and parental lifestyle factors, have a major influence on children's health and development. Due to increasing interest in the early-life developmental origins of diseases, many birth cohorts have been established. These studies constitute a repository of data which researchers use over many years to investigate emerging research questions. However, no such databank or cohort study is available in the United Arab Emirates (UAE). This project aims to establish a prospective mother and child cohort study in Al Ain (Abu Dhabi, UAE) to investigate the maternal and early-life determinants of infant, child, adolescent, and maternal health of the Emirati population.

Methods and analysis: During the period 2017-2021, this study aims to recruit 10,000 pregnant women at approximately 12 weeks of gestation from hospitals and clinics in Al Ain city. For each mother/newborn pair, an initial dataset will be collected including anthropometric, physiological, and biochemical measurements, medical interventions, circumstances of pregnancy, delivery details, and neonatal and perinatal growth and health using a combination of questionnaires, interviews, and medical record extractions. Baseline data will act as the starting point from which the children will be followed up and re-surveyed at intervals throughout their life course until the age of 16 years, to explore how familial, socioeconomic, and lifestyle factors interact with genetic and environmental factors to influence health outcomes and achievements later in life.

Ethics and dissemination: Ethical approval has been granted by the United Arab Emirates University Human Research Ethics Committee and the ethical committees of the participating institutions. Results will be widely disseminated via peer reviewed manuscripts, conference presentations, media outlets and reports to relevant authorities.

ARTICLE SUMMARY

Strength and Limitations of this study

- This study is the first and largest mother and child cohort study to be established in Al Ain, Abu Dhabi, UAE
- The study will have a large sample size of 10,000 mothers and child dyads as well as a long follow up period (16 years).
- We intend to recruit pregnant women from the Emirati population who would be more likely to follow up till the Emirati children are 16 years of age
- Standardized scales and clinical assessments and records from hospitals are carefully designed to reduce any misreporting and ensure a large cohesive dataset
- We are not recruiting other expatriates as it might lead to a large amount of attrition, so the study may not be generalizable to populations elsewhere.

INTRODUCTION

Although the causes of non-communicable disease epidemics have not yet been fully determined, emerging evidence suggests causal associations between their occurrence and exposures during pregnancy and early-life (1, 2). The Developmental Origins of Health and Disease hypothesis speculates that the risk of chronic disease in adult life is related to biological programming of the fetus or infant in response to early environmental signals (3). Moreover, there is convincing evidence that physical and psychosocial exposures in the first months of life and later in childhood have important effects on health, well-being, and development during adolescence and adulthood (4-6). For instance, numerous studies have reported the beneficial effect of breastfeeding on some of the major components of the metabolic syndrome (i.e. obesity, blood pressure, cholesterol metabolism, and insulin resistance) and thereafter on the risk of cardiovascular disease (7, 8).

Research based on the available medical record systems or on cross-sectional data usually involve small samples of the general population with limited information on specific exposures and disease outcomes of interest. Firstly, this will significantly narrow exposure-outcome relationships. Secondly, these studies will face methodological and analytical problems of residual confounding due to the lack of data on other important lifestyle, socioeconomic, nutritional, physical, and environmental exposures not routinely captured in medical records. Therefore, new datasets that support research in a life course perspective are urgently needed. Datasets with rich information on exposures and outcomes, that include social and biological factors, can be used by researchers in different fields with widely different types of causal models to produce original research. For over half a century, there has been a proliferation of birth cohort studies fueled by the recognition of the importance of the *in utero* environment on health outcomes in later life (9). The main distinctive feature of a cohort study is the longitudinal follow-up time frame and the frequency of

the follow up that could be extended indefinitely (4). A longitudinal design allows the quantification of the temporal relationship between a specific exposure and outcome, observance of the natural history, and calculation of the incidence of a specific outcome. Despite the surge in the number of cohort studies, there is a lack of longitudinal studies in the United Arab Emirates (UAE) with follow-ups across the lifespan to help understand the etiology of numerous health conditions in the community.

This study protocol describes the research design and methods used to establish a large prospective cohort study focusing on maternal and child health in the UAE. This study aims to establish a prospective mother and child cohort study in Al Ain city to investigate the maternal, genetic, social, environmental, lifestyle, and other early childhood determinants of infant, child, and adolescent health, as well as the mother's health.

The study objectives are: i) identify and collect data on relevant exposures of the mother and child during pregnancy, delivery, and the post-natal period; ii) identify and collect relevant outcomes of the mother and child during delivery, post-natal period, and early life; iii) associate relevant exposures and health outcomes; and iv) establish a prospective and updated databank.

METHODS AND ANALYSIS

Study Design

Mutaba'ah, (meaning "follow up" in Arabic), the Mother and Child Health Study is a prospective cohort study in Al Ain city.

Study Setting

Al Ain is the second largest city in the Emirate of Abu Dhabi (the largest UAE emirate in terms of land mass and population size) and has the largest and relatively stable population of Emirati

citizens compared to other parts of the country. This makes it an ideal setting for a birth cohort study with longitudinal follow-ups. In 2016, the Emirate of Abu Dhabi population was estimated to be approximately 2.9 million, of which, less than 19% were Emiratis and around 41% of these Emiratis lived in the Al Ain region (10). The population of Al Ain is approximately 766,900 (mid-2016) of which 226,300 are Emirati citizens and of these 53,995 are women of reproductive age (15-44 years) (10). Levels and standards of antenatal care are high, and all births take place in hospital. Although this study has the potential to expand to involve many health institutions, the initial recruitment has been confined to three major hospitals in Al Ain: the only two public hospitals and one large private hospital; Al Ain Hospital, Tawam Hospital, and Oasis Hospital, respectively. As all of the Emirati population has full health insurance allowing them to have the same level of health care at any health facility, there is no difference in health care access between pregnant women attending these three hospitals and those who use other institutions. Therefore, a representative sample of the Emirati population in Al Ain can be recruited from these three hospitals.

Participants

The study aims to recruit 10,000 mother and baby pairs. Invitation for participation is limited to the Emirati population attending any of the above three hospitals for their antenatal care management, regardless of parity.

All invited participants will be at least 18 years old, resident in Al Ain, ideally in their first trimester (approximately 12 weeks of gestation) and be able to provide informed consent. Women who conceive multiple times during the study period, as well as their offspring will be included in the study so long as they provide consent. Women and their children can choose to withdraw from the study at any time. The study will exclude expatriates as they are less likely than the Emirati

population to be available for long-term follow-up. Women younger than 18 years, or those who have already delivered will also be excluded. Recruitment began in May 2017 and will proceed till 2021 or until the desired sample size has been reached. There are approximately 6,600 births of Emirati children each year in Al Ain, of which, the clear majority take place in the three participating hospitals. With the current participation rate of 80%, it is expected that over 6,000 pregnant women could realistically be recruited during the first two-year period with the remainder to be recruited in the third year of the study.

Eligible participants are identified via a health care provider (nurse or physician) at each hospital's registration point and are approached by an on-site research assistant with an information sheet detailing the project. If they express interest, participants provide informed consent. This consent allows for follow-up interviews and the extraction of their and their babies' health information from medical records up until the child is 16 years old. The study is conducted in accordance with the principles of the Declaration of Helsinki. Each participant has the right to withdraw from the study at any time without giving any reason. Should a participant wish to withdraw from the study, and wish for their collected data to be destroyed, this will be done in a prompt and secure manner and a message will be sent to the woman to confirm study withdrawal. The reason for withdrawal, if given, will be recorded in the database.

Patient involvement

Participants provide input during their recruitment process on their thoughts on how best to follow them and their children up after delivery, and how to access more participants. This information is usually collected verbatim by the data collectors or collected via administrative forms. Participants were not consulted about study outcomes or interpretation of the results.

Data sources and measurements

Collected data will include but are not limited to: demographic, socioeconomic, lifestyle, environmental, education, employment, physical and mental health, household and family information, parental health, social support, local community and services, mother and child nutrition, previous pregnancies and birth outcomes, health and development of child, and childcare information.

Data will be collected around the following time points: 12 weeks of gestation; 25 weeks of gestation; at the time of delivery; and at six and 12 months for the infants. Further time points for follow-up during childhood and adolescence will be decided later. In addition to data abstracted from the medical records (MR), data will be obtained using three tablet-assisted self-administered questionnaires; a short questionnaire (SQ), long questionnaire (LQ), and a food frequency questionnaire (FFQ). The research database will be linked using the medical record number and unique identification number assigned to each participant when consenting to the study. Medical records of the mother will provide information on the progress of the pregnancy, imaging and laboratory test results such as Complete Blood Counts (CBC) and Oral Glucose Tolerance Tests (OGTT). All medical outcomes will be ascertained from the woman's and child's medical records as standardized definitions are employed following the regulations and guidelines of the Department of Health of Abu Dhabi (11). Official birth notification and delivery records will provide data on the delivery and birth outcomes. Interviews using the infant questionnaire (IQ) will be conducted via follow-up hospital visits, home visits, or telephone when the child is six and 12 months old. In the future, we plan to collect data when the child is aged from five to 16 years using interviews or specifically designed child questionnaires (CQ) and adolescent questionnaires (AQ).

Table 1 shows examples of the types and sources of data collected during the study. The SQ is administered at the first point of contact and comprises 67 questions on varying socio-demographic and psychosocial measures. Questions were pooled and adapted from the Avon Longitudinal Study of Parents and Children (12), the Norwegian Mother and Child Study (13, 14), the Danish Birth Cohort Study (15), and the Born in Bradford study (16). The FFQ will be administered during the second or third trimester to ascertain diet, supplement intake, and herbal use during the pregnancy. The FFQ has been created and validated in the UAE (17).

