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Antenatal and Postnatal Depressive symptoms in Kuwait: results from the TRACER Study

PhD Thesis

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Approval Page

PhD Dissertation

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Abstract

Introduction: The perinatal period is characterized by hormonal and neurobiological changes which may result in mood changes, making women more susceptible to depression. Prenatal depression and postnatal depression are common in women and have been associated with adverse outcomes of both the child and the mother. Limited evidence exists in the Gulf countries about depression during and after pregnancy, as well as for their correlates. The aims of this PhD dissertation work were: a) to provide an estimate of the prevalence of antenatal depressive symptoms in Kuwait, as an indicator of depression, and identify the risk factors associated with it; b) to examine whether antenatal depressive symptoms and other potential risk factors are associated with adverse perinatal outcomes, such as preterm birth, small for gestational age, and large for gestational age; and c) to estimate the prevalence of postnatal depressive symptoms and identify the risk factors associated with it as well as examine the link with antenatal depressive symptoms.

Methods: This was a secondary analysis of data collected from 1938 women who participated in the TRansgenerational Assessment of Children's Environmental Risk (TRACER) Study - a longitudinal prospective birth cohort study in Kuwait. A baseline questionnaire was administered to all participants at enrollment while a stress questionnaire, that also included the Edinburgh Postnatal Depression Scale (EPDS), was administered at a later visit in person or through a phone-interview. A postnatal phone interview was conducted to obtain information about the birth date, birth weight, adverse outcomes during pregnancy, and postnatal depressive symptoms using the EPDS. A score of 10 or greater in the EPDS was used as a cut-off point to determine the presence of depressive symptoms antenatally and postnatally. Chi-square tests, crude and multiple logistic regression models were used to identify the risk factors of antenatal

and postnatal depressive symptoms, preterm birth, small and large for gestational age babies and assess their effect.

Results: The prevalence of antenatal depressive symptoms was 20.2% (95% CI: 18.4-22.1) while that of postnatal depressive symptoms was 11.7% (95% CI: 10.1-13.5). Antenatal depressive symptoms were reported more by women in the third trimester compared to those in the second trimester, women of lower family income, those who had experienced more than five traumatic events during their lifetime, and those women that had self-reported history of depression prior to pregnancy. Pregnancy-related anxiety, moderate and higher perceived stress, post-traumatic stress disorder symptoms, and fair or poor quality of mental health, as well as poor quality of physical health during pregnancy were also associated with the presence of antenatal depressive symptoms. In our sample, antenatal depressive symptoms did not predict adverse birth outcomes; preterm birth was associated with in vitro fertilization and previous preterm delivery, small for gestational age was associated with lower family income and a female baby, while large for gestational age was associated with a non-Kuwaiti nationality, parity, and a male baby. Antenatal depressive symptoms were the strongest risk factor for developing postnatal depressive symptoms. Other determinants of postnatal depressive symptoms included lower family income, being Kuwaiti, and reporting post-traumatic stress disorder symptoms in pregnancy. In the group of women with no depressive symptoms in pregnancy the mother's mental well-being and social support from her network were also significant risks factors for postnatal depressive symptoms.

Conclusions: Our results showed that in Kuwait, 1 in 5 women experiences depressive symptoms antenatally and 1 in 9 women postnatally. We recommend that antenatal and postnatal depression screening is performed as a routine test, especially among women who are at a higher risk of experiencing depression during the perinatal period. Improving the mental well-being of

women during pregnancy, helping them reduce their anxiety related to pregnancy, and making them feel less isolated, could also potentially lower the risk for postnatal depressive symptoms and their sequelae.

Περίληψη

Εισαγωγή: Η περιγεννητική περίοδος χαρακτηρίζεται από ορμονικές και νευροβιολογικές αλλαγές που μπορεί να οδηγήσουν σε μεταβολές της διάθεσης, καθιστώντας τις γυναίκες πιο ευάλωτες στην κατάθλιψη. Η κατάθλιψη κατά τη διάρκεια της εγκυμοσύνης και η επιλόχεια κατάθλιψη συναντούνται συχνά και έχουν συσχετιστεί με ανεπιθύμητα αποτελέσματα τόσο στη μητέρα όσο και στο παιδί. Στις χώρες του Αραβικού Κόλπου τα στοιχεία για τον επιπολασμό τους καθώς και για τους παράγοντες που σχετίζονται με αυτά είναι περιορισμένα. Οι στόχοι της παρούσας διδακτορικής διατριβής ήταν: α) να υπολογιστεί ο επιπολασμός των συμπτωμάτων κατάθλιψης στην εγκυμοσύνη και να διερευνηθούν οι παράγοντες κινδύνου τους, β) να εξεταστεί εάν τα συμπτώματα κατάθλιψης στην εγκυμοσύνη σχετίζονται με τον πρόωρο τοκετό και με την γέννηση νεογνών μικρότερων ή μεγαλύτερων με βάση την ηλικία κύησης τους και να διερευνηθούν περαιτέρω παράγοντες κινδύνου με αυτές τις δυσμενείς εκβάσεις, και γ) να εκτιμήσει τον επιπολασμό των συμπτωμάτων επιλόχειας κατάθλιψης, να προσδιορίσει τους παράγοντες που αυξάνουν τον κίνδυνο εκδήλωσής τους και να εξετάσει τη σχέση τους με τα συμπτώματα κατάθλιψης στην εγκυμοσύνη.

Μέθοδοι: Έγινε μία δευτερογενής ανάλυση των δεδομένων που συλλέχθηκαν από 1938 γυναίκες στο Κουβέιτ οι οποίες συμμετείχαν στην προοπτική μελέτη κοορτής TRansgenerational Assessment of Children's Environmental Risk (TRACER). Ένα αρχικό ερωτηματολόγιο με βασικές πληροφορίες είχε δοθεί στους συμμετέχοντες κατά την εγγραφή τους στην μελέτη ενώ ένα εκτενές ερωτηματολόγιο που είχε ως κύριο σκοπό να αξιολογήσει την ψυχική υγεία των εγκύων και το οποίο περιλάμβανε και την κλίμακα επιλόχειας κατάθλιψης του Εδιμβούργου (EPDS) διεξήχθη σε μεταγενέστερη επίσκεψη κατά την διάρκεια της εγκυμοσύνης. Τέλος, διεξήχθη μια τηλεφωνική συνέντευξη των μητέρων μετά τον τοκετό για να ληφθούν πληροφορίες σχετικά με την ημερομηνία και το βάρος γέννησης του βρέφους, δυσμενείς

εκβάσεις κατά τη διάρκεια της εγκυμοσύνης και του τοκετού, και συμπτώματα επιλόχειας κατάθλιψης χρησιμοποιώντας το EPDS. Εάν η βαθμολογία στο EPDS ήταν μεγαλύτερη ή ίση με το 10, τότε θεωρούμε ότι υπήρχαν συμπτώματα κατάθλιψης. Οι στατιστικές αναλύσεις έγιναν με τη χρήση απλών και πολλαπλών μοντέλων λογιστικής παλινδρόμησης καθώς και με τη χρήση της δοκιμασίας χ^2.

Αποτελέσματα: Ο επιπολασμός συμπτωμάτων κατάθλιψης κατά την διάρκεια της εγκυμοσύνης ήταν 20,2% (95% CI: 18,4-22,1) ενώ των συμπτωμάτων επιλόχειας κατάθλιψης ήταν 11,7% (95% CI: 10,1-13,5). Τα συμπτώματα κατάθλιψης ήταν πιο συχνά σε γυναίκες στο τρίτο τρίμηνο της εγκυμοσύνης τους σε σύγκριση με εκείνες του δευτέρου τριμήνου, σε γυναίκες με χαμηλότερο οικογενειακό εισόδημα, σε αυτές που είχαν βιώσει περισσότερα από πέντε τραυματικά γεγονότα κατά τη διάρκεια της ζωής τους και σε αυτές που είχαν ιστορικό κατάθλιψης (αυτό-αναφορές). Το άγχος που σχετίζεται με την εγκυμοσύνη, περισσότερο αντιληπτό στρες, συμπτώματα Συνδρόμου Μετατραυματικού Στρες, η κακή ποιότητα ψυχικής υγείας και η κακή ποιότητα σωματικής υγείας κατά τη διάρκεια της εγκυμοσύνης συσχετίζονταν επίσης με την παρουσία συμπτωμάτων κατάθλιψης. Στο δείγμα μας, τα συμπτώματα κατάθλιψης στην εγκυμοσύνη δεν συνδέονταν με δυσμενή αποτελέσματα στη γέννηση -- ο πρόωρος τοκετός συσχετίζεται με την εξωσωματική γονιμοποίηση και με το ιστορικό πρόωρου τοκετού σε προηγούμενη εγκυμοσύνη, η γέννηση μικρότερου για την ηλικία κύησης νεογνού συσχετίζεται με ένα χαμηλότερο οικογενειακό εισόδημα και το φύλο του νεογνού (θηλυκό), ενώ αυτό της γέννησης μεγαλύτερου για την ηλικία κύησης νεογνού συσχετίζεται με την εθνικότητα (εκτός Κουβέιτ) και με το φύλο του νεογνού (αρσενικό). Τα συμπτώματα κατάθλιψης στην εγκυμοσύνη ήταν ο ισχυρότερος παράγοντας κινδύνου για την ανάπτυξη συμπτωμάτων επιλόχειας κατάθλιψης. Άλλοι καθοριστικοί παράγοντες για την επιλόχεια κατάθλιψη ήταν το χαμηλότερο οικογενειακό εισόδημα, η εθνικότητα (Κουβέιτ) και τα συμπτώματα Συνδρόμου

Μετατραυματικού Στρες κατά την εγκυμοσύνη. Η ψυχική ευεξία της μητέρας και η υποστήριξη από το κοινωνικό της δίκτυο ήταν επίσης σημαντικοί παράγοντες κινδύνου για τα συμπτώματα επιλόχειας κατάθλιψης στην ομάδα των γυναικών που δεν είχαν συμπτώματα κατάθλιψης κατά την εγκυμοσύνη.

Συμπεράσματα: Σύμφωνα με τα αποτελέσματα μας, στο Κουβέιτ 1 στις 5 γυναίκες παρουσιάζει συμπτώματα κατάθλιψης πριν τον τοκετό και 1 στις 9 παρουσιάζει συμπτώματα κατάθλιψης μετά τον τοκετό. Συνιστούμε όπως μια διαδικασία διαλογής για την κατάθλιψη πριν και μετά τον τοκετό πραγματοποιείται ως εξέταση ρουτίνας, ειδικά σε γυναίκες που διατρέχουν μεγαλύτερο κίνδυνο να παρουσιάσουν κατάθλιψη κατά την περιγεννητική περίοδο. Η βελτίωση της ψυχικής ευεξίας των γυναικών κατά τη διάρκεια της εγκυμοσύνης, βοηθώντας τις να μειώσουν το άγχος που σχετίζεται με την εγκυμοσύνη και να νιώσουν λιγότερο απομονωμένες, θα μπορούσε επίσης να μειώσει την πιθανότητα κατάθλιψης και τα επακόλουθα της.