The LQ will be a combination of questions asked in the four cohort studies previously mentioned that were used to develop the SQ as well. However, it will delve deeper into psychosocial dimensions of health including mental health using scales such as the Edinburgh Depression Scale (18) and the Spielberger State Trait Anxiety Inventory (19). All questionnaires were translated from English to Arabic by one group of study researchers and then back translated from Arabic to English by a different group of study researchers.

During childhood and adolescence, we will use previously validated measures such as the Childhood Trauma Questionnaire (20), Adverse Child Experiences (21), a child-relevant FFQ (22), and the Physical Activity Questionnaire for Older Children (PAQ-C) and Physical Activity Questionnaire for Adolescents (PAQ-A) (23).

Clinical data will be abstracted by the research team using a standardized chart abstraction tool to ascertain pre- and perinatal conditions, anthropometrics of both mother and child, delivery and birth outcomes, and childhood diseases. Some examples of the above are mentioned in Table 1. The ideal timeline of data collection is shown in Figure 1. We will not be collecting any biological samples at this stage of the study.

Sample Size

Assuming an exposure level of 10% and a relatively common outcome of 5% (for instance, sickle cell trait (24)) in the unexposed group, a cohort of 10,000 mothers or newborns will allow the detection of true relative risks of approximately 0.61 or 1.45 in exposed group relative to unexposed group with 80% power and a 5% Type I error probability that this relative risk equals 1. Accounting for a 20% attrition rate, Table 2 shows the minimum detectable relative risks for different levels of exposure and proportions of affected unexposed based on a cohort of 8,000 and 80% power and a 5% Type I error probability.

Statistical Methods

Crude and adjusted prevalence and incidence of key outcomes will be estimated with their 95% confidence intervals. Descriptive statistics will be performed to show the distribution of the study population characteristics. Continuous variables will be presented as means with standard deviations or medians with interquartile range where appropriate, while categorical variables will be presented as counts (percentages). Continuous variables with a normal distribution will be compared using a Student t-test or analysis of variance (ANOVA). Categorical data will be compared using the Pearson Chi-square test. Univariate and multivariate regression models will be used to quantify the association between potential exposures and the different outcomes. Logistic and linear models will be used for binary and continuous outcome variables, respectively. Propensity score analysis, survival analyses, and proportional hazard models will be used when applicable. Crude and adjusted odds ratios, relative risks, and hazard ratios with 95% confidence intervals will be reported. Statistical analyses will be performed using STATA and R statistical packages. P value ≤ 0.05 will define statistical significance.

ETHICS AND DISSEMINATION

Ethical approvals have been granted by the United Arab Emirates University Human Research Ethics Committee (previously known as Al Ain Medical District Human Research Ethics Committee) (ERH-2017-5512), Al Ain Hospital Research Ethics Committee (AAHEC-03-17-058) and Tawam Human Research Ethics Committee (T-HREC–494). Informed written consent is obtained from the participant prior to the data collection.

It is anticipated that Mutaba'ah will receive widespread interest in the UAE as well as neighboring regions and media attention. We also anticipate our results to be published in highly ranked international scientific journals, presented at conferences and meetings as well as reported to appropriate authorities for interventions and services.

DISCUSSION

In this paper, we present the design, data collection methods, and expected analyses of a mother and child cohort study in Al Ain; the Mutaba'ah study. The study aims to investigate the maternal and early childhood determinants of infant, child, and adolescent health, as well as maternal health. The pregnant women recruited from the three participating hospitals are expected to be representative of the local population and will provide a rich depiction of the risk and protective factors experienced by the cohort as a whole.

The strengths of the study include the establishment of the first longitudinal cohort of pregnant women and their children in the UAE. The prospective population-based design with the planned long follow-up of a large cohort of mothers and children has great advantages. The study will be able to collect high-quality clinical data from medical records which will reduce missing data and imprecision in variables such as body mass and gestational age. Therefore, Mutaba'ah will secure

epidemiological data and provide a pioneering platform for maternal and child health research. As in most epidemiologic studies, self-reported data and loss to follow-up (at least beyond birth) are potential weaknesses to this study.

Exposures to various risk factors *in utero* and during childhood have a major influence on health and development in adulthood. The impact of this study will extend beyond exposing factors that will be risky and protective for delivery and birth outcomes, childhood, and adolescent health. Mutaba'ah will create a databank for like-minded researchers to conduct work on maternal and child health in the country. It will provide insights into unique exposures and outcomes present in the region such as consanguinity (25), increasing rates of obesity in women and childrem (26, 27) gestational diabetes (28), and smoking practices such as shisha (29).

Cohort studies with such breadth and depth of data can provide important information to the public and authorities. This study will allow researchers to relate different health outcomes to a variety of early-life exposures using appropriate statistical methods based on the robust longitudinal cohort design. Study findings will provide the local, regional, and international scientific community with evidence of the burden and impact of diseases in maternal and child health in a high-income Arab country. Clinicians and public health policy makers can translate this evidence into health policies and practices to improve the health status and services for mothers and children.

ABBREVIATIONS

UAE: United Arab Emirates

MR: Medical Record

SQ: Short Questionnaire

LQ: Long Questionnaire

FFQ: Food Frequency Questionnaire

IQ: Infant Questionnaire

CQ: Child Questionnaire

AQ: Adolescent Questionnaire

CBC: Complete Blood Count

OGTT: Oral Glucose Tolerance Test

PAQ-C: Physical Activity Questionnaire for Older Children

PAQ-A: Physical Activity Questionnaire for Adolescents

ANOVA: Analysis of Variance

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Authors' contributions

LAA, TL and IB conceived, designed and initiated the study. LAA, FAM, HN, CB, SGA, FMA, AZ, TL and IB contributed to the planning of the study. LAA, AAH, NA, IE, HE, TL and IB contributed to the implementation, coordination and management of the study. LAA, AAH, NA, HE and TL drafted this manuscript. All authors read and approved the final version of the manuscript.

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Competing interests

The authors declare that they have no competing interests

Ethics approval

The study was approved by the United Arab Emirates University Human Research Ethics Committee (previously known as Al Ain Medical District Human Research Ethics Committee) (ERH-2017-5512), Al Ain Hospital Research Ethics Committee (AAHEC-03-17-058), and Tawam Human Research Ethics Committee (T-HREC–494). Informed written consent is obtained from the participant prior to the data collection.

Data sharing statement

Data sharing is not applicable to this article as no datasets were analyzed for this manuscript.

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FIGURE LEGEND

Figure 1: Data collection time points during the Mutaba'ah study

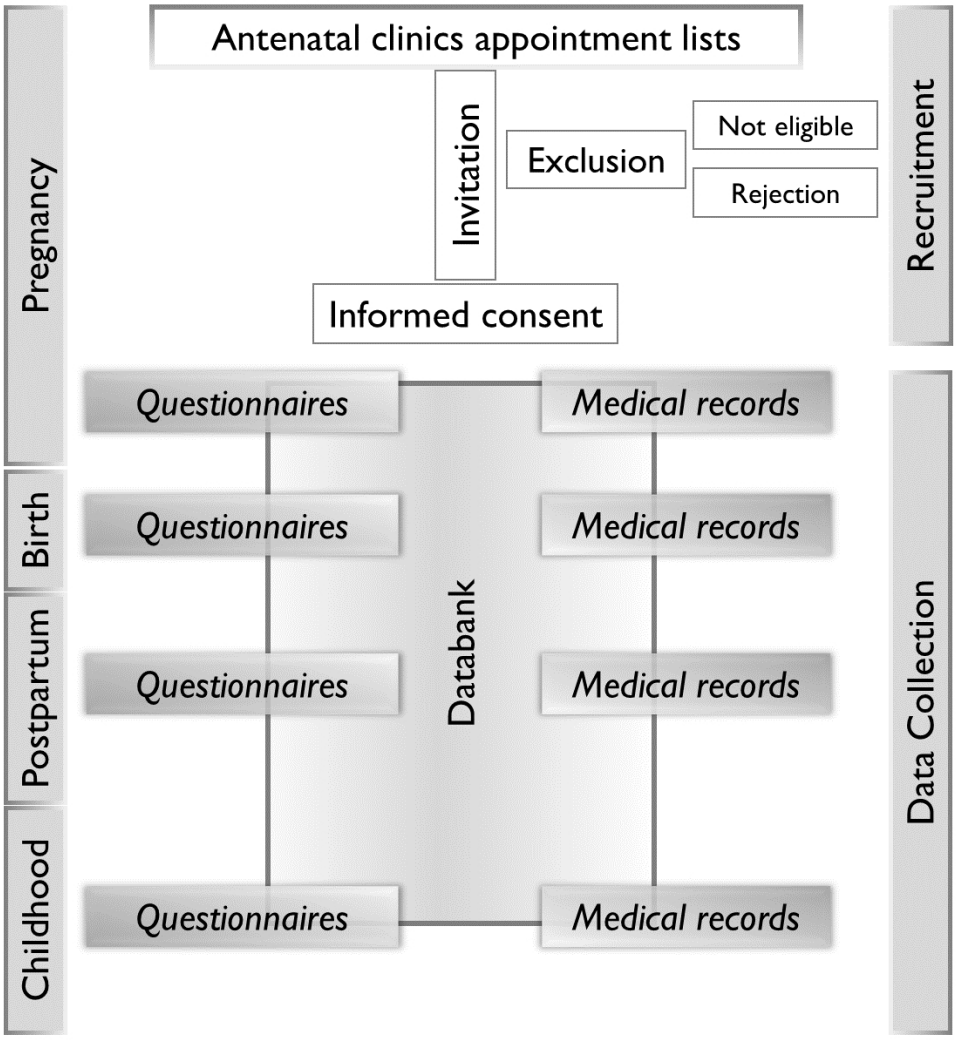
Table 1: Examples of data collected at different time points in the study

	Data	Source
Pregnancy	Past and current pregnancy, health, fertility, supplements, smoking, physical activity, and occupation	SQ
	More details on previous and current pregnancy, lifestyle, home and indoor air quality, mental health, and family health	LQ
	Diet, supplements, and herbal use	FFQ
	Anthropometric data on mother and laboratory test results	MR
Birth and delivery	Length of pregnancy, premature birth, pre-eclampsia, mode of delivery, maternal weight gain and weight after birth, gestational diabetes, birth weight, birth injury, and congenital malformations	MR
Infancy	Breastfeeding and nutrition	IQ
	Growth and development, diseases, and vaccination	MR
Childhood	Diet, physical activity, lifestyle, and medication	CQ
	Childhood diseases, asthma, diabetes, atopy, allergy, cognitive function, psychological behavior, and language skills	MR
Adolescence	Maltreatment, development, diet, physical activity, and lifestyle	AQ
	Any health issues	MR

(SQ) short questionnaire, (LQ) long questionnaire, (FFQ) food frequency questionnaire, (MR) medical records. (IQ) infant questionnaire, (CQ) child questionnaire, (AQ) adolescent questionnaire.

Table 2: Minimum detectable Relative Risks for different levels of exposure and proportions of affected unexposed based on a cohort of 8,000 with 80% power and 5% Type I error probability.

	Exposure level (%)	Proportion of outcome in unexposed group				
		1%	5%	10%	25%	50%
Protective exposure	**1%**	-	-	*0.202*	*0.491*	*0.688*
	5%	-	*0.425*	*0.588*	*0.753*	*0.853*
	10%	*0.125*	*0.562*	*0.69*	*0.816*	*0.891*
	25%	*0.332*	*0.68*	*0.775*	*0.867*	*0.922*
	50%	*0.427*	*0.727*	*0.808*	*0.887*	*0.934*
Harmful exposure	**50%**	*1.76*	*1.307*	*1.207*	*1.117*	*1.066*
	25%	*1.897*	*1.362*	*1.244*	*1.138*	*1.078*
	10%	*2.276*	*1.51*	*1.342*	*1.192*	*1.109*
	5%	*2.782*	*1.701*	*1.468*	*1.261*	*1.147*
	1%	*5.341*	*2.612*	*2.051*	*1.57*	*1.312*



Data collection time points during the Mutaba'ah study

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Mutaba'ah: Mother and Child Health Study - Protocol for a prospective cohort study investigating the maternal and early-life determinants of infant, child, adolescent, and maternal health in the United Arab Emirates

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ABSTRACT

Introduction: Early-life exposures, particularly environmental and parental lifestyle factors, have a major influence on children's health and development. Due to increasing interest in the early-life developmental origins of diseases, many birth cohorts have been established. These studies constitute a repository of data which researchers use over many years to investigate emerging research questions. However, no such databank or cohort study is available in the United Arab Emirates (UAE). This project aims to establish a prospective mother and child cohort study in Al Ain (Abu Dhabi, UAE) to investigate the maternal and early-life determinants of infant, child, adolescent, and maternal health of the Emirati population.

Methods and analysis: During the period 2017-2021, this study aims to recruit 10,000 pregnancies at approximately 12 weeks of gestation from hospitals and clinics in Al Ain city. For each mother/newborn pair, an initial dataset will be collected including anthropometric, physiological, and biochemical measurements, medical interventions, circumstances of pregnancy, delivery details, and neonatal and perinatal growth and health using a combination of questionnaires, interviews, and medical record extractions. Baseline data will act as the starting point from which the children will be followed up and re-surveyed at intervals throughout their life course until the age of 16 years, to explore how familial, socioeconomic, and lifestyle factors interact with genetic and environmental factors to influence health outcomes and achievements later in life.

Ethics and dissemination: Ethical approval has been granted by the United Arab Emirates University Human Research Ethics Committee and the ethical committees of the participating institutions. Results will be widely disseminated via peer reviewed manuscripts, conference presentations, media outlets and reports to relevant authorities.

ARTICLE SUMMARY

Strength and Limitations of this study

- This study is the largest mother and child cohort study to be established in the UAE, and the first conducted in the emirate of Abu Dhabi.
- The study will have a large sample size of 10,000 pregnancies as well as a long follow up period (16 years).
- We intend to recruit pregnant women from the Emirati population who would be more likely to follow up till the Emirati children are 16 years of age
- Standardized scales and clinical assessments and records from hospitals are carefully designed to reduce any misreporting and ensure a large cohesive dataset
- We are not recruiting other expatriates as it might lead to a large amount of attrition, so the study may not be generalizable to populations elsewhere.

INTRODUCTION

Although the causes of non-communicable disease epidemics have not yet been fully determined, emerging evidence suggests causal associations between their occurrence and exposures during pregnancy and early-life (1, 2). The Developmental Origins of Health and Disease hypothesis speculates that the risk of chronic disease in adult life is related to biological programming of the fetus or infant in response to early environmental signals (3). Moreover, there is convincing evidence that physical and psychosocial exposures in the first months of life and later in childhood have important effects on health, well-being, and development during adolescence and adulthood (4-6). For instance, numerous studies have reported the beneficial effect of breastfeeding on some of the major components of the metabolic syndrome (i.e. obesity, blood pressure, cholesterol metabolism, and insulin resistance) and thereafter on the risk of cardiovascular disease (7, 8).

Research based on the available medical record systems or on cross-sectional data usually involve small samples of the general population with limited information on specific exposures and disease outcomes of interest. Firstly, this will significantly narrow exposure-outcome relationships. Secondly, these studies will face methodological and analytical problems of residual confounding due to the lack of data on other important lifestyle, socioeconomic, nutritional, physical, and environmental exposures not routinely captured in medical records. Therefore, new datasets that support research in a life course perspective are urgently needed. Datasets with rich information on exposures and outcomes, that include social and biological factors, can be used by researchers in different fields with widely different types of causal models to produce original research. For over half a century, there has been a proliferation of birth cohort studies fueled by the recognition of the importance of the *in utero* environment on health outcomes in later life (9). The main distinctive feature of a cohort study is the longitudinal follow-up time frame and the frequency of

the follow up that could be extended indefinitely (4). A longitudinal design allows the quantification of the temporal relationship between a specific exposure and outcome, observance of the natural history, and calculation of the incidence of a specific outcome. Despite the surge in the number of cohort studies, there is a lack of longitudinal studies in the United Arab Emirates (UAE) with follow-ups across the lifespan to help understand the etiology of numerous health conditions in the community.

This protocol describes the research design and methods used to establish the Mutaba'ah study which is a large prospective cohort study focusing on maternal and child health in the UAE. This study aims to establish a prospective mother and child cohort study in Al Ain city to investigate the maternal, genetic, social, environmental, lifestyle, and other early childhood determinants of infant, child, and adolescent health, as well as the mother's health.

The study objectives are to: i) identify and collect data on relevant exposures of the mother and child during pregnancy, delivery, and the post-natal period; ii) identify and collect relevant outcomes of the mother and child during delivery, post-natal period, and early life; iii) associate relevant exposures and health outcomes; and iv) establish a prospective and updated databank.

METHODS AND ANALYSIS

Study Design

Mutaba'ah, (meaning "follow up" in Arabic), the Mother and Child Health Study is a prospective cohort study in Al Ain city.

Study Setting

Al Ain is the second largest city in the Emirate of Abu Dhabi (the largest UAE emirate in terms of land mass and population size) and has the largest and relatively stable population of Emirati

citizens compared to other parts of the country. This makes it an ideal setting for a birth cohort study with longitudinal follow-ups. In 2016, the Emirate of Abu Dhabi population was estimated to be approximately 2.9 million, of which, less than 19% were Emiratis and around 41% of these Emiratis lived in the Al Ain region (10). The population of Al Ain is approximately 766,900 (mid-2016) of which 226,300 are Emirati citizens and of these 53,995 are women of reproductive age (15-44 years) (10). Levels and standards of antenatal care are high, and all births take place in hospital. Although this study has the potential to expand to involve many health institutions, the initial recruitment has been confined to three major hospitals in Al Ain: the only two public hospitals and one large private hospital; Al Ain Hospital, Tawam Hospital, and Oasis Hospital, respectively. As all of the Emirati population has full health insurance allowing them to have the same level of health care at any health facility, there is no difference in health care access between pregnant women attending these three hospitals and those who use other institutions. Therefore, a representative sample of the Emirati population in Al Ain can be recruited from these three hospitals.

Participants

The study aims to recruit 10,000 mother and baby pairs with each pair suggesting a pregnancy.

Inclusion Criteria

Invitation for participation is limited to the Emirati population. All pregnant women from this population attending any of the three participating hospitals for their antenatal care management who are at least 18 years old, resident in Al Ain, ideally in their first trimester (approximately 12 weeks of gestation), able to provide informed consent, and their newborns will be included in the study. Women with multiple pregnancies (pregnant with more than one fetus) and those who

conceive multiple times during the study period, as well as their offspring will also be included in the study so long as they provide consent.

Exclusion Criteria

The study will exclude expatriates as they are less likely than the Emirati population to be available for long-term follow-up. Pregnant women younger than 18 years or those who are unable to provide consent and women who are not currently pregnant, will also be excluded.