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Chapter 1 – Overview, Rationale, and Aims of dissertation

Brief overview

The period of pregnancy is considered in general as a period of anticipation for women but the hormonal and lifestyle changes that occur may result in mood changes, making women more susceptible to mental diseases such as depression. Depression in pregnancy, referred to as antenatal, prenatal, or antepartum depression, is a relatively common mental health problem with prevalence rates varying from 5 to 30% in developed countries (Pereira et al., 2011). However, despite the effects that antenatal depression may have on the health of the mother and the baby, it is usually overlooked (Grigoriadis et al., 2013; Rubertsson et al., 2003).

Depression in pregnancy has been linked with adverse pregnancy and birth outcomes, such as preeclampsia and delivery with obstetric forceps or cesarean section (Grigoriadis et al., 2013; Hu et al., 2015). A lower Apgar score has also been observed among newborns from mothers with depression (Goedhart et al., 2010). Some studies have shown that antenatal depression is linked to preterm delivery, low birth weight, and small for gestational age (SGA) babies, though these associations remain unclear, with the results of different studies being contradictory (Berle et al., 2005; Bindt et al., 2013; Fransson et al., 2011; Grigoriadis et al., 2013; Grote et al., 2010; Rahman et al., 2007; Szegda et al., 2016).

Women with antenatal depression are more likely to engage in unhealthy activities during pregnancy, such as smoking, using alcohol and drugs, and having poor nutrition (Zuckerman et al., 1989), and less likely to initiate breastfeeding (Grigoriadis et al., 2013). Furthermore, antenatal depression is a risk factor for postnatal depression. Postnatal, or postpartum, depression is another common problem that occurs after birth and has adverse effects on the mother-child bonding, the mother's health, and the development of the child (Logsdon et al., 2006).

Epidemiologic studies conducted in different countries have identified several risk factors associated with perinatal depression, i.e. depression experienced during pregnancy (antenatal) and/or within 12 months after childbirth (postnatal) (Dmitrovic, Dugalic, Balkoski, Dmitrovic, & Soldatovic, 2014) with the majority of them focusing on the determinants of postnatal depression. Apart from the biological risk factors, a number of socio-demographic and pregnancy related factors have also been reported, including maternal anxiety, life stress, history of depression, lack of social support, unintended pregnancy, lower income, lower education, being single, or not having a good relationship with the father (Lancaster et al., 2010). These factors may in fact vary depending on the location of the study. Determining the risk factors associated with perinatal depression in a particular area is important in planning strategies to reduce the magnitude of this problem, as well as the risk of its sequelae.

Aims

Major depressive disorders are on the rise in several high income countries of the Arab World, such as Kuwait, and they are a major cause of reduced disability-adjusted life-years (DALYs) (Mokdad et al., 2014). The impact of major depression is higher among females in the reproductive ages (Mokdad et al., 2014). Despite the importance of mental health, there is still very limited evidence about depression, and pregnancy related depression, in Kuwait and the neighboring countries. Identifying the potential determinants for developing antenatal and postnatal depression is important in understanding the problem and for designing successful screening and intervention programs. Thus, the main aims of this dissertation work are to:

1) Provide an estimate of the prevalence of self-reported antenatal depressive symptoms in Kuwait, as an indicator of depression, and identify the risk factors associated with it;

2) Examine whether antenatal depressive symptoms and other potential risk factors are associated with adverse perinatal outcomes, such as preterm birth, small and large for gestational age; and

3) Estimate the prevalence and identify the risk factors of self-reported postnatal depressive symptoms and examine the link with antenatal depressive symptoms.

Outline

The rationale and the aims of this work are explained in Chapter 1.

Chapter 2 provides background information about Kuwait and describes the TRansgenerational Assessment of Children's Environmental Risk (TRACER) study, including details about the participants, measures, and outcomes of interest.

Chapter 3 focuses on antenatal depressive symptoms. It provides the literature review on the topic, followed by the methods and results on the prevalence and the determination of risk factors of antenatal depressive symptoms in Kuwait using data from the TRACER Study. It concludes with a discussion of the estimates of the prevalence and the risk factors identified.

Chapter 4 presents a brief literature review on adverse pregnancy outcomes that can occur at birth, such as preterm delivery, small and large for gestational age, and the evidence available of their association with antenatal depression. The association of these outcomes with antenatal depressive symptoms and other potential risk factors is also investigated in this chapter with the use of the TRACER data.

Chapter 5 deals with the definition and determinants of postnatal depression and examines the association of antenatal depressive symptoms and postnatal depressive symptoms. Other potential risk factors of postnatal depressive symptoms are also investigated.

Chapter 6 summarizes the conclusive points of this work, its major limitations and strengths, and discusses future directions.

Finally, an Appendix is provided at the end of this work which includes additional figures and tables, as well as the different measures used in this study.

Chapter 2 – Kuwait and the TRACER Study

Kuwait

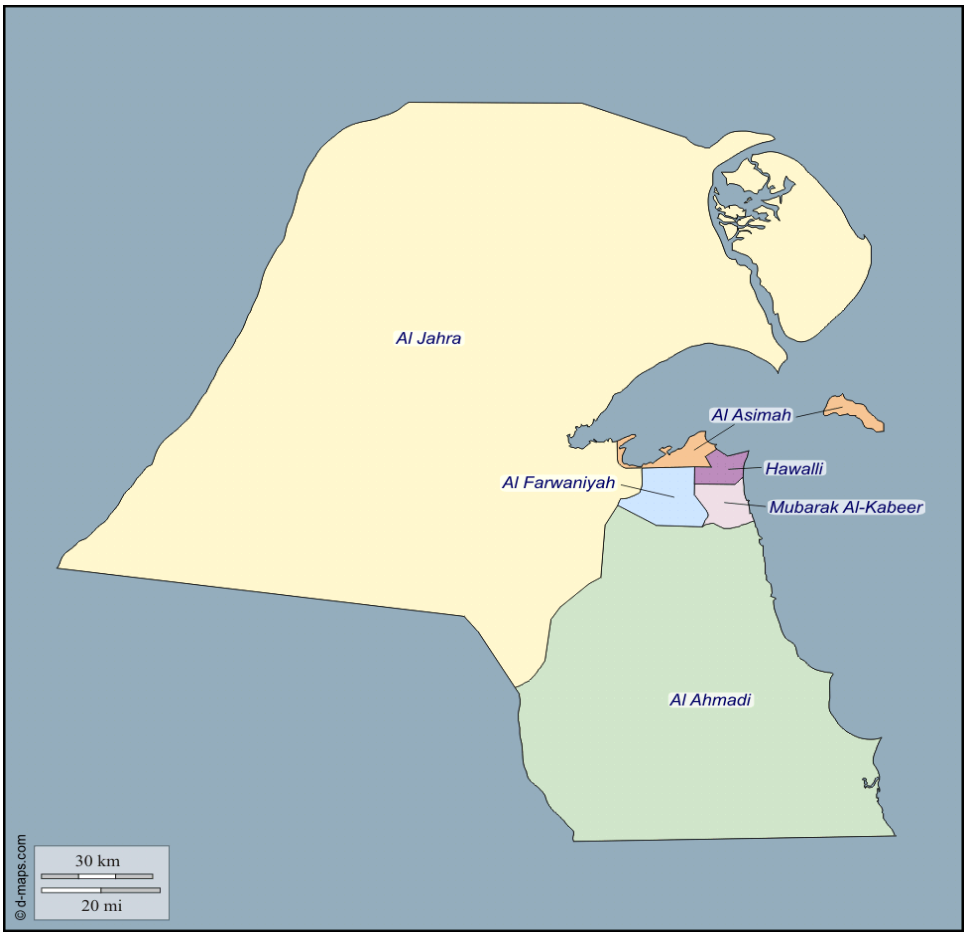
Kuwait is an Arab country which is located in the Gulf region (Figure 2.1). According to the World Bank, Kuwait is one of the wealthiest countries in the world and the second wealthiest in the Middle East region, after Qatar (Gregson Jonathan, 2017).

Figure 2.1 – Location of Kuwait, adapted from Map data © Google, Mapa GISrael, ORION-ME (Maps data ©2017 Google, Mapa GISrael, n.d.).

The country is small with an area of 6880 square miles. As shown in Figure 2.2, the country is divided into six governorates (D-maps.com, n.d.). The governorate of Jahra is the largest in area but the population is mostly concentrated in Hawalli, Farwaniya, and Ahmadi governorates (The Public Authority For Civil Information, n.d.). In August 1990 Kuwait experienced an invasion by Iraq which was followed by an occupation that lasted approximately 7 months. Despite the fact that this was a relatively short period of conflict, human rights were violated and civilians lived in rough conditions and suffered the consequences of the warfare (Kälin, 1992; Wright et

al., 2010). This recent war experience is one more of the unique characteristics of the Kuwait population.

Figure 2.2 – Map of Kuwait



The population of Kuwait, as reported by the Kuwaiti Public Authority for Civil Information, is approximately 4.4 million, out of whom only 1.3 million are Kuwaitis (The Public Authority for Civil Information, n.d.). The majority of women in the reproductive period (20-44 years old) are non-Kuwaitis (Figure 2.3) and most of them are married (Figure 2.4). In 2016, there were 57561 births, with more than half (33004) being among Kuwaitis (Figure 2.5). The majority of mothers for these births were aged from 20-44 years (The Public Authority for Civil Information, n.d.). [Figures 2.3, 2.4, and 2.5 were created based on data obtained from the Kuwait Public Authority for Civil Information (The Public Authority for Civil Information, n.d.).]

Figure 2.3 – Nationality of women in their reproductive age by age group

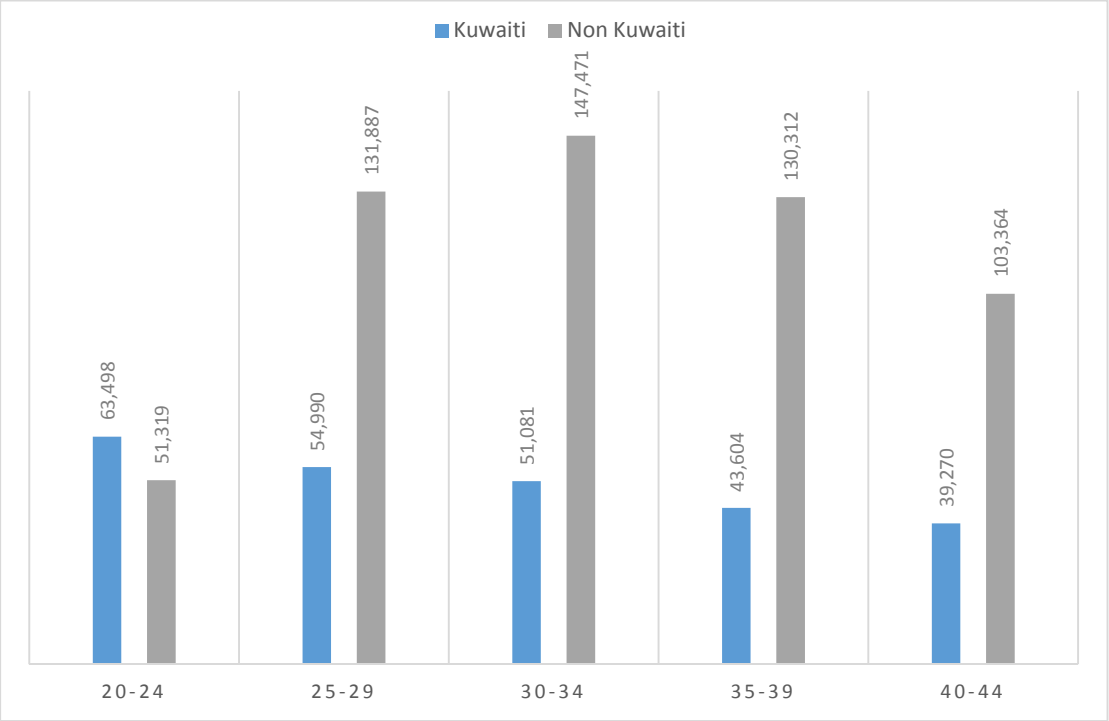


Figure 2.4 – Marital status of women in their reproductive age by age group

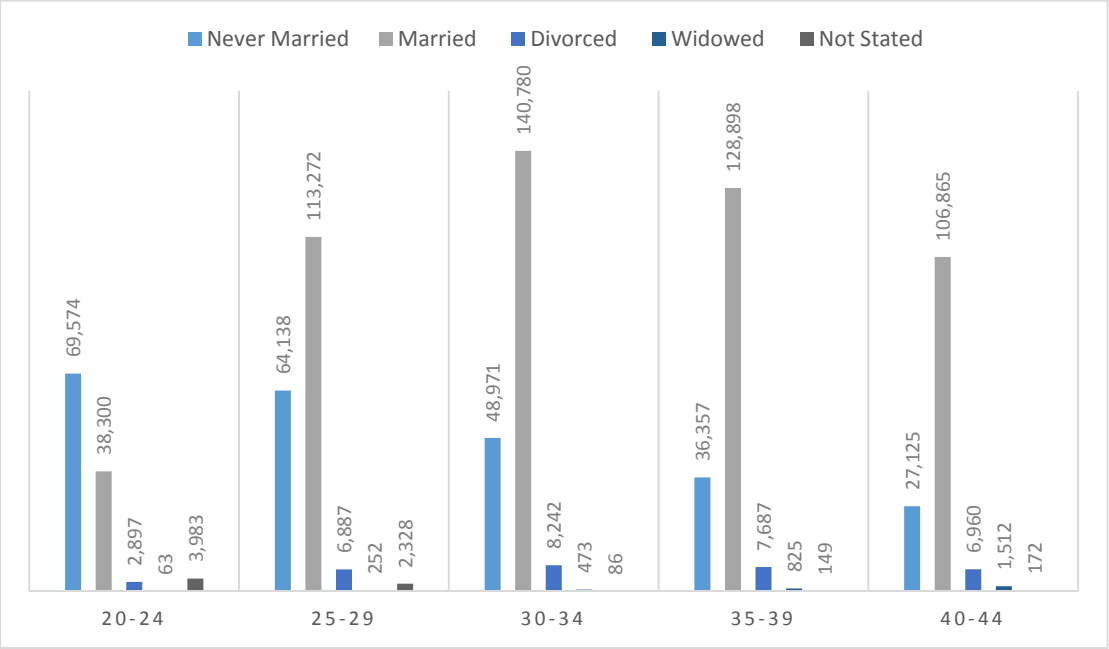
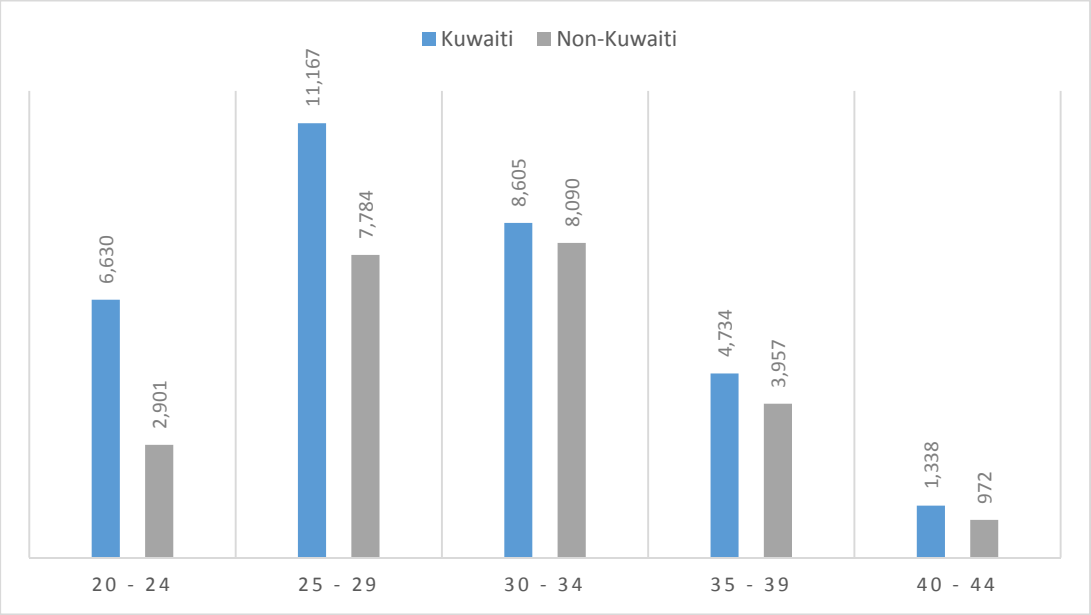


Figure 2.5 – Births in 2016 by age group (20-44) and nationality



The TRACER Study

This dissertation work is based on secondary analyses of the data collected in the TRansgenerational Assessment of Children's Environmental Risk (TRACER) Study. Details of the TRACER study have been published elsewhere (AlSeaidan et al., 2016). Briefly, the TRACER Study is a longitudinal prospective birth cohort study conducted in Kuwait with the goal of examining prenatal risk factors for early childhood obesity. In addition, the objectives of the study are to look at allergies and early programming for future chronic diseases. This study was set up by the Harvard T.H. Chan School of Public Health, the Dasman Diabetes Institute, and the Cyprus University of Technology. Ethical approval for the TRACER Study was obtained from the institutional review boards at both Harvard T.H. Chan School of Public Health and the Dasman Diabetes Institute and permission to recruit participants was provided by the participating health centers. Women were eligible to participate, if they were 18 to 45 years old, fluent in Arabic or English, and were willing to participate. Pregnant women who attended public and private health care centers were provided with a brochure of the project. Those who

were interested in participating were then referred to a member of the TRACER research team who provided further details of the study and obtained a signed informed consent from the pregnant woman and her husband. Women were enrolled usually in the visit following the receipt of signed consents. Women were excluded from the study if they were found to have a multiple pregnancy or the baby was to be born with a fetal abnormality. Participants were recruited and enrolled primarily during their second trimester (48%) after pregnancy was confirmed, but pregnant women in their first (16%) and third (36%) trimester were also enrolled in the study.

The data collection process included a series of interviewer-administered questionnaires to assess demographics, medical history, diet, physical activity, psychological stress, and the health of the mother and the baby. Biological samples were also collected and banked, although these samples were not used in this dissertation work. The data collection process started in May 2012 and ended in August 2015. The questionnaires used in this thesis are listed below.

(a) Baseline Questionnaire

The Baseline Questionnaire was administered at enrollment and included questions on demographics, socio-economic status, and medical history of the mother.

(b) Stress Questionnaire

The Stress Questionnaire was administered at a later visit, nominally during a clinic visit at 22 to 26 weeks gestation or by a phone interview. It included sections examining factors both before and during pregnancy, such as antenatal depressive symptoms, childhood emotional neglect, lifetime traumatic events, pregnancy-related anxiety, perceived stress, post-traumatic stress disorder (PTSD) symptoms, support from social network, and summary scales for physical and mental quality of health (see Appendix).

If a woman was enrolled at a later stage of her pregnancy both the Baseline Questionnaire and the Stress Questionnaire were administered at that time.