Sampling and Recruitment

There are approximately 6,600 births of Emirati children each year in Al Ain, of which, the clear majority take place in the three participating hospitals. The study employs a consecutive sampling strategy whereby all eligible pregnant women that present at one of three hospitals are invited to participate in the study. Eligible participants are identified via a health care provider (nurse or physician) at each hospital's registration point and are approached by an on-site research assistant with an information sheet detailing the project. If they express interest, participants provide informed consent. This consent allows for follow-up interviews and the extraction of their and their babies' health information from medical records up until the child is 16 years old. The study is conducted in accordance with the principles of the Declaration of Helsinki. Each participant has the right to withdraw from the study at any time without giving any reason. Should a participant wish to withdraw from the study, and wish for their collected data to be destroyed, this will be completed in a prompt and secure manner and a message will be sent to the woman to confirm study withdrawal. The reason for withdrawal, if given, will be recorded in the database.

Patient involvement

Participants provide input during their recruitment process on their thoughts on how best to follow them and their children up after delivery, and how to access more participants. This information is

usually collected verbatim by the data collectors or collected via administrative forms. Participants were not consulted about study outcomes or interpretation of the results.

Data sources and measurements

Collected data will include but are not limited to: demographic, socioeconomic, lifestyle, environmental, education, employment, physical and mental health, household and family information, parental health, social support, local community and services, mother and child nutrition, previous pregnancies and birth outcomes, health and development of child, and childcare information.

Data will be collected around the following time points: 12 weeks of gestation; 25 weeks of gestation; at the time of delivery; and at six and 12 months for the infants. Further time points for follow-up during childhood and adolescence will be decided later. In addition to data abstracted from the medical records (MR), data will be obtained using three tablet-assisted self-administered questionnaires; a short questionnaire (SQ), long questionnaire (LQ), and a food frequency questionnaire (FFQ). The research database will be linked using the medical record number and unique identification number assigned to each participant when consenting to the study. Medical records of the mother will provide information on the progress of the pregnancy, imaging and laboratory test results such as Complete Blood Counts (CBC) and Oral Glucose Tolerance Tests (OGTT). All medical outcomes will be ascertained from the woman's and child's medical records as standardized definitions are employed following the regulations and guidelines of the Department of Health of Abu Dhabi (11). Official birth notification and delivery records will provide data on the delivery and birth outcomes. Interviews using the infant questionnaire (IQ) will be conducted via follow-up hospital visits, home visits, or telephone when the child is six and

12 months old. In the future, we plan to collect data when the child is aged from five to 16 years using interviews or specifically designed child questionnaires (CQ) and adolescent questionnaires (AQ).

Table 1 shows examples of the types and sources of data collected during the study. The SQ is administered at the first point of contact and comprises 67 questions on varying socio-demographic and psychosocial measures. Questions were pooled and adapted from the Avon Longitudinal Study of Parents and Children (12), the Norwegian Mother and Child Study (13, 14), the Danish Birth Cohort Study (15), and the Born in Bradford study (16). The FFQ will be administered during the second or third trimester to ascertain diet, supplement intake, and herbal use during the pregnancy. The FFQ has been created and validated in the UAE (17).

The LQ will be a combination of questions asked in the four cohort studies previously mentioned that were used to develop the SQ as well. However, it will delve deeper into psychosocial dimensions of health including mental health using scales such as the Edinburgh Depression Scale (18) and the Spielberger State Trait Anxiety Inventory (19). All questionnaires were translated from English to Arabic by one group of study researchers and then back translated from Arabic to English by a different group of study researchers.

During childhood and adolescence, we will use previously validated measures such as the Childhood Trauma Questionnaire (20), Adverse Child Experiences (21), a child-relevant FFQ (22), and the Physical Activity Questionnaire for Older Children (PAQ-C) and Physical Activity Questionnaire for Adolescents (PAQ-A) (23).

Clinical data will be abstracted by the research team using a standardized chart abstraction tool to ascertain pre- and perinatal conditions, anthropometrics of both mother and child, delivery and birth outcomes, and childhood diseases. Some examples of the above are mentioned in Table 1.

The ideal timeline of data collection is shown in Figure 1. We will not be collecting any biological samples at this stage of the study.

Sample Size

Assuming an exposure level of 10% and a relatively common outcome of 5% (for instance, sickle cell trait (24)) in the unexposed group, a cohort of 10,000 pregnancies will allow the detection of true relative risks of approximately 0.61 or 1.45 in exposed group relative to unexposed group with 80% power and a 5% Type I error probability that this relative risk equals 1. Accounting for a 20% attrition rate, Table 2 shows the minimum detectable relative risks for different levels of exposure and proportions of affected unexposed based on a cohort of 8,000 and 80% power and a 5% Type I error probability.

Statistical Methods

Crude and adjusted prevalence and incidence of key outcomes will be estimated with their 95% confidence intervals. Descriptive statistics will be performed to show the distribution of the study population characteristics. Continuous variables will be presented as means with standard deviations or medians with interquartile range where appropriate, while categorical variables will be presented as counts (percentages). Continuous variables with a normal distribution will be compared using a Student t-test or analysis of variance (ANOVA). Categorical data will be compared using the Pearson Chi-square test. Univariate and multivariate regression models will be used to quantify the association between potential exposures and the different outcomes. Multiple imputation, complete-case analyses, and sensitivity analyses will be used to deal with missing data. Logistic and linear models will be used for binary and continuous outcome variables, respectively. Propensity score analysis, survival analyses, and proportional hazard models will be

used when applicable. Crude and adjusted odds ratios, relative risks, and hazard ratios with 95% confidence intervals will be reported. Statistical analyses will be performed using STATA and R statistical packages. P value ≤0.05 will define statistical significance.

ETHICS AND DISSEMINATION

Ethical approvals have been granted by the United Arab Emirates University Human Research Ethics Committee (previously known as Al Ain Medical District Human Research Ethics Committee) (ERH-2017-5512), Al Ain Hospital Research Ethics Committee (AAHEC-03-17-058) and Tawam Human Research Ethics Committee (T-HREC–494). Informed written consent is obtained from the participant prior to the data collection.

It is anticipated that Mutaba'ah will receive widespread interest in the UAE as well as neighboring regions and media attention. We also anticipate our results to be published in highly ranked international scientific journals, presented at conferences and meetings as well as reported to appropriate authorities for interventions and services.

STATUS OF PROJECT

Pilot recruitment was performed between May and August 2017 (100 participants), while active recruitment began in October 2017 and will proceed till 2021 or until the desired sample size has been reached. Around 5000 participants completed the SQ (among them 844 participants completed LQ) until May 2019. With the current participation rate of over 80%, it is expected that over 6,000 pregnant women could realistically be recruited by the end of second year (October 2019) with the remainder to be recruited in the third year of the study. The refusal rate is around 17.5%. Women who refuse generally indicated either fatigue or lack of time as their reasons for

refusal. We have had 3 withdrawals so far citing personal reasons. Despite a steady enrolment, we face some challenges as most longitudinal cohorts with respect to partial responses and loss to follow up. The total number of variables in our dataset currently amounts up to more than 1800 variables from the two questionnaires and medical records.

DISCUSSION

In this paper, we present the design, data collection methods, and expected analyses of a mother and child cohort study in Al Ain; the Mutaba'ah study. The study aims to investigate the maternal and early childhood determinants of infant, child, and adolescent health, as well as maternal health. The pregnant women recruited from the three participating hospitals are expected to be representative of the local population and will provide a rich depiction of the risk and protective factors experienced by the cohort as a whole.

Currently, there is only one ongoing two-year prospective birth cohort study (Mother-Infant Study Cohort; MISC) which recruited 256 of both UAE national and expatriate pregnant women late during their pregnancy in three emirates (Dubai, Sharjah and Ajman) of the UAE (25). The two-year follow-up period in the MISC study focuses on exploring the association between nutrition and lifestyle characteristics on birth outcomes, infant nutritional status, and cognitive development. Mutaba'ah on the other hand aims to recruit pregnant women during the first trimester of their pregnancy to enable exploring the early pregnancy exposures that influence maternal and fetal health during the second and third trimester, in addition to delivery complications and birth outcomes. Moreover, the planned long-term follow-up (16 years) will permit Mutaba'ah to investigate the prenatal and neonatal exposures that might be associated with

infant, child, and adolescent health outcomes. Both the MISC and Mutaba'ah studies will enrich the scant body of maternal and child health research in the UAE.

The strengths of the Mutaba'ah study include the establishment of the largest longitudinal cohort of pregnant women and their children in the UAE. The prospective population-based design with the planned long follow-up of a large cohort of mothers and children has great advantages. The study will be able to collect high-quality clinical data from medical records which will reduce missing data and imprecision in variables such as body mass and gestational age. Therefore, Mutaba'ah will secure epidemiological data and provide a pioneering platform for maternal and child health research. As in most epidemiologic studies, self-reported data and loss to follow-up (at least beyond birth) are potential weaknesses to this study.

Exposures to various risk factors *in utero* and during childhood have a major influence on health and development in adulthood. The impact of this study will extend beyond exposing factors that will be risky and protective for delivery and birth outcomes, childhood, and adolescent health. Mutaba'ah will create a databank for like-minded researchers to conduct work on maternal and child health in the country. It will provide insights into unique exposures and outcomes present in the region such as consanguinity (26), increasing rates of obesity in women and childrem (27, 28) gestational diabetes (29), and smoking practices such as shisha (30). The study will also aim to initiate regional and international collaborations with similar onging mother and child cohort studies to enable performing international comparisons and generating more research prospects.

Cohort studies with such breadth and depth of data can provide important information to the public and authorities. This study will allow researchers to relate different health outcomes to a variety of early-life exposures using appropriate statistical methods based on the robust longitudinal cohort design. Study findings will provide the local, regional, and international scientific

community with evidence of the burden and impact of diseases in maternal and child health in a high-income Arab country. Clinicians and public health policy makers can translate this evidence into health policies and practices to improve the health status and services for mothers and children.