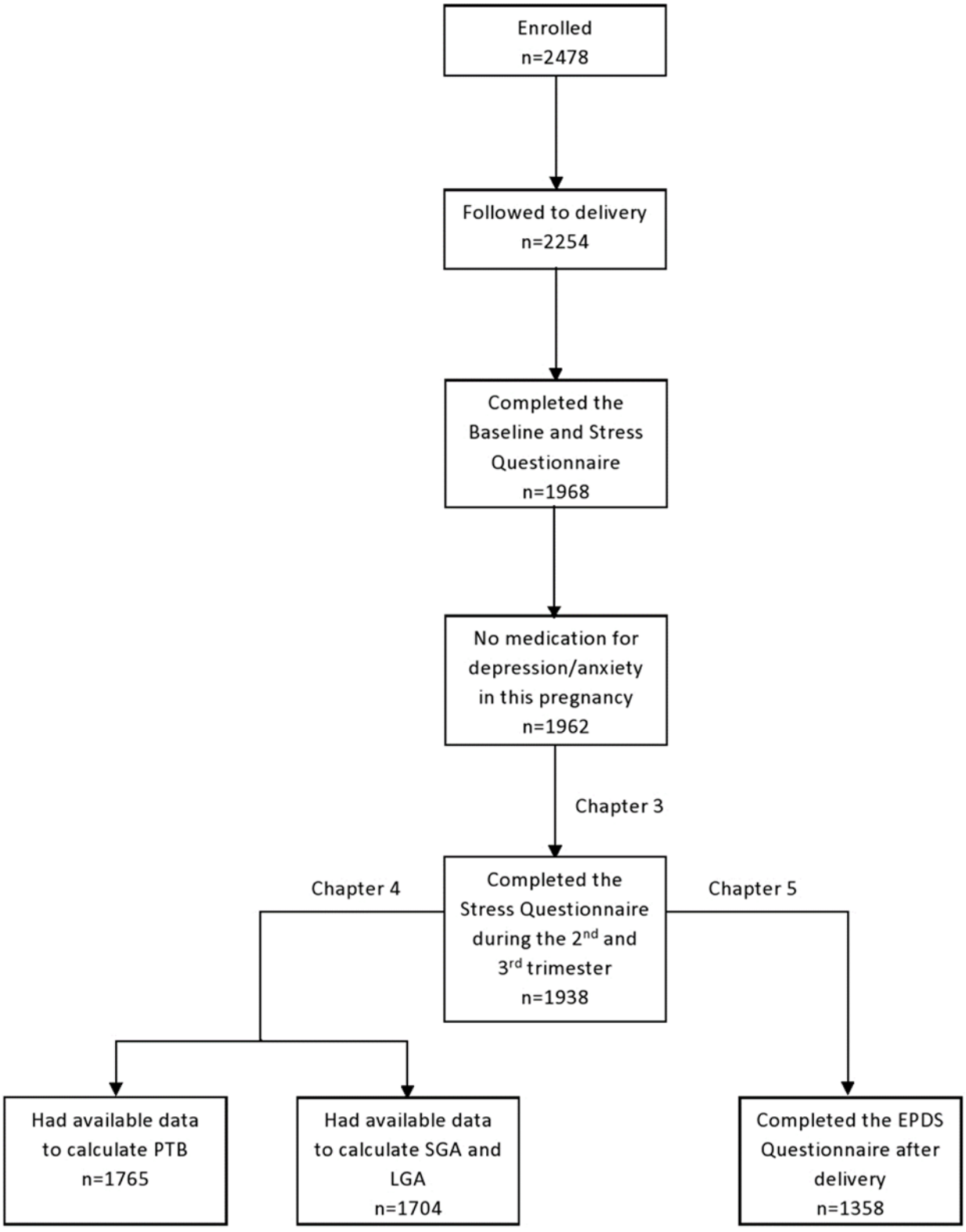
(c) Postnatal Questionnaire

A postnatal phone interview was conducted to obtain information about the birth date, birth weight, and adverse outcomes during pregnancy, such as gestational diabetes and gestational hypertension. During that same interview a questionnaire was used to evaluate the health and diet of the baby, as well as to assess postnatal depressive symptoms.

Participants

A total of 2478 women (739 Kuwaiti and 1739 non-Kuwaiti) were enrolled in this prospective cohort study, in a ratio that reflected the heterogeneity in the population of Kuwait where about 70% of the residents are non-Kuwaitis. Out of the enrolled participants, 2254 (91%) of them were followed to delivery. There were 1968 women who completed both the baseline and the stress questionnaires with usable data. We excluded women who took anxiety or depression medication during the current pregnancy (n=6) and we further restricted the sample only to women who had answered the section on depressive symptoms in the Stress Questionnaire during their second or third trimester of the pregnancy (n=24 women that completed the questionnaire in the first semester were excluded because according to the study protocol women should complete the questionnaire during the second or third trimester), thus ending with a sample of 1938 women for the subsequent analyses (Figure 2.6).

Figure 2.6 – Description of sample



Measures

(a) Outcomes of interest

1) Antenatal depressive symptoms

Depressive symptoms during pregnancy were assessed using the Edinburgh Depression Scale (EDS). This is the same tool as the Edinburgh Postnatal Depression Scale (EPDS) which was originally used to assess postnatal depression, but it has been validated in different languages for use in women who are not in the postnatal period (Cox et al., 1996). There are 10 items in the EDS, each scoring from 0 to 3, for a total score of 0-30. More specifically, these 10 items examine if the participant in the last 7 days:

- was able to laugh
- looked forward with enjoyment to things
- blamed herself unnecessarily
- felt anxious or worried
- felt scared or panicky
- felt overwhelmed
- felt so unhappy that she could not sleep
- felt so unhappy that she has been crying
- felt sad or miserable
- had thoughts of self-harm

Higher EDS scores indicate higher levels of depressive symptoms. Therefore, the ordering for the first two items listed, i.e. ability to laugh and looking forward to things with enjoyment had to be reversed, so that a higher score would indicate inability to laugh and inability to look forward to things with enjoyment. Different cut-off points for defining depressive symptoms have been recommended in the literature, such as 10, 12, 13, and 15 (Bisetegn, Mihretie, &

Muche, 2016; Coll et al., 2017; Giardinelli et al., 2012; Matthey, Henshaw, Elliott, & Barnett, 2006). For our study we selected the cut-off point of EDS≥10, which was used in studies conducted in multi-ethnic populations (Nasreen et al., 2010; Shakeel et al., 2015), and was also the recommended cut-off for the Arabic version of the EPDS for the antenatal period by the State Perinatal Mental Health Reference Group of Western Australia (Department of Health, Government of Western Australia, 2006). EDS is used for screening for the presence of depressive symptoms and not for diagnosis of depression, which requires a psychiatric examination.

2) Preterm Birth

The date of last menstrual period and the birth date were used to calculate the gestational age at birth. Preterm birth (PTB) was defined as a gestational age at birth that was less than 37 weeks.

3) Small and Large for Gestational Age

Small for gestational age (SGA) was estimated based on the World Health Organization birth weight percentiles for gestational week. If the birth weight was lower than the 10^{th} percentile for the gestational age then the neonate was characterized as SGA. Similarly, large for gestational age (LGA) was defined by a birth weight greater than the 90^{th} percentile.

4) Postnatal depressive symptoms

The Edinburgh Postnatal Depression Questionnaire was used to examine depression in the postpartum period. Similar to antenatal depressive symptoms, we used a cut-off of EPDS≥10 to define the presence of depressive symptoms in the postpartum period.

(b) Covariates of interest

1) Childhood emotional neglect

In order to assess the emotional neglect of the mother in childhood, the Child Trauma Questionnaire (Bernstein et al., 1994) was included in the Stress Questionnaire of TRACER. A likert scale from 1-5 (with 1 being "very often" and 5 being "never") was utilized to describe each of the following statements:

- "I felt like there was someone in my family who wanted me to be a success"
- "There was someone in my family who helped me feel that I was important or special"
- "My family was a source of strength and support"
- "People in my family felt close to each other"
- "Someone in my family believed in me"

A higher total score indicates less support and more emotional neglect from the family during childhood years. Three categories were created based on the tertiles of the total score in our sample; least, moderately, and most emotionally neglected during childhood.

2) Traumatic events

The Stress Questionnaire also examined exposure to lifetime traumatic events, both war and non-war related. Questions from the Brief Trauma Questionnaire that examined events in which the woman experienced fear or witnessed a situation where she feared for someone being seriously injured or killed, or feared that she would be injured or killed, were included in this scale, along with other related questions added by the investigators of TRACER (including war related events witnessed or experienced by the woman herself, or experienced by a person close to her, such as house searching, house destruction, hiding, assault, rape, threats, attack or injury, arrest, torture etc. as well as non-war related events, including experiencing death of one of her children,

emotional or psychological mistreatment, witnessing an attack etc.). Three categories were created, based on the tertiles of the total number of traumatic events, namely, 0-1, 2-4, and 5 or more lifetime traumatic events.

3) Pregnancy related anxiety

Concerns about pregnancy, delivery, and the health of the baby were examined using a 7-item questionnaire previously used by Fairlie et al. (2009). The women had to indicate which of the following statements applied to them:

- I am concerned or worried about how the baby is growing and developing inside me
- I am concerned or worried about having a hard or difficult delivery
- I am worried that the baby could be abnormal
- I am afraid that I will be harmed during delivery
- I am concerned or worried about losing the baby
- I have a lot of fear regarding the health of my baby
- I am concerned or worried about developing medical problems during my pregnancy

Each of these items had four possible responses: "Not at all", "Somewhat", "Moderately", and "Very much". Pregnancy-related anxiety was defined by three or more responses of "Very much", while all other women were categorized in the low-moderate anxiety group (Fairlie et al., 2009).

4) Perceived stress

The short version of the Cohen Perceived Stress Scale Questionnaire (Cohen & Williamson, 1988) was used to calculate the perceived stress score. This measure has 4 items which examine how often in the previous month the women felt:

- That difficulties were piling up so high that they could not overcome them

- Unable to control the important things in their life
- Not confident about their ability to handle their personal problems
- That things were not going their way

Each component was evaluated on a scale from 0-4, with 4 indicating higher levels of perceived stress, and the total score ranged from 0-16. The tertiles of the total score were used to classify women into three groups; lower (0-4), moderate (5-7), and higher (8-16) levels of perceived stress.

5) PTSD symptoms

The presence of post-traumatic stress disorder (PTSD) symptoms, following either war experiences or their worst stressor in the case of no war-related experience, was evaluated using the Breslau 7-item questionnaire (Breslau et al., 1999). There are seven items in this screening test examining whether there have been times when women:

- Tried to stay away from activities or situations that reminded them of any of their war experiences (or worst stressor)
- Were less interested in important activities that once gave them pleasure, such as sports, hobbies, or social activities
- Felt distant or cut off from those around them
- Felt emotionally numb, had trouble experiencing feelings such as love or happiness
- Felt that there was no need to plan for the future and that somehow their future would be cut short (apart from life-threatening events or illnesses)
- Had problems falling or staying asleep

- Experienced strong startle reactions to loud, unexpected noises (e.g., car backfires, fireworks, doorslams, etc.) or things that they saw (e.g., movement in the corner of their eye)

Each item was answered with a "yes" or a "no" and a total of 4 or more "yes" responses was considered as an indication of the presence of PTSD symptoms (Breslau et al., 1999).

6) SF36v2 (Mental and physical component summaries)

The Short Form 36 questionnaire is the short version of the Medical Outcomes Study questionnaire designed to measure physical and mental health status in population surveys (Ware et al., 1993). The questionnaire administered in our study is the second version of this questionnaire (SF-36v2). There are 36 items in the questionnaire, which are grouped in 8 scales, namely:

- Physical functioning
- Role limitations due to physical health
- Bodily pain
- General health perceptions
- Vitality
- Social functioning
- Role limitations due to emotional problems
- Mental health

The scores from the first 4 scales are used to calculate a summary measure for physical health, the physical component summary (PCS), while the sum of the other 4 scales provides a summary for the mental component summary (MCS), with a higher score indicating better self-reported health. We adopted the statistical program used by Fryback et al. (2007) in the National Health

Measurement Study, as provided in the "Explanation of Computed Variables" guide to compute PCS and MCS. More explicitly, the means and standard deviations of the PCS and MCS from the 1998 US National Survey of Functional Health Status were used to calculate z-scores for PCS and MCS in our population (Fryback et al., 2007). The z-scores were then multiplied by 10 and the product was added to 50, as the scoring used in SF36v2 is norm-based, with the mean set to 50 and the standard deviation to 10. Then, we created three categories for both mental and physical component summaries using the tertiles of the norm-based scores. The first, second, and third tertiles of the score corresponded to poor, fair, and good health, respectively.