ABBREVIATIONS

UAE: United Arab Emirates

MR: Medical Record

SQ: Short Questionnaire

LQ: Long Questionnaire

FFQ: Food Frequency Questionnaire

IQ: Infant Questionnaire

CQ: Child Questionnaire

AQ: Adolescent Questionnaire

CBC: Complete Blood Count

OGTT: Oral Glucose Tolerance Test

PAQ-C: Physical Activity Questionnaire for Older Children

PAQ-A: Physical Activity Questionnaire for Adolescents

ANOVA: Analysis of Variance

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Authors' contributions

LAA, TL and IB conceived, designed and initiated the study. LAA, FAM, HN, CB, SGA, FMA, AZ, TL and IB contributed to the planning of the study. LAA, AAH, NA, IE, HE, TL and IB contributed to the implementation, coordination and management of the study. LAA, AAH, NA, HE and TL drafted this manuscript. All authors read and approved the final version of the manuscript.

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Competing interests

The authors declare that they have no competing interests

Ethics approval

The study was approved by the United Arab Emirates University Human Research Ethics Committee (previously known as Al Ain Medical District Human Research Ethics Committee) (ERH-2017-5512), Al Ain Hospital Research Ethics Committee (AAHEC-03-17-058), and Tawam Human Research Ethics Committee (T-HREC–494). Informed written consent is obtained from the participant prior to the data collection.

Data sharing statement

Data sharing is not applicable to this article as no datasets were analyzed for this manuscript.

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FIGURE LEGEND

Figure 1: Data collection time points during the Mutaba'ah study

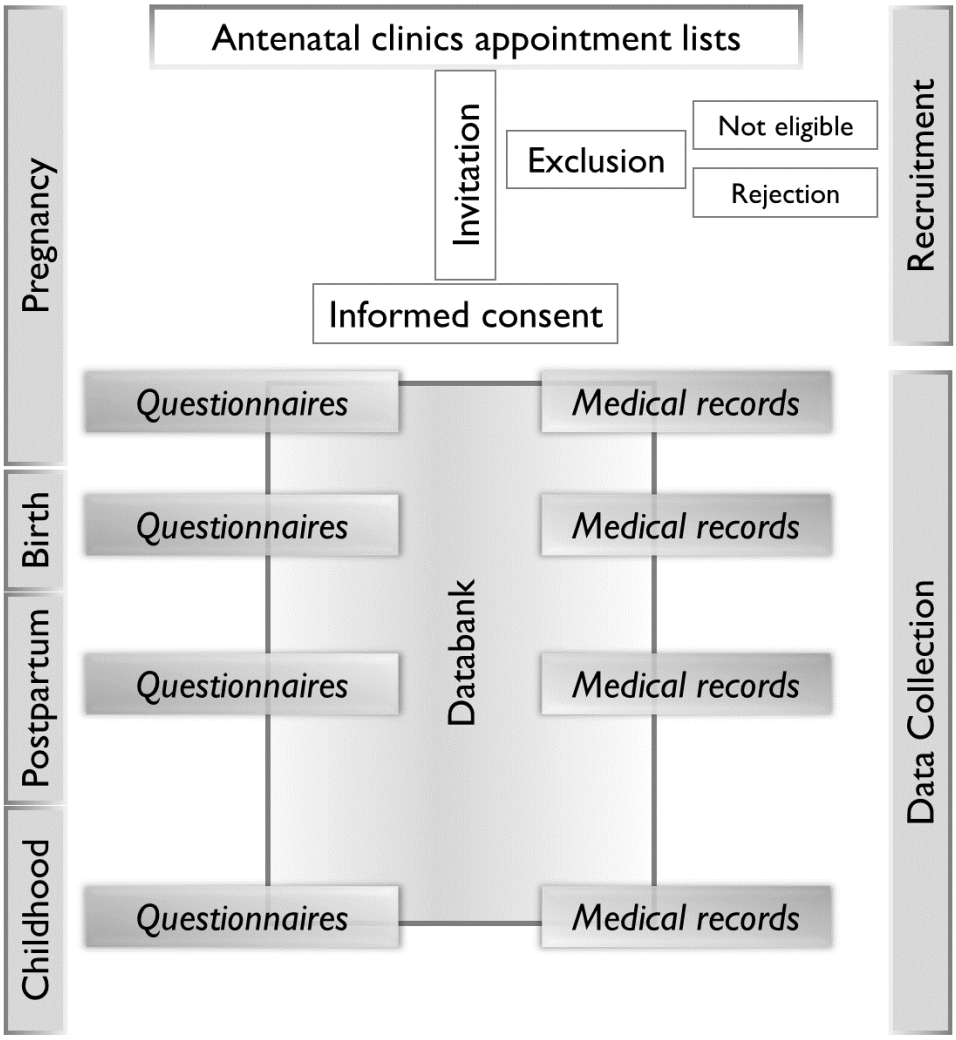
Table 1: Examples of data collected at different time points in the study

	Data	Source
Pregnancy	Past and current pregnancy, health, fertility, supplements, smoking, physical activity, and occupation	SQ
	More details on previous and current pregnancy, lifestyle, home and indoor air quality, mental health, and family health	LQ
	Diet, supplements, and herbal use	FFQ
	Anthropometric data on mother and laboratory test results	MR
Birth and delivery	Length of pregnancy, premature birth, pre-eclampsia, mode of delivery, maternal weight gain and weight after birth, gestational diabetes, birth weight, birth injury, and congenital malformations	MR
Infancy	Breastfeeding and nutrition	IQ
	Growth and development, diseases, and vaccination	MR
Childhood	Diet, physical activity, lifestyle, and medication	CQ
	Childhood diseases, asthma, diabetes, atopy, allergy, cognitive function, psychological behavior, and language skills	MR
Adolescence	Maltreatment, development, diet, physical activity, and lifestyle	AQ
	Any health issues	MR

(SQ) short questionnaire, (LQ) long questionnaire, (FFQ) food frequency questionnaire, (MR) medical records. (IQ) infant questionnaire, (CQ) child questionnaire, (AQ) adolescent questionnaire.

Table 2: Minimum detectable Relative Risks for different levels of exposure and proportions of affected unexposed based on a cohort of 8,000 with 80% power and 5% Type I error probability.

	Exposure level (%)	Proportion of outcome in unexposed group				
		1%	5%	10%	25%	50%
Protective exposure	**1%**	-	-	*0.202*	*0.491*	*0.688*
	5%	-	*0.425*	*0.588*	*0.753*	*0.853*
	10%	*0.125*	*0.562*	*0.69*	*0.816*	*0.891*
	25%	*0.332*	*0.68*	*0.775*	*0.867*	*0.922*
	50%	*0.427*	*0.727*	*0.808*	*0.887*	*0.934*
Harmful exposure	**50%**	*1.76*	*1.307*	*1.207*	*1.117*	*1.066*
	25%	*1.897*	*1.362*	*1.244*	*1.138*	*1.078*
	10%	*2.276*	*1.51*	*1.342*	*1.192*	*1.109*
	5%	*2.782*	*1.701*	*1.468*	*1.261*	*1.147*
	1%	*5.341*	*2.612*	*2.051*	*1.57*	*1.312*



Data collection time points during the Mutaba'ah study

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Mutaba'ah: Mother and Child Health Study - Protocol for a prospective cohort study investigating the maternal and early-life determinants of infant, child, adolescent, and maternal health in the United Arab Emirates

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Mutaba'ah: Mother and Child Health Study - Protocol for a prospective cohort study investigating the maternal and early-life determinants of infant, child, adolescent, and maternal health in the United Arab Emirates

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ABSTRACT

Introduction: Early-life exposures, particularly environmental and parental lifestyle factors, have a major influence on children's health and development. Due to increasing interest in the early-life developmental origins of diseases, many birth cohorts have been established. These studies constitute a repository of data which researchers use over many years to investigate emerging research questions. However, no such databank or cohort study is available in the United Arab Emirates (UAE). This project aims to establish a prospective mother and child cohort study in Al Ain (Abu Dhabi, UAE) to investigate the maternal and early-life determinants of infant, child, adolescent, and maternal health of the Emirati population.

Methods and analysis: During the period 2017-2021, this study aims to recruit 10,000 pregnancies at approximately 12 weeks of gestation from hospitals and clinics in Al Ain city. For each mother/newborn pair, an initial dataset will be collected including anthropometric, physiological, and biochemical measurements, medical interventions, circumstances of pregnancy, delivery details, and neonatal and perinatal growth and health using a combination of questionnaires, interviews, and medical record extractions. Baseline data will act as the starting point from which the children will be followed up and re-surveyed at intervals throughout their life course until the age of 16 years, to explore how familial, socioeconomic, and lifestyle factors interact with genetic and environmental factors to influence health outcomes and achievements later in life.

Ethics and dissemination: Ethical approval has been granted by the United Arab Emirates University Human Research Ethics Committee and the ethical committees of the participating institutions. Results will be widely disseminated via peer reviewed manuscripts, conference presentations, media outlets and reports to relevant authorities.

ARTICLE SUMMARY

Strength and Limitations of this study

- This study is the largest mother and child cohort study to be established in the UAE, and the first conducted in the emirate of Abu Dhabi.
- The study will have a large sample size of 10,000 pregnancies as well as a long follow up period (16 years).
- We intend to recruit pregnant women from the Emirati population who would be more likely to follow up till the Emirati children are 16 years of age
- Standardized scales and clinical assessments and records from hospitals are carefully designed to reduce any misreporting and ensure a large cohesive dataset
- We are not recruiting other expatriates as it might lead to a large amount of attrition, so the study may not be generalizable to populations elsewhere.