7) Social network

The mother's social network status was examined by using an adapted version of the Berkman-Syme Social Network Index (Berkman and Syme, 1979), as used in Barrett and Mosca (2013). The four components of this questionnaire, namely marital status, number and frequency of contacts with family and friends, participation in religious services, and participation in social or community groups, provided an indication of whether the participant was socially isolated or socially integrated. Each component received a score of 0 or 1, with 1 indicating the more socially integrated person, i.e. women who were married, had at least 2 people to support them, participated in religious services weekly, and were members of social or community groups. The total score could range from 0 to 4 with a score of less than 2 corresponding to the most isolated women, a score of 2 to the moderately isolated women, 3 to the moderately integrated ones, and 4 to the most integrated women (Loucks et al., 2006).

8) Other variables

Apart from the measures mentioned above, which were all assessed using the Stress Questionnaire, we also examined other variables collected at enrollment that could be associated with the outcomes of interest investigated in this thesis. These variables included age, nationality

(Kuwaiti vs. non-Kuwaiti), employment status, educational level, household income, parity, pre-pregnancy BMI, and type of clinic (private, public or other). The gestational age in weeks at the time of completion of the Stress Questionnaire was calculated as the date at the Stress Questionnaire minus the self-reported date of the woman's last menstrual period. Similarly, the gestational age at birth was calculated as the birth date minus the self-reported date of the last menstrual period.

Furthermore, we considered the role of complications in previous pregnancies, such as miscarriages, preterm labor, bleeding not related to miscarriage, gestational diabetes or gestational hypertension, as well as history of depression prior to the current pregnancy on antenatal depressive symptoms. History of depression was self-reported and was defined as a physician's diagnosis of depression or use of anti-depressive medication. Conception by in-vitro fertilization (IVF), gestational diabetes, and gestational hypertension in current pregnancy, as well as the sex of the neonate were considered as risk factors for the adverse birth outcomes examined in Chapter 4. More details about which variables were used to predict each outcome of interest are provided in each of the corresponding chapters.

Chapter 3 – Prevalence and Risk Factors of Antenatal Depressive Symptoms

Introduction

Antenatal depression is defined as the depression that occurs during pregnancy, prior to delivery. Even though it is a common problem and may result in complications before, during, and after birth, screening for antenatal depression is not common. Moreover, the number of epidemiologic studies that examined antenatal depression is limited, especially when compared to the large number of studies that focused on postnatal depression.

The levels of antenatal depression vary widely and rates are usually higher in low and middle income countries (Fisher et al., 2012). According to the systematic review of Pereira et al. (2011) the prevalence of antenatal depression in developed countries ranges from 5% to 30%. In the Arab speaking countries, only a few studies have examined the prevalence of depression during pregnancy and the factors associated with this condition. For example, the prevalence of antenatal depression in Jordanian women was reported to be 19% (K. I. Mohammad, Gamble, & Creedy, 2011) and in Omani women 24% (Al-Azri et al., 2016).

Demographic and socioeconomic factors have been previously identified as risk factors for antenatal depression. Studies have suggested that women who face financial problems or those coming from lower income groups are more likely to develop depression (K. I. Mohammad et al., 2011). Similarly, women who are unemployed (Marcus, Flynn, Blow, & Barry, 2003) or housewives (Matteo et al., 2012) are more likely to report antenatal depressive symptoms. In addition, higher depression rates are observed among women with a lower educational status (Abuidhail & Abujilban, 2014; Coll et al., 2017; Marcus et al., 2003) and among migrant women (Giardinelli et al., 2012). Women with different ethnicities show different levels of antenatal depression (Waldie et al., 2015).

The marital status, the relationship of the mother with her partner, and the support that a woman receives during the antepartum period also contribute to the development of antenatal depression. Women who are unmarried (Marcus et al., 2003), who have difficult relationships with their partner (Giardinelli et al., 2012), who lack marital support (Ratcliff, Sharapova, Suardi, & Borel, 2015), or those who experience domestic violence (Lancaster et al., 2010) are more likely to report antenatal depressive symptoms. Family members other than the partner may provide support to the woman and thus reduce her risk of developing depression in pregnancy. A relationship of low quality between the woman and her mother, or her mother-in-law, is associated with depression (K. I. Mohammad et al., 2011; Senturk, Abas, Berksun, & Stewart, 2011). Similarly, the lack of social support was reported in the systematic review of Lancaster et al. (2010) as a risk factor for antenatal depression.

Several mental health problems have been found to be associated with depression in pregnancy. Firstly, antenatal depression is more common among women who self-reported history of depression or had lifetime psychiatric disorders (Bisetegn et al., 2016; Giardinelli et al., 2012; Marcus et al., 2003; Shakeel et al., 2015). Women who report greater levels of stress and anxiety before or during pregnancy and those who show low self-efficacy are at greater risk of developing antenatal depressive symptoms (Lancaster et al., 2010; K. I. Mohammad et al., 2011; Rubertsson et al., 2003; Waldie et al., 2015). Moreover, the risk is higher among women who have previously experienced adverse stressful life events (Lancaster et al., 2010; Rubertsson et al., 2003).

Adverse events in previous pregnancies, including stillbirth and abortion, lower health status, and a higher pre-conception BMI are strong risk factors of antenatal depression (Bisetegn et al., 2016; Marcus et al., 2003; Molyneaux, Poston, Ashurst-williams, & Howard, 2014). Other determinants of antenatal depression include unplanned pregnancy (Bisetegn et al., 2016; K. I.

Mohammad et al., 2011), high parity (Coll et al., 2017), and smoking before and during pregnancy (Abuidhail & Abujilban, 2014; Marcus et al., 2003). However, the link with smoking may reflect the effect of depressive symptoms on an increased tendency to smoke. Lastly, women in their third trimester seem to have higher depression rates compared to women in other trimesters (Bisetegn et al., 2016).

Aim

The aim of this analysis was to provide an estimate of the prevalence of antenatal depressive symptoms as an indicator of antenatal depression and identify the risk factors associated with antenatal depressive symptoms using data from the TRansgenerational Assessment of Children's Environmental Risk (TRACER) Study in Kuwait. Identifying the potential determinants for developing antenatal depression in this geographic area is important in understanding the problem and for designing successful screening tools and interventions.

Methods

Sample

A total of 1938 women who had completed the Stress Questionnaire, were included in this analysis (see Figure 2.6).

Statistical analysis

We first examined the distribution of the EDS scores and we calculated the prevalence of antenatal depressive symptoms and the corresponding 95% confidence intervals (CIs) separately among Kuwaitis and non-Kuwaitis, as the majority of the Kuwaiti population are non-Kuwaitis (The Public Authority for Civil Information website, n.d.). We calculated the prevalence of antenatal depressive symptoms for different cut-off points encountered in the literature, namely

EDS≥10, 12, 13, and 15. We further identified the most common antenatal depressive symptoms reported by women in the study. For the primary analysis, the participants were classified as women with depressive symptoms using EDS≥10, as recommended for the Arabic EDS, and as women without depressive symptoms if EDS<10, and their baseline characteristics were compared using the chi-square test of association.

Logistic regression models were utilized to explore potential risk factors for the presence of antenatal depressive symptoms. Crude ORs and 95% CIs were obtained from univariate logistic regression models. The variables examined included age, nationality, monthly income, employment status, educational level, trimester, pre-pregnancy BMI, type of clinic, childhood emotional neglect, traumatic events, history of depression, history of adverse outcomes in prior pregnancies (miscarriage, bleeding, preterm birth, gestational diabetes or gestational hypertension), pregnancy-related anxiety, stress, PTSD symptoms, mental and physical quality of health, and support from the social environment. A multiple logistic regression model was then built using forward selection. The role of nationality, trimester, and depression history as effect-modifiers of the relationship of anxiety, stress, and MCS with depressive symptoms was also investigated by introducing interaction terms in the models.

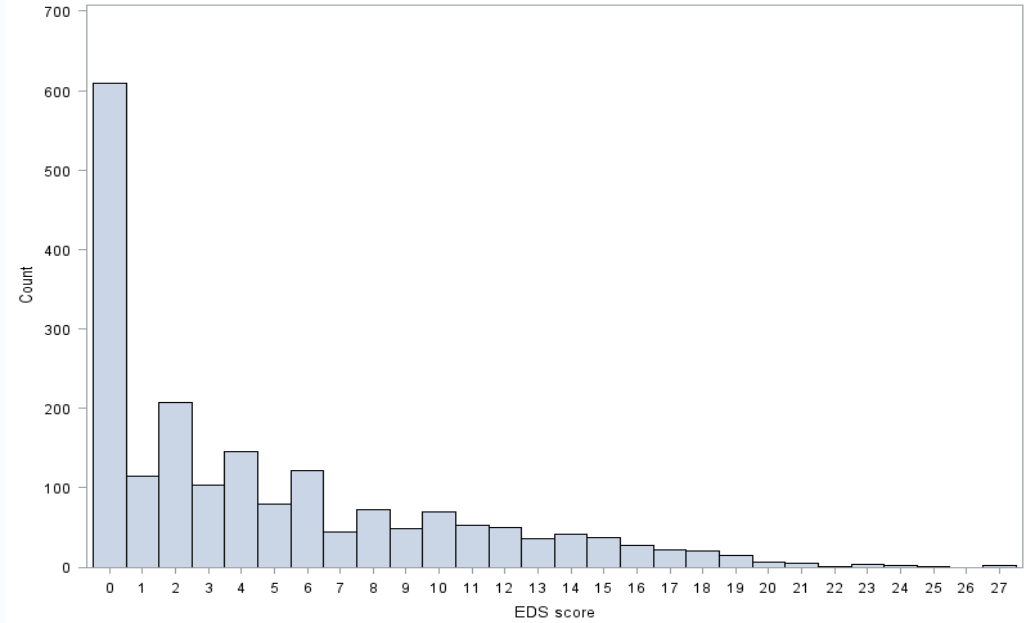
Sensitivity analysis was performed to examine whether the stricter cut-off point of EDS≥13, as recommended elsewhere (Abuidhail and Abujilban, 2014; Al-Azri et al., 2016; Alder et al, 2011), provided different results.

All statistical analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC, USA) and statistical significance was defined as a p-value<0.05 using two-sided tests.

Results

The EDS score distribution was skewed to the right with a median EDS score of 3 (interquartile range 0-8) and a mode of 0 (Figure 3.1). Overall, 20.2% (95% CI: 18.4, 22.1) of the participants had depressive symptoms, defined by an EDS score of 10 or greater and 11.4% (95% CI: 10.0, 12.9) had a score of 13 or greater. Kuwaitis and non-Kuwaitis had similar levels of depressive symptoms under all different cut-off points considered for defining depression (Appendix Table 1).

Figure 3.1 – Distribution of EDS score



The specific questions used in the EDS and the corresponding percentages of positive or negative responses for each are shown in the Appendix Table 2 and Table 3. The most common antenatal depressive symptom reported by the women in the study was that they felt overwhelmed (with 25% reporting feeling overwhelmed some of the time or most of the time). The least reported symptom was the thought of harming themselves, with only 1.0% of the women reporting having had such a thought ever, even if not very often. Similarly, when the sample was stratified into

women with and without depressive symptoms, feeling overwhelmed was the most common symptom and the thought of harming themselves the least one reported in both groups.

The baseline characteristics of the participants, overall and for those with an EDS score of greater than or equal to 10, are presented in Table 3.1. The majority of the characteristics examined had a similar distribution among those with EDS score <10 and those with EDS score ≥10. Statistically significant differences were observed for educational level, gestational age (trimester), and parity (see also Appendix Table 4). Women who had completed primary or middle school only were more likely to show depressive symptoms compared to women that had completed higher education (OR=1.59; 95% CI: 1.26-2.00). Furthermore, a household income of less than <400 KWD (1 Kuwaiti Dinar = approximately 2.85 Euros) compared with ≥1600 KWD was a significant predictor of depressive symptoms in pregnancy (OR=1.69; 95% CI: 1.15-2.48). On the other hand, women who were in their second trimester (OR=0.54; 95% CI: 0.42-0.70) or were nulliparous (OR=0.73; 95% CI: 0.57-0.94) showed lower odds of antenatal depressive symptoms compared to women in their third trimester and women who have already given birth at least once, respectively.

Table 3.1 – Baseline characteristics and antenatal depressive symptoms - Frequencies and unadjusted ORs.

	Overall		**EDS≥10**		**Unadjusted OR**	
	n	**%**	**n**	**%**	**OR**	**95% CI**
DEMOGRAPHIC CHARACTERISTICS						
Age group						
<25	483	25	84	17	0.79	0.59-1.07
25-30	739	38	155	21	1	-
30-35	480	25	104	22	1.04	0.79-1.38
>35	236	12	49	21	0.99	0.69-1.42
Nationality						
Kuwaiti	492	25	105	21	1	-
Non- Kuwaiti	1446	75	287	20	0.91	0.71- 1.17
Employment status						

Employed	873	46	163	19	1	-
Housewife	852	44	190	22	1.25	0.99-1.58
Unemployed	191	10	32	17	0.88	0.58-1.33
Education						
Up to Middle/secondary	585	31	149	25	**1.59**	**1.26-2.00**
Higher education	1331	69	236	18	1	-
Household Income (KWD)						
<400	575	31	132	23	**1.69**	**1.15-2.48**
400-800	647	35	126	19	1.37	0.93- 2.01
800-1600	373	20	79	21	1.52	1.00-2.30
≥1600	273	15	41	15	1	-
PREGNANCY CHARACTERISTICS						
Trimester of EDS evaluation						
2nd	645	34	91	14	**0.54**	**0.42- 0.70**
3rd	1259	66	293	23	1	-
Parity						
0	639	34	108	17	**0.73**	**0.57-0.94**
≥1	1268	66	276	22	1	-
Pre-pregnancy BMI						
<18.5	43	2	9	21	1.09	0.51-2.31
18.5-25	826	43	162	20	1	-
25-30	627	33	123	20	1.00	0.77-1.30
≥30	409	22	87	21	1.11	0.83-1.48
Clinic						
Private	336	17	67	20	0.95	0.70-1.27
Public	1449	75	302	21	1	-
Other	153	8	23	15	0.67	0.42-1.07

Table 3.2 includes mental and physical health indicators that could potentially be associated with depressive symptoms. The crude ORs show that history of depression, being neglected in childhood, having experienced six or more lifetime traumatic events, pregnancy related anxiety, moderate and higher levels of perceived stress, the presence of PTSD symptoms, fair or poor mental health, poor physical health, and being mostly isolated in terms of social network were all associated with antenatal depressive symptoms in unadjusted models (see also Appendix Table 5). The strongest effect was observed for poor mental health, described by a low mental component summary score, with OR=17.93 (95% CI: 11.75-27.36).

Table 3.2 – Mental and physical health indicators of antenatal depressive symptoms- Frequencies and unadjusted ORs.

	Overall		EDS≥10		Unadjusted OR	
	n	%	n	%	OR	95% CI
RISKS BEFORE PREGNANCY						
Prior depression						
No	1866	96	363	19	1	-
Yes	41	2	21	51	4.35	2.33-8.11
Adverse outcomes in previous pregnancies						
No previous pregnancy	533	28	85	16	0.78	0.57-1.06
No	606	32	119	19	1	-
Yes	768	40	180	23	1.25	0.97-1.63
Childhood emotional neglect						
Least neglected (score 5-7)	826	43	152	18	1	-
Moderately neglected (8-10)	496	25	92	19	1.01	0.76-1.35
Most neglected (11-25)	616	32	148	24	**1.40**	**1.09-1.81**
Traumatic Events						
0-1	716	37	115	16	1	-
2-5	612	32	87	14	0.87	0.64-1.17
6 or more	610	31	190	31	**2.36**	**1.82-3.08**
PREGNANCY RELATED						
Pregnancy related anxiety						
No	1657	86	266	16	1	-
Yes	281	14	126	45	**4.25**	**3.25-5.56**
Perceived Stress Levels						
Lower (score 0-4)	685	36	38	6	1	-
Moderate (score 5-7)	717	37	108	15	**3.02**	**2.05-4.44**
Higher (score 8-16)	522	27	236	45	**14.05**	**9.71-20.34**
PTSD symptoms						
No	1265	65	114	9	1	-
Yes	673	35	278	41	**7.10**	**5.56-9.09**
Mental Component Summary						
Poor	636	33	274	43	**17.93**	**11.75-27.36**
Fair	660	34	92	14	**3.84**	**2.45-6.02**
Good	642	33	26	4	1	-
Physical Component Summary						
Poor	643	33	195	30	**2.69**	**2.03-3.55**
Fair	657	34	108	16	1.21	0.90-1.65
Good	638	33	89	14	1	-
COPING DURING PREGNANCY						
Social Network						
Most integrated	136	7	27	20	1	-
Moderately integrated	327	17	61	19	0.93	0.56-1.53

Moderately isolated	1118	58	198	18	0.87	0.56-1.36
Most isolated	334	17	99	30	**1.70**	**1.05-2.76**

The results of a multiple logistic regression model, modeling the probability of antenatal depressive symptoms as the outcome of interest, which was obtained with the use of forward selection, are shown in Table 3.3. The variables that were initially added in the model included age, nationality, employment status, educational level, trimester, pre-pregnancy BMI, type of clinic, childhood emotional neglect, traumatic events, history of depression, history of adverse pregnancy outcomes, pregnancy-related anxiety, stress, PTSD symptoms, mental and physical component scales, and support from the social environment. Model 1 suggests that lower household income (<400, 400-800, and 800-1600 KWD), history of depression, greater gestational age, experience of traumatic events, pregnancy-related anxiety, moderate and higher levels of stress, PTSD symptoms, fair and poor mental health, and poor physical health were all significant risk factors for having depressive symptoms, defined as EDS≥10, even after adjusting for all the other covariates in the model. Based on this multivariate model, a poor mental health (vs. good) was the most significant factor associated with the outcome with an odds ratio of 7.45 (95% CI: 4.54-12.23). Higher perceived stress was the second most significant factor (OR=4.49; 95% CI: 2.90-6.94). The model had a good fit (Hosmer-Lemeshow p-value=0.16) and the C-statistic was equal to 0.87 (Appendix Figure 1). The validity of the final model was also assessed using regression diagnostics; we examined the residuals of the final model and both Pearson and Deviance residuals did not present any violation of the assumptions of regression and no influential points were identified.

Model 2 presents the same analyses but conducted under a stricter level of antenatal depressive symptoms (EDS≥13). Trimester, anxiety, perceived stress, PTSD symptoms, poor mental health,

and depression history all remained significant risk factors for depressive symptoms, as did lower educational level.

Table 3.3 – Multivariate logistic regression models for antenatal depressive symptoms.

	Model 1 (EDS≥10)		Model 2 (EDS≥13)	
	OR	**95% CI**	**OR**	**95% CI**
Household Income (KWD)				
<400	1.97	1.23-3.16	-	-
400-800	1.99	1.14-3.19	-	-
800-1600	2.22	1.33-3.71	-	-
≥1600	1	-		
Education				
Up to Middle/secondary	-	-	1.61	1.13-2.30
Higher education	-	-	1	-
Trimester of EDS evaluation				
2nd	0.65	0.47-0.89	0.54	0.36-0.82
3rd	1	-	1	-
Prior depression				
No	1	-	1	-
Yes	2.83	1.17-6.86	3.11	1.27-7.62
Traumatic Events				
0-1	1	-	-	-
2-5	1.02	0.70-1.50	-	-
6 or more	1.52	1.08-2.14	-	-
Pregnancy-related anxiety				
No	1	-	1	-
Yes	2.02	1.44-2.83	3.44	2.38-4.99
Perceived Stress				
Lower (0-4)	1	-	1	-
Moderate (5-7)	1.76	1.13-2.74	1.53	0.82-2.85
Higher (8-16)	4.49	2.90-6.94	3.97	2.20-7.16
PTSD symptoms				
No	1	-	1	-
Yes	2.61	1.92-3.55	2.63	1.80-3.86
Mental Component Summary				
Poor	7.45	4.54-12.23	7.80	3.75-16.22
Fair	2.48	1.49-4.11	2.32	1.06-5.08
Good	1	-	1	-
Physical Component Summary				
Poor	1.74	1.21-2.53	-	-
Fair	1.10	0.75-1.60	-	-
Good	1	-	-	-

The models were obtained using forward selection from the following variables age, nationality, monthly income, job, education, trimester, pre-pregnancy BMI, type of clinic, childhood emotional neglect, traumatic events, history of depression, history of adverse pregnancy outcomes, pregnancy-related anxiety, stress, PTSD symptoms, mental and physical quality of health, and support from the social environment. Education was not significant in forward selection with a cut-off of 10 while household income and traumatic events were not significant for depressive symptoms defined by a cut-off of 13.

Potential effect modifiers of the association of (i) anxiety, (ii) perceived stress, symptoms, and (iii) MCS, with depressive symptoms were considered, such as nationality, trimester, and depression history. However, no significant effect modification was detected when interaction terms were introduced in the model or when stratified analysis was used (data not shown). Kuwaitis and non-Kuwaitis had similar levels of depressive symptoms and stratification analysis revealed similar important covariates for depressive symptoms among Kuwaitis and non-Kuwaitis.