INTRODUCTION

Although the causes of non-communicable disease epidemics have not yet been fully determined, emerging evidence suggests causal associations between their occurrence and exposures during pregnancy and early-life (1, 2). The Developmental Origins of Health and Disease hypothesis speculates that the risk of chronic disease in adult life is related to biological programming of the fetus or infant in response to early environmental signals (3). Moreover, there is convincing evidence that physical and psychosocial exposures in the first months of life and later in childhood have important effects on health, well-being, and development during adolescence and adulthood (4-6). For instance, numerous studies have reported the beneficial effect of breastfeeding on some of the major components of the metabolic syndrome (i.e. obesity, blood pressure, cholesterol metabolism, and insulin resistance) and thereafter on the risk of cardiovascular disease (7, 8).

Research based on the available medical record systems or on cross-sectional data usually involve small samples of the general population with limited information on specific exposures and disease outcomes of interest. Firstly, this will significantly narrow exposure-outcome relationships. Secondly, these studies will face methodological and analytical problems of residual confounding due to the lack of data on other important lifestyle, socioeconomic, nutritional, physical, and environmental exposures not routinely captured in medical records. Therefore, new datasets that support research in a life course perspective are urgently needed. Datasets with rich information on exposures and outcomes, that include social and biological factors, can be used by researchers in different fields with widely different types of causal models to produce original research. For over half a century, there has been a proliferation of birth cohort studies fueled by the recognition of the importance of the *in utero* environment on health outcomes in later life (9). The main distinctive feature of a cohort study is the longitudinal follow-up time frame and the frequency of

the follow up that could be extended indefinitely (4). A longitudinal design allows the quantification of the temporal relationship between a specific exposure and outcome, observance of the natural history, and calculation of the incidence of a specific outcome. Despite the surge in the number of cohort studies, there is a lack of longitudinal studies in the United Arab Emirates (UAE) with follow-ups across the lifespan to help understand the etiology of numerous health conditions in the community.

This protocol describes the research design and methods used to establish the Mutaba'ah study which is a large prospective cohort study focusing on maternal and child health in the UAE. This study aims to establish a prospective mother and child cohort study in Al Ain city to investigate the maternal, genetic, social, environmental, lifestyle, and other early childhood determinants of infant, child, and adolescent health, as well as the mother's health.

The study objectives are to: i) identify and collect data on relevant exposures of the mother and child during pregnancy, delivery, and the post-natal period; ii) identify and collect relevant outcomes of the mother and child during delivery, post-natal period, and early life; iii) associate relevant exposures and health outcomes; and iv) establish a prospective and updated databank.

METHODS AND ANALYSIS

Study Design

Mutaba'ah, (meaning "follow up" in Arabic), the Mother and Child Health Study is a prospective cohort study in Al Ain city.

Study Setting

Al Ain is the second largest city in the Emirate of Abu Dhabi (the largest UAE emirate in terms of land mass and population size) and has the largest and relatively stable population of Emirati

citizens compared to other parts of the country. This makes it an ideal setting for a birth cohort study with longitudinal follow-ups. In 2016, the Emirate of Abu Dhabi population was estimated to be approximately 2.9 million, of which, less than 19% were Emiratis and around 41% of these Emiratis lived in the Al Ain region (10). The population of Al Ain is approximately 766,900 (mid-2016) of which 226,300 are Emirati citizens and of these 53,995 are women of reproductive age (15-44 years) (10). Levels and standards of antenatal care are high, and all births take place in hospital. Although this study has the potential to expand to involve many health institutions, the initial recruitment has been confined to three major hospitals in Al Ain: the only two public hospitals and one large private hospital; Al Ain Hospital, Tawam Hospital, and Oasis Hospital, respectively. As all of the Emirati population has full health insurance allowing them to have the same level of health care at any health facility, there is no difference in health care access between pregnant women attending these three hospitals and those who use other institutions. Therefore, a representative sample of the Emirati population in Al Ain can be recruited from these three hospitals.

Participants

The study aims to recruit 10,000 mother and baby pairs with each pair suggesting a pregnancy.

Inclusion Criteria

Invitation for participation is limited to the Emirati population. All pregnant women from this population attending any of the three participating hospitals for their antenatal care management who are at least 18 years old, resident in Al Ain, ideally in their first trimester (approximately 12 weeks of gestation), able to provide informed consent, and their newborns will be included in the study. Women with multiple pregnancies (pregnant with more than one fetus) and those who

conceive multiple times during the study period, as well as their offspring will also be included in the study so long as they provide consent.

Exclusion Criteria

The study will exclude expatriates as they are less likely than the Emirati population to be available for long-term follow-up. Pregnant women younger than 18 years or those who are unable to provide consent and women who are not currently pregnant, will also be excluded.

Sampling and Recruitment

There are approximately 6,600 births of Emirati children each year in Al Ain, of which, the clear majority take place in the three participating hospitals. The study employs a consecutive sampling strategy whereby all eligible pregnant women that present at one of three hospitals are invited to participate in the study. Eligible participants are identified via a health care provider (nurse or physician) at each hospital's registration point and are approached by an on-site research assistant with an information sheet detailing the project. If they express interest, participants provide informed consent. This consent allows for follow-up interviews and the extraction of their and their babies' health information from medical records up until the child is 16 years old. The study is conducted in accordance with the principles of the Declaration of Helsinki. Each participant has the right to withdraw from the study at any time without giving any reason. During enrolment, the participant is provided with a detailed information sheet on the Mutaba'ah study description, contact details (telephone number and email address), and the withdrawal process. In addition, the withdrawal process is explained verbally to the participant. The participant is informed verbally and in writing that they can call or email at any time to execute their right to withdraw from the study. Should a participant wish to withdraw from the study, and wish for their collected data to be destroyed, this will be completed in a prompt and secure manner and a message will be sent to

the woman to confirm study withdrawal. The reason for withdrawal, if given, will be recorded in the database.

Patient involvement

Participants provide input during their recruitment process on their thoughts on how best to follow them and their children up after delivery, and how to access more participants. This information is usually collected verbatim by the data collectors or collected via administrative forms. Participants were not consulted about study outcomes or interpretation of the results.

Data sources and measurements

Collected data will include but are not limited to: demographic, socioeconomic, lifestyle, environmental, education, employment, physical and mental health, household and family information, parental health, social support, local community and services, mother and child nutrition, previous pregnancies and birth outcomes, health and development of child, and childcare information.

Data will be collected around the following time points: 12 weeks of gestation; 25 weeks of gestation; at the time of delivery; and at six and 12 months for the infants. The ideal timeline of data collection is shown in Figure 1. Further time points for follow-up during childhood and adolescence will be decided later. In addition to data abstracted from the medical records (MR), data will be obtained using three tablet-assisted self-administered questionnaires; a short questionnaire (SQ), long questionnaire (LQ), and a food frequency questionnaire (FFQ). The research database will be linked using the medical record number and unique identification number assigned to each participant when consenting to the study. Medical records of the mother will provide information on the progress of the pregnancy and pregnancy outcomes. Information will be extracted from the laboratory tests and imaging results which are performed routinely on all

women. These routine antenatal care screenings and tests include among others, complete blood count, vitamin D (plasma 25-hydroxyvitamin D3), infectious disease screening (i.e. hepatitis B virus, human immunodeficiency virus, rubella, syphilis, varicella), cervical cancer screening, haemoglobinopathy screening, anomaly scan, gestational diabetes mellitus screening, and repeated measures of proteinuria, fetal growth, heart tones, fundal height measurements, maternal body mass, body mass index, and blood pressure. All medical outcomes will be ascertained from the woman's and child's medical records as standardized definitions are employed following the regulations and guidelines of the Department of Health of Abu Dhabi (11). Official birth notification and delivery records will provide data on the delivery and birth outcomes. Important information on genetic exposures and outcomes will be collected from the medical records and questionnaires. Examples of genetic data include degree of consanguinity, family history of diseases, and routine genetic screening results of the mother and child such as thalassemia, glucose-6-phosphate dehydrogenase deficiency, and sickle cell trait. Interviews using the infant questionnaire (IQ) will be conducted via follow-up hospital visits, home visits, or telephone when the child is six and 12 months old. In the future, we plan to collect data when the child is aged from five to 16 years using interviews or specifically designed child questionnaires (CQ) and adolescent questionnaires (AQ). We plan to collaborate with federal institutions to set-up linkages between the Mutaba'ah study data and UAE population registries to ensure continued access to the child's health and education records during their childhood and adolescence.

Table 1 shows examples of the types and sources of data collected during the study. The SQ is administered at the first point of contact and comprises 67 questions on varying socio-demographic and psychosocial measures. Questions were pooled and adapted from the Avon Longitudinal Study of Parents and Children (12), the Norwegian Mother and Child Study (13, 14), the Danish Birth

Cohort Study (15), and the Born in Bradford study (16). The semi-quantitative FFQ will be completed by the mother during the second or third trimester to ascertain diet (i.e. energy intake, macro- and micro-nutrient intake), supplement intake, and herbal use during the pregnancy. The FFQ has been created and validated in the UAE and the nutrient intake calculations will be based on a newly developed food composition database developed specifically for the UAE (17).

The LQ will be a combination of questions asked in the four cohort studies previously mentioned that were used to develop the SQ as well. However, it will delve deeper into psychosocial dimensions of health including mental health using scales such as the Edinburgh Depression Scale (18) and the Spielberger State Trait Anxiety Inventory (19). All questionnaires were translated from English to Arabic by one group of study researchers and then back translated from Arabic to English by a different group of study researchers.

During childhood and adolescence, we will use previously validated measures such as the Childhood Trauma Questionnaire (20), Adverse Child Experiences (21), a child-relevant FFQ (22), and the Physical Activity Questionnaire for Older Children (PAQ-C) and Physical Activity Questionnaire for Adolescents (PAQ-A) (23).