Discussion

Despite the fact that there are some studies on postnatal depression, research on antenatal depression in the Gulf countries is limited. To the best of our knowledge, this is the first study that provides an estimate of the levels of depressive symptoms during pregnancy in Kuwait and identifies the factors that are associated with higher levels of depressive symptoms. Using a cut-off of EDS of 10 or greater, we found that the prevalence of depressive symptoms in a sample of 1938 women was 20.2%. This is very similar to the antenatal depression prevalence observed among participants from the Middle East in a multiethnic cohort study conducted in Oslo (Shakeel et al., 2015) that had 15% of the participants being of Middle-Eastern origin. Our results are also consistent with the prevalence of antenatal depression in different ethnicities, such as the prevalence of 21.9% reported in the study of Giardinelli et al. (2012) in Italy. Higher levels of depression have also been detected recently in Oman (Al-Azri et al., 2016), where the prevalence based on an even greater cut-off point (EDS≥13) was 24.3%.

Some of the socio-demographic factors explored in this study were found to be potential predictors of depressive symptoms in pregnancy. Depressive symptoms were more common among women of lower family income which is consistent with studies conducted elsewhere (Leigh and Milgrom, 2008; Silva et al., 2012). A low family income is usually accompanied by stress regarding finances, which in turn is a risk factor for antenatal depression (Mohammad et al., 2011). We also observed, in unadjusted analysis, that women with lower educational levels were more likely to show antenatal depressive symptoms. Similar results were reported in studies conducted in neighboring countries, such as Jordan (Abuidhail and Abujilban, 2014), but also in different settings, such as the large cohort study conducted in New Zealand (Waldie et al., 2015). Abuidhail and Abujilban (2014) suggested that depression affects more women from a lower educational background as they may have not developed defense mechanisms against stress.

We also found a significant association between trimester and depressive symptoms. More advanced gestational age seems to be associated with depressive symptoms, even after adjusting for other covariates. This could be explained by the fact that women closer to their due date are more worried about the forthcoming delivery and the health of the baby. In fact, pregnancy-related anxiety was one of the most significant psychological factors that were associated with depressive symptoms in our study. Our results are somewhat higher than the summary estimates provided in the systematic review and meta-analysis of Bennett et al. (2004), where the prevalence rate for the second (12.8%) and for the third trimester (12.0%) were not significantly different, compared to our results of 14.1% and 23.3%, respectively.

The majority of psychological factors examined were also co-morbid with depressive symptoms. A higher perceived stress score was observed among women with EDS≥10, which is in agreement with the work of Waldie et al. (2015), who used the 10-item Cohen Perceived Stress Scale. Similar to our results, other studies have found that lifetime stressful and traumatic events

are potential risk factors for antenatal depression (Leigh and Milgrom, 2008; Shakeel et al., 2015). We further observed that the mental health component of the participants' health and physical component summaries, obtained from the SF36v2 questionnaire, was associated with depressive symptoms. Nicholson et al. (2006) examined the health related quality of life during pregnancy and demonstrated that the median scores for both mental and physical health items of the SF36 were significantly lower among women with depression. The role of the social network and support was not significant in our study which was consistent with research conducted elsewhere (Biratu and Haile, 2015; Waldie et al., 2015). Women with a history of depression in our study had a greater risk of developing depressive symptoms during pregnancy which was similar to results obtained in the recent study of Coll et al. (2017).

Conclusion

Our findings emphasize the need for addressing mental health problems in women with antenatal depression. During pregnancy, a lot of hormonal changes occur which may affect the mental health of the pregnant woman and indirectly the health of the embryo. Women with antenatal depression have greater odds of developing postnatal depression which in turn can be detrimental for the health of the baby and of the mother, as well as of the mother-baby bonding. Moreover, women who experience depression in pregnancy could be at a greater risk of adverse birth outcomes. This hypothesis will be further investigated in the following chapter.

Chapter 4 – Antenatal depression and other risk factors of adverse pregnancy outcomes

Introduction

The perinatal period, defined as the period of pregnancy and the first 12 months after childbirth, is a very important time for the development of the fetus and the newborn, as well as of the further development as a child later on. Adverse outcomes may occur during pregnancy or at birth which have a direct or indirect impact on the health of the newborn and may result in long-term sequelae. Examples of such outcomes include preterm birth (PTB), low birth weight, small for gestational age (SGA), and large for gestational age (LGA) (Chiavaroli et al., 2014; Grissom & Reyes, 2013; Longo et al., 2013; Saigal & Doyle, 2008). These events are complex and are associated with a number of factors, including biological, obstetrical, behavioral, psychological, and socio-economic. Understanding the determinants of these outcomes is important in predicting and monitoring them. We were particularly interested in the potential association of antenatal depression with PTB, SGA, and LGA. In this chapter, a short literature review is provided first that includes the risk factors and the consequences of these outcomes, as well as the epidemiological evidence available for the association of antenatal depression with these outcomes, followed by an evaluation of the relationship of antenatal depression with these outcomes using data from the TRACER study.

Preterm birth

According to the World Health Organization, 15 million babies are born preterm (defined as a gestational age at birth less than 37 weeks) every year and the rate ranges from 5-18% across different countries (Blencowe et al., 2012). Several complications are associated with preterm delivery making it the leading cause of perinatal mortality and a major cause of child death in many middle and high income countries (Blencowe et al., 2013). PTB puts a serious burden on

the healthcare system as babies who are born prematurely present both short and long term complications and are at a higher risk of morbidity (Jelliffe-Pawlowski et al., 2015). In addition, PTB increases the psychosocial, emotional, and economic challenges faced by the family (Blencowe et al., 2013).

Babies who are born prematurely have a shorter gestation age and thus their organ systems do not develop completely. As a result, these immature organ systems cannot fully support the neonate outside the uterus and may even have lifelong health consequences (Committee on Understanding Premature Birth and Assuring Healthy Outcomes Policy Institute of Medicine (US), 2007). To start with, PTB affects the function of the lungs and may result in acute respiratory distress syndrome which in turn can lead to chronic problems, such as broncho-pulmonary dysplasia, due to the inflammation and scarring of the airways and the alveoli. The neonate may also have apnea episodes, which usually go away after some weeks. Moreover, PTB can lead to feeding intolerance and necrotizing enterocolitis, both of which may require parenteral nutrition something that in turn may result in further complications, especially if it is provided for a long time. Infections are also common in preterm babies as their immune system cannot fight pathogens (Committee on Understanding Premature Birth and Assuring Healthy Outcomes Policy Institute of Medicine (US), 2007). Premature babies often present intraventricular hemorrhage which sometimes leads to permanent damage of the central nervous system (Saigal & Doyle, 2008). When the development of the nervous system is impaired, cerebral palsy, mental retardation, hearing, and vision problems may emerge as well.

Saigal and Doyle (2008) summarized the evidence on the behavioral problems and traits associated with PTB. Problems include a higher risk of attention deficit hyperactivity disorder (ADHD) and emotional problems at school age, which have an impact on the academic

functioning of these children, while reported traits include shyness, unassertiveness, social maladaptation, anxiety, and a tendency to withdraw.

Preterm delivery is usually classified into spontaneous preterm birth, which is the result of spontaneous onset of labor or premature rupture of membranes, and provider-initiated PTB, which is the result of maternal or fetal indications that require induction of labor or a cesarean section. The latter may occur even for non-medical reasons (Blencowe et al., 2013; Goldenberg, Culhane, Iams, & Romero, 2008).

Even though the exact mechanisms of preterm birth are not clear, a range of risk factors for PTB have been identified, including infections, obstetric, clinical, lifestyle, socio-economic, psychological, genetic, and other factors (Goldenberg et al., 2008). Infections of the uterus are one of the major mechanisms that can result in a PTB (Goldenberg, Hauth, & Andrews, 2000). History of previous PTB is also a strong risk factor for a recurrent PTB (Mercer et al., 1999). The risk of preterm birth is also associated with primiparity and with multiple pregnancies (López & Bréart, 2013; K. Mohammad, Abu Dalou, Kassab, Gamble, & Creedy, 2015; Shiozaki et al., 2014). Conception by in vitro fertilization (IVF) or other assisted reproductive technology (ART) also increase the risk for PTB, mostly because they result in multiple gestation (Centers for Disease Control and Prevention, n.d.). Medical conditions that can occur prior to or during pregnancy, such as hypertension and gestational hypertension, preeclampsia, diabetes and gestational diabetes, history of delivery with cesarean section, and large time intervals between pregnancies may also trigger PTB (Jelliffe-Pawlowski et al., 2015; NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development, n.d.).

PTB rates seem to be different across different racial or ethnic groups, with black women being at a higher risk of a PTB and East Asian and Hispanic women usually having lower risk

(Goldenberg et al., 2008). In many countries in the Middle East the incidence of PTB ranges from 10-15%, while in a few other countries in the same region this is less than 10% (Blencowe et al., 2012). These differences could be partially explained by the different socio-economic and lifestyle factors as well as the genetic predisposition of the different ethnic groups (Blencowe et al., 2013). Socio-economic characteristics, such as lower educational level (Oftedal, Busterud, Irgens, Haug, & Rasmussen, 2016; Shiozaki et al., 2014) and lower socioeconomic status in general (L. K. Smith, Draper, Manktelow, Dorling, & Field, 2007; Thompson, Irgens, Rasmussen, & Daltveit, 2006) are also found to be associated with PTB. Joseph et al. (2014) argued that lower family income can predict spontaneous PTB but not clinically initiated PTB.

Other maternal characteristics linked with PTB are maternal age and body mass index (BMI). Women of lower and higher age or of lower BMI have a greater risk for PTB while a higher BMI seems to be protective against PTB (Goldenberg et al., 2008; Hendler et al., 2005). However, this is controversial, as being overweight or obese in pregnancy has been identified as a risk factor for preterm delivery (Cnattingius et al., 2013). According to the American College of Obstetricians and Gynecologists, smoking in pregnancy and substance abuse are also lifestyle factors contributing to PTB ("Preterm (Premature) Labor and Birth (FAQ087)- ACOG," 2016).

In addition, the psychological well-being of the mother has been linked to PTB. Women who had experienced stressful events or suffer from anxiety or chronic stress are at a greater risk for delivering before 37 weeks (Committee on Understanding Premature Birth and Assuring Healthy Outcomes Policy Institute of Medicine (US), 2007; Garn, Nagulesapillai, Metcalfe, Tough, & Kramer, 2015). Lack of support may also trigger PTB (Committee on Understanding Premature Birth and Assuring Healthy Outcomes Policy Institute of Medicine (US), 2007). Studies conducted in various countries showed that single motherhood is a risk factor for PTB, which highlights the importance of the support of the partner (López & Bréart, 2013; Oftedal et al.,

2016). Depression has also been identified as a potential risk factor for PTB but its effect is not clear (Committee on Understanding Premature Birth and Assuring Healthy Outcomes Policy Institute of Medicine (US), 2007). More epidemiological evidence on the association of depression and PTB is provided later in this chapter.