Clinical data will be abstracted by the research team using a standardized chart abstraction tool to ascertain pre- and perinatal conditions, anthropometrics of both mother and child, delivery and birth outcomes, and childhood diseases. We will not be collecting any biological samples at this stage of the study. The Supplementary Table provides more details on the proposed and projected variables, time points, and data sources in the Mutaba'ah study.

Sample Size

Assuming an exposure level of 10% and a relatively common outcome of 5% (for instance, sickle cell trait (24)) in the unexposed group, a cohort of 10,000 pregnancies will allow the detection of

true relative risks of approximately 0.61 or 1.45 in exposed group relative to unexposed group with 80% power and a 5% Type I error probability that this relative risk equals 1. Accounting for a 20% attrition rate, Table 2 shows the minimum detectable relative risks for different levels of exposure and proportions of affected unexposed based on a cohort of 8,000 and 80% power and a 5% Type I error probability.

Statistical Methods

Crude and adjusted prevalence and incidence of key outcomes will be estimated with their 95% confidence intervals. Descriptive statistics will be performed to show the distribution of the study population characteristics. Continuous variables will be presented as means with standard deviations or medians with interquartile range where appropriate, while categorical variables will be presented as counts (percentages). Continuous variables with a normal distribution will be compared using a Student t-test or analysis of variance (ANOVA). Categorical data will be compared using the Pearson Chi-square test. Univariate and multivariate regression models will be used to quantify the association between potential exposures and the different outcomes. Multiple imputation, complete-case analyses, and sensitivity analyses will be used to deal with missing data. Logistic and linear models will be used for binary and continuous outcome variables, respectively. Propensity score analysis, survival analyses, and proportional hazard models will be used when applicable. Crude and adjusted odds ratios, relative risks, and hazard ratios with 95% confidence intervals will be reported. Statistical analyses will be performed using STATA and R statistical packages. P value ≤ 0.05 will define statistical significance.

ETHICS AND DISSEMINATION

Ethical approvals have been granted by the United Arab Emirates University Human Research Ethics Committee (previously known as Al Ain Medical District Human Research Ethics Committee) (ERH-2017-5512), Al Ain Hospital Research Ethics Committee (AAHEC-03-17-058) and Tawam Human Research Ethics Committee (T-HREC–494). Informed written consent is obtained from the participant prior to the data collection.

It is anticipated that Mutaba'ah will receive widespread interest in the UAE as well as neighboring regions and media attention. We also anticipate our results to be published in highly ranked international scientific journals, presented at conferences and meetings as well as reported to appropriate authorities for interventions and services.

STATUS OF PROJECT

Pilot recruitment was performed between May and August 2017 (100 participants), while active recruitment began in October 2017 and will proceed till 2021 or until the desired sample size has been reached. Around 5000 participants completed the SQ (among them 844 participants completed LQ) until May 2019. With the current participation rate of over 80%, it is expected that over 6,000 pregnant women could realistically be recruited by the end of second year (October 2019) with the remainder to be recruited in the third year of the study. The refusal rate is around 17.5%. Women who refuse generally indicated either fatigue or lack of time as their reasons for refusal. We have had 3 withdrawals so far citing personal reasons. Despite a steady enrolment, we face some challenges as most longitudinal cohorts with respect to partial responses and loss to follow up. The total number of variables in our dataset currently amounts up to more than 1800 variables from the two questionnaires and medical records.

DISCUSSION

In this paper, we present the design, data collection methods, and expected analyses of a mother and child cohort study in Al Ain; the Mutaba'ah study. The study aims to investigate the maternal and early childhood determinants of infant, child, and adolescent health, as well as maternal health. The pregnant women recruited from the three participating hospitals are expected to be representative of the local population and will provide a rich depiction of the risk and protective factors experienced by the cohort as a whole.

Currently, there is only one ongoing two-year prospective birth cohort study (Mother-Infant Study Cohort; MISC) which recruited 256 of both UAE national and expatriate pregnant women late during their pregnancy in three emirates (Dubai, Sharjah and Ajman) of the UAE (25). The two-year follow-up period in the MISC study focuses on exploring the association between nutrition and lifestyle characteristics on birth outcomes, infant nutritional status, and cognitive development. Mutaba'ah on the other hand aims to recruit pregnant women during the first trimester of their pregnancy to enable exploring the early pregnancy exposures that influence maternal and fetal health during the second and third trimester, in addition to delivery complications and birth outcomes. Moreover, the planned long-term follow-up (16 years) will permit Mutaba'ah to investigate the prenatal and neonatal exposures that might be associated with infant, child, and adolescent health outcomes. Both the MISC and Mutaba'ah studies will enrich the scant body of maternal and child health research in the UAE.

The strengths of the Mutaba'ah study include the establishment of the largest longitudinal cohort of pregnant women and their children in the UAE. The prospective population-based design with the planned long follow-up of a large cohort of mothers and children has great advantages. The study will be able to collect high-quality clinical data from medical records which will reduce

missing data and imprecision in variables such as body mass and gestational age. Therefore, Mutaba'ah will secure epidemiological data and provide a pioneering platform for maternal and child health research. As in most epidemiologic studies, self-reported data and loss to follow-up (at least beyond birth) are potential weaknesses to this study.

Exposures to various risk factors *in utero* and during childhood have a major influence on health and development in adulthood. The impact of this study will extend beyond exposing factors that will be risky and protective for delivery and birth outcomes, childhood, and adolescent health. Mutaba'ah will create a databank for like-minded researchers to conduct work on maternal and child health in the country. It will provide insights into unique exposures and outcomes present in the region such as consanguinity (26), increasing rates of obesity in women and childrem (27, 28) gestational diabetes (29), and smoking practices such as shisha (30). The study will also provide opportinuities to use case-cohort and nested case-control designs for some unique research questions and to perform validation studies. Mutaba'ah will aim to initiate regional and international collaborations with similar onging mother and child cohort studies to enable performing international comparisons and generating more research prospects.

Cohort studies with such breadth and depth of data can provide important information to the public and authorities. This study will allow researchers to relate different health outcomes to a variety of early-life exposures using appropriate statistical methods based on the robust longitudinal cohort design. Study findings will provide the local, regional, and international scientific community with evidence of the burden and impact of diseases in maternal and child health in a high-income Arab country. Clinicians and public health policy makers can translate this evidence into health policies and practices to improve the health status and services for mothers and children.

ABBREVIATIONS

UAE: United Arab Emirates

MR: Medical Record

SQ: Short Questionnaire

LQ: Long Questionnaire

FFQ: Food Frequency Questionnaire

IQ: Infant Questionnaire

CQ: Child Questionnaire

AQ: Adolescent Questionnaire

CBC: Complete Blood Count

OGTT: Oral Glucose Tolerance Test

PAQ-C: Physical Activity Questionnaire for Older Children

PAQ-A: Physical Activity Questionnaire for Adolescents

ANOVA: Analysis of Variance

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Authors' contributions

LAA, TL and IB conceived, designed and initiated the study. LAA, FAM, HN, CB, SGA, FMA, AZ, TL and IB contributed to the planning of the study. LAA, AAH, NA, IE, HE, TL and IB contributed to the implementation, coordination and management of the study. LAA, AAH, NA, HE and TL drafted this manuscript. All authors read and approved the final version of the manuscript.

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Competing interests

The authors declare that they have no competing interests

Ethics approval

The study was approved by the United Arab Emirates University Human Research Ethics Committee (previously known as Al Ain Medical District Human Research Ethics Committee) (ERH-2017-5512), Al Ain Hospital Research Ethics Committee (AAHEC-03-17-058), and Tawam Human Research Ethics Committee (T-HREC–494). Informed written consent is obtained from the participant prior to the data collection.

Data sharing statement

Data sharing is not applicable to this article as no datasets were analyzed for this manuscript.

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FIGURE LEGEND

Figure 1: Data collection time points during the Mutaba'ah study

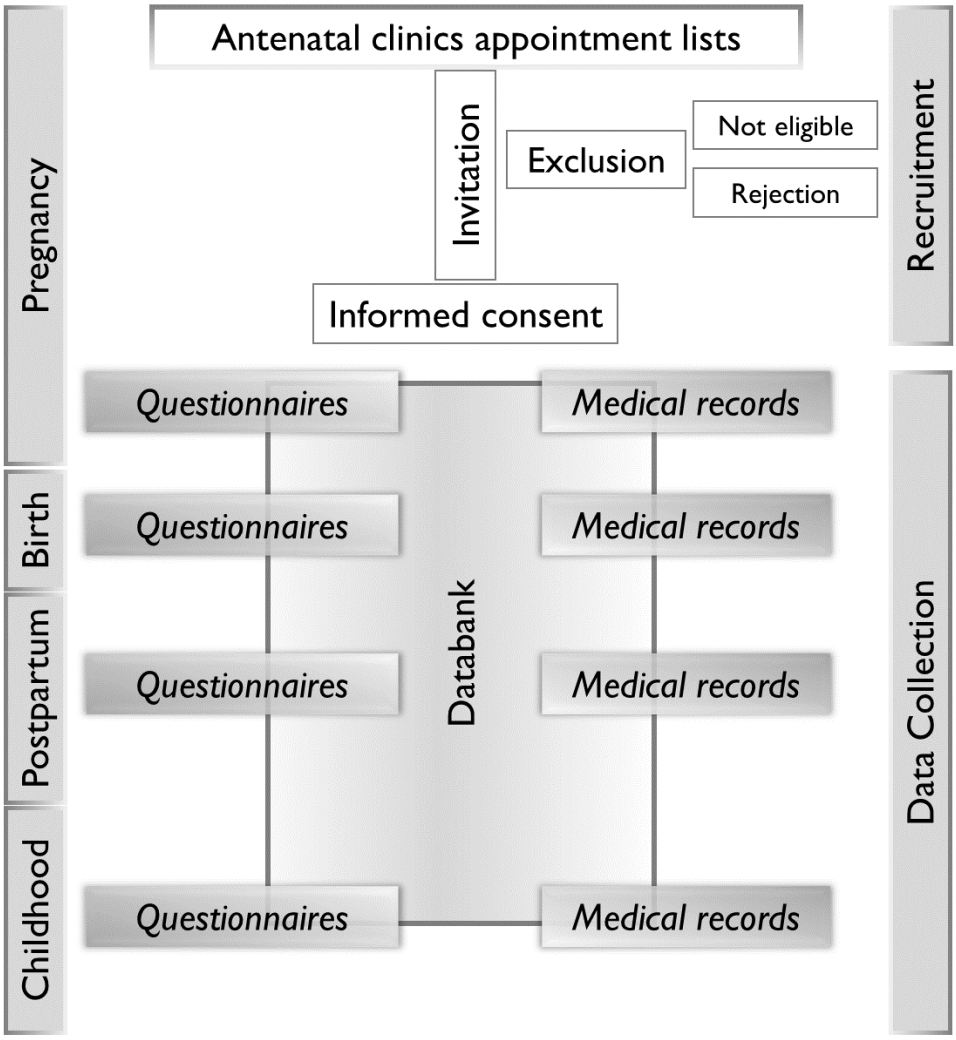
Table 1: Examples of data collected at different time points in the study

	Data	Source
Pregnancy	Past and current pregnancy, health, fertility, supplements, smoking, physical activity, and occupation	SQ
	More details on previous and current pregnancy, lifestyle, home and indoor air quality, mental health, and family health	LQ
	Diet, supplements, and herbal use	FFQ
	Anthropometric data on mother and laboratory test results	MR
Birth and delivery	Length of pregnancy, premature birth, pre-eclampsia, mode of delivery, maternal weight gain and weight after birth, gestational diabetes, birth weight, birth injury, and congenital malformations	MR
Infancy	Breastfeeding and nutrition	IQ
	Growth and development, diseases, and vaccination	MR
Childhood	Diet, physical activity, lifestyle, and medication	CQ
	Childhood diseases, asthma, diabetes, atopy, allergy, cognitive function, psychological behavior, and language skills	MR
Adolescence	Maltreatment, development, diet, physical activity, and lifestyle	AQ
	Any health issues	MR

(SQ) short questionnaire, (LQ) long questionnaire, (FFQ) food frequency questionnaire, (MR) medical records. (IQ) infant questionnaire, (CQ) child questionnaire, (AQ) adolescent questionnaire.

Table 2: Minimum detectable Relative Risks for different levels of exposure and proportions of affected unexposed based on a cohort of 8,000 with 80% power and 5% Type I error probability.

	Exposure level (%)	Proportion of outcome in unexposed group				
		1%	5%	10%	25%	50%
Protective exposure	**1%**	-	-	*0.202*	*0.491*	*0.688*
	5%	-	*0.425*	*0.588*	*0.753*	*0.853*
	10%	*0.125*	*0.562*	*0.69*	*0.816*	*0.891*
	25%	*0.332*	*0.68*	*0.775*	*0.867*	*0.922*
	50%	*0.427*	*0.727*	*0.808*	*0.887*	*0.934*
Harmful exposure	**50%**	*1.76*	*1.307*	*1.207*	*1.117*	*1.066*
	25%	*1.897*	*1.362*	*1.244*	*1.138*	*1.078*
	10%	*2.276*	*1.51*	*1.342*	*1.192*	*1.109*
	5%	*2.782*	*1.701*	*1.468*	*1.261*	*1.147*
	1%	*5.341*	*2.612*	*2.051*	*1.57*	*1.312*



Data collection time points during the Mutaba'ah study

Supplementary Table - Proposed/projected variables, time points and data source.

Dataset *(Approx. number of variables)*	**Data format and source**	**Collection period**	**Examples of types of exposures ascertained***	**Examples of types of outcomes ascertained***
Currently already in progress				
Short questionnaire *(200 variables)*	Self-administered via online portal using a tablet. Source: Mother	Pregnancy (ideally first trimester before 12 weeks, leeway: before delivery) Between 2017-2021	• Parity • Gravidity • Psychosocial details (social support, number of household members) • Age of menarche • Contraceptives • Education • Employment	• Previous pregnancy complications such as miscarriages and stillbirth • Congenital malformations • Current pregnancy issues including anxiety • Happiness levels
Long questionnaire *(330 variables)*	Self-administered via online portal using a tablet. Source: Mother	Pregnancy (ideally third trimester. However, any time before delivery) Between 2018-2022	• Ethnicity of paternal and maternal family • Infertility • Oral health • Menstrual cycle • Pregnancy planning • Previous Caesarean sections • Smoking • Alcohol consumption	• Mental health including depression (EPPDS), anxiety (STAI) and social support (MOS-SS) • Health Literacy (BRIEF) • Work absenteeism • Husband's health
Medical record extraction exercise 1 *(600 variables)*	Extracted from multiple portals according to hospital location by trained staff. Extracted onto offline app. Source: Hospital	Pregnancy and delivery collection period: Between 2018 – 2023	• Length of gestation • Consanguinity • Complete blood count • Gestational age at presentation at hospital	• Length of labor • Complications during pregnancy • Down's syndrome • Pregnancy outcome (live birth, still birth) • Gestational diabetes • Gestational hypertension • Anemia

Currently being processed or will be processed in the future; All details resemble data collected by predecessors and are prone to changes.				
Food frequency questionnaire for mother *(approx. 300 variables)*	Self-administered via online portal using a tablet. Source: Mother	At any time during pregnancy Collection period: 2019 – 2021	Dietary habits	Food related illness, allergies and consumption habits
Infant Questionnaire 1 and 2 (in progress) *(approx. 1000 variables)*	Self-administered via online portal using a tablet. Source: Mother	At 6 months and 12 months of child's life Collection period: 2020 – 2022	• Baby anthropometrics • Baby feeding practices • Sleeping patterns of the baby • Pregnancy intervals of future babies	• Onset of illness, if any • Milestones • Post-partum issues with respect to the mother
Medical record extraction exercises 2 and 3 *(approx. 600 variables)*	Extracted from multiple portals according to hospital location by trained staff. Extracted into offline app. Source: Hospital	Birth till 12 months of life Collection period: 2020-2022	• Baby birth details including gender, head and abdominal circumference • Other baby anthropometrics • Laboratory and imaging results • Discharge details	• Birth complications • Admission to NICU • APGAR score • Hospital admissions
Child Questionnaires (in progress) *(approx. 1500 variables)*	Self-administered via online portal using a tablet. Source: Mother and child	At 18, 36 months and 5 and 7 years of child's life Collection period: 2021-2028	• Child anthropometrics • Diet and lifestyle • Immunization • Sleeping patterns	• Onset of illness, if any • Milestones • Motor and behavioral developments • Relationships with family • Emotions and behavior (ASEBA; BASC-2; CRS-R; CSI-4; DMSD; PSC; RBPC; SDQ)
Medical record extraction exercise 4, 5, 6 and 7 *(approx. 1500 variables)*	Extracted from multiple portals according to hospital location by trained staff. Extracted into offline app. Source: Hospital	From 18 months till 7 years (at least 4) Collection period: 2021-2028	• Immunizations • Exposure to allergens • Genetic testing • Lab and imaging results (if any)	• Onset of illness, if any (if missed out by mother) • Hospital admissions • Anthropometry including BMI • Allergies

Adolescent Questionnaires *(approx. 1000 variables)*	Self-administered via online portal using a tablet. Source: Mother and child	At 11, 14 and 16 years Collection period: 2027-2038	• Diet • Physical activity • Education • Lifestyle	• Health issues • Maltreatment • Psychological behavior • Emotions and behavior (ASEBA; BASC-2; CRS-R; CSI-4; DMSD; PSC; RBPC; SDQ)
Medical record extraction exercise 8, 9, 10 *(approx. 1000 variables)*	Extracted from multiple portals according to hospital location by trained staff. Extracted into offline app. Source: Hospital	From 11 years to 16 years Collection period: 2027-2038	• Allergies • Psychological behavior • Personality traits • Anthropometry	• Onset of illness, if any (if missed out in questionnaires) • Hospital admissions • Obesity • Reproductive health (puberty)

* Please note that due to the longitudinal design of the Mutaba'ah study many outcomes during pregnancy will become exposures for outcomes during infancy, childhood, and adolescence. For example, we are interested in the lifestyle behaviours (exposures) associated with gestational diabetes mellitus (GDM; outcome during pregnancy) and then GDM becomes an exposure for specific outcomes late in the pregnancy (e.g. preeclampsia, delivery complications), birth (e.g. macrosomia), infancy (e.g. growth and development), and childhood (e.g. obesity), and adolescence (e.g. non-alcoholic fatty liver disease). APGAR denotes Appearance, Pulse, Grimace, Activity, and Respiration Score; ASEBA denotes Achenbach System of Empirically Based Assessment; BASC-2 denotes Behavior Assessment System for Children, Second Edition; BMI denotes Body Mass Index; BRIEF denotes the Brief Health Literacy Screening Tool; CSI-4 denotes the Child Symptom Inventory-4; CRS-R denotes Conners' Rating Scale – Revised; DMSD denotes the Devereux Scales of Mental Disorders; EPDS denotes Edinburgh Peri/Post-Natal Depression Scale; MOS-SS denotes Medical Outcomes Study Social Support Scale; NICU denotes Neonatal Intensive Care Unit; PSC denotes Pediatric Symptom Checklist; RBPC denotes Revised Behavior Problem Checklist; SDQ denotes Strengths and Difficulties Questionnaire; STAI denotes State-Trait Anxiety Inventory.