Small for gestational age

Small for gestational age (SGA) is defined by a birth weight below the population's 10^{th} percentile for the gestational age. Neonates who are born SGA are at an increased risk of morbidity and mortality (McCowan & Horgan, 2009). The mortality rates are higher in lower and middle income countries, with more than a quarter of the infant deaths being attributable to SGA (Katz, Lee, Kozuki, & Black, 2015). It is often used as an indicator of intrauterine growth restriction (Kozuki et al., 2015). The restricted growth has both acute and long term consequences. Short-term consequences include a greater risk of developing respiratory distress syndrome, necrotizing enterocolitis, retinopathy of prematurity, and intraventricular hemorrhage, and it is a major cause of perinatal morbidity (Longo et al., 2013). In the long term, SGA has an impact on the growth, metabolism, and neurodevelopment of the child. A shorter stature is observed among children and adults born with intrauterine growth retardation, but the effect is different based on predisposing risk factors (Longo et al., 2013; Meas, Deghmoun, Armoogum, Alberti, & Levy-Marchal, 2008). Apart from stunting, intrauterine growth restriction has also been linked to premature adrenarche and polycystic ovarian syndrome (Longo et al., 2013).

In a follow-up study conducted in France, adults who were born SGA had different body composition compared to adults who were born appropriate for their gestational age. Specifically, adults born SGA had a larger percentage of body fat and their BMI and waist circumference gains were significantly greater (Meas et al., 2008). Moreover, these individuals were more likely to have hypertension, dyslipidemia, insulin resistance, and type 2 diabetes. All

these metabolic consequences contribute to the risk of developing cardiovascular diseases prematurely (Longo et al., 2013).

The neuro-developmental sequelae of SGA add to the burden of this outcome. Children born SGA experience school problems and their intellectual and psychological performance is lower (Van Wassenaer, 2005). Moreover, a number of studies have showed that SGA increases the risk of attention deficit hyperactivity disorder, autism, anxiety, and depression (Colman, Ataullahjan, Naicker, & Van Lieshout, 2012; Heinonen et al., 2010; Lahti et al., 2006; Moore, Kneitel, Walker, Gilbert, & Xing, 2012).

Several maternal characteristics have been associated with an increased risk of delivering a SGA baby. Lifestyle risk factors include smoking before and during pregnancy, using cocaine, and a diet low in dairy, meat, fish, nuts, and seeds (Bakketeig et al., 1993; Ford, 2011; Räisänen et al., 2013). On the other hand a diet rich in green leafy vegetables and fruit reduces this risk (McCowan & Horgan, 2009). Moreover, women of lower BMI or who have inadequate weight gain in their pregnancy are at a greater risk of having a baby born SGA (Clausson, Cnattingius, & Axelsson, 1998; Heaman et al., 2013; Räisänen et al., 2013). Interestingly, obesity was also identified as a potential risk factor for SGA, with obese women having higher odds of delivering SGA babies (Anderson, Sadler, Stewart, Fyfe, & McCowan, 2013). Shorter stature is another maternal characteristic linked to SGA.

Predisposing diseases, including chronic hypertension, renal disease, and anemia, are shown to be positively associated with SGA. On the other hand, type 1 diabetes was found to be protective (Anderson et al., 2013). Small for gestational age babies are more common among women who are nulliparous or experience complications in pregnancy, such as heavy bleeding, placental abruption, gestational hypertension, pre-eclampsia, and eclampsia, and is less common among

women who develop gestational diabetes (Anderson et al., 2013; Sebastian, Yadav, Jeyaseelan, Vijayaselvi, & Jose, 2015).

Socio-demographic variables, such as lower socioeconomic status, lower educational level, and Indian or Asian ethnicity were also found to be associated with SGA (Clausson et al., 1998; McCowan & Horgan, 2009; Räisänen et al., 2013).

Large for gestational age

Fetal overgrowth can be characterized as macrosomia, which is defined by the American College of Obstetricians and Gynecologists (American College of Obstetricians and Gynecologists, 2016) as a birth weight of greater than 4000 g or 4500g irrespective of gestational age, or as large for gestational age (LGA), which is defined as a birth weight above the population's 90th percentile for that gestational age (American College of Obstetricians and Gynecologists, 2016). Despite the fact that sometimes excessive fetal growth may not be viewed as a public health problem, it can be as unhealthy as SGA. Macrosomia increases the risk of prolonged labor, cesarean delivery, shoulder dystocia, and the need for labor augmentation by oxytocin, which in turn increase perinatal morbidity and mortality (Fuchs, Bouyer, Rozenberg, & Senat, 2013; Modanlou, Dorchester, Thorosian, & Freeman, 1980). The consequences are even worse for neonates that have a birth weight of greater than 4500 g, as they have an increased risk of stillbirth, neonatal asphyxia, and therefore neonatal mortality, injury at birth, meconium aspiration, and cesarean delivery (Zhang, Decker, Platt, Kramer, & Club, 2008). Furthermore, babies with a higher birth weight have a greater chance to be admitted to a neonatal intensive care unit, mostly due to birth complications as a result of their size. Fetal overgrowth may not only affect the life of the newborn but it has implications in childhood and adolescence. Children that are born macrosomic are at a greater risk for developing dental caries (Yokomichi et al., 2015). Chiavaroli et al. (2014) examined the cardio-metabolic profile of children by assessing

their BMI, blood pressure, insulin resistance, and lipids and then following them up to adolescence. Their results suggested that children that were LGA or SGA had an adverse cardio-metabolic profile, as compared to children that were born with a weight appropriate for their gestational age, and their cardio-metabolic profile worsened during adolescence. Similarly, in a recent study conducted in Kaunas, Lithuania, adolescents that had a high birth weight or were born LGA were found to have higher odds of having high blood pressure (Kuciene, Dulskiene, & Medzioniene, 2017). Adding to these adverse effects, in a review of Grissom et al. (2013), LGA was linked to mental and neuro-developmental disorders, including depression, anxiety, autism, attention deficit hyperactivity disorder, and cognitive delay.

Macrosomia is positively associated with multiparity, maternal age, and history of another macrosomic baby, or history of gestational diabetes (Essel & Tetteh, 1990; Modanlou et al., 1980), and is more common among male babies (Modanlou et al., 1980). One of the most significant risk factors for macrosomia is abnormal glucose metabolism. The incidence of macrosomic or LGA babies is higher among women who have abnormal glucose tolerance, especially at the early or later stages of their pregnancy, have pre-gestational diabetes mellitus, are diagnosed with gestational diabetes, or have a history of gestational diabetes (Ehrenberg, Mercer, & Catalano, 2004; Frick, Syngelaki, Zheng, Poon, & Nicolaides, 2016; Mello et al., 1997; Modanlou et al., 1980; Poon, Karagiannis, Stratieva, Syngelaki, & Nicolaides, 2011). Indicators of maternal body composition, such as pre-pregnancy BMI, weight gain during pregnancy, body weight at delivery, or maternal waist-to-hip ratio are also associated with macrosomia (Modanlou et al., 1980; Morikawa et al., 2013; Salem, Adler, Lee, & Smith, 2012). On the other hand, smoking, as well as Afro-Caribbean and South Asian racial origins, seem to be protective against delivering a LGA baby (Frick et al., 2016).

Antenatal depression and adverse pregnancy outcomes

The association of antenatal depression with adverse pregnancy and neonatal outcomes has been an item of scientific interest over the last decade. Several studies examined the effect of depression in pregnancy on preterm birth and found a positive association (Fransson et al., 2011; Li, Liu, & Odouli, 2009; Niemi et al., 2013; Straub, Adams, Kim, & Silver, 2012). Antenatal depression has also been identified as a risk factor for low birth weight (Niemi et al., 2013). Furthermore, several meta-analyses reported that antenatal depression is associated with a higher risk of preterm birth and low birth weight (Grote et al., 2010; Jarde et al., 2016). In addition, women with depression in pregnancy, especially in mid-pregnancy, were shown to experience greater odds of delivering a baby with SGA (Szegda et al., 2016) while for LGA the evidence is still limited (Jarde et al., 2016).

Despite the fact that there is some scientific evidence which supports that antenatal depression is associated with these adverse outcomes, these associations are not consistent, even when comparing results from studies conducted in the same country (Berle et al., 2005; Eastwood et al., 2017; Grigoriadis et al., 2013; N Husain et al., 2014; Varela, Spyropoulou, Kalogerakis, Moraitou, & Zervas, 2015; Stavena et al., 2017).

Apart from depression, other psychosocial problems that may exist before or during pregnancy have been described as potential risk factors in the etiology of perinatal adverse outcomes. A study conducted among a group of African-American women in the USA suggested that a poor psychosocial profile was significantly associated with preterm delivery as well as low birth weight infants (Neggers, Goldenberg, Cliver, & Hauth, 2006). Yonkers et al. (2014) argued that women with PTSD are at a greater risk of preterm birth and Shapiro et al. (2013) summarized the results from different studies and concluded that psychosocial stress is associated with preterm

birth, with perceived stress and pregnancy-related anxiety being the two indicators most consistently reported to increase the risk of PTB.

The mechanism underlying the association of depression or psychosocial stress with birth weight is not clear (Neggers et al., 2006). Cortisol levels in pregnancy are shown to be inversely proportional to birth weight but these levels cannot be explained by prenatal stress (Bolten et al., 2011). In regards to the association with preterm birth, different mechanisms have been suggested. Depressed mood is linked to a decrease in the activity of natural killer cells and a rise in the plasma levels of inflammatory cytokines, suggesting that the effect of depression on PTB may be mediated through inflammations (Goldenberg et al., 2008). Moreover, the depression-PTB association could be mediated by behavioral factors related to depression, including smoking and alcohol consumption, which may in turn increase the risk of PTB. Also, as commented in Dean et al. (2013), if women engage in risky sexual activities then the risk of being infected with sexually transmitted pathogens increases substantially. In the review of Shapiro et al. (2013) other possible mechanisms for the effect of psychosocial stress on PTB have been provided. These include infectious, neuro-inflammatory, and neuro-endocrine pathways (Shapiro et al., 2013). Briefly, stress is correlated with a rise in cortisols and corticotropin-releasing hormone levels, as well as with dopamine release and dopaminergic activity in the prefrontal complex. In addition, stress can result in excessive production of pro-inflammatory cytokines and abnormal levels of inflammatory cytokines which can then stimulate the expression of toll-like receptors and the production of prostaglandins which can then result in uterine contractions. Infections are also considered as a potential mechanism, with bacterial vaginosis being identified as a risk factor for PTB. A relatively newer idea is that infections lead to alterations in the maternal microbiome, which can then activate an inflammatory response (Shapiro et al., 2013).

Aim

The aim of this study is to examine whether antenatal depressive symptoms are associated with adverse perinatal outcomes, including preterm birth, small for gestational age, and large for gestational age, and to identify any additional risk factors of these three outcomes in women who enrolled in TRACER.

Methods

Sample

The population and methods of the TRACER study were described in detail in Chapter 2 and the diagram showing how the sample for this analysis was selected is presented in Figure 2.6. In brief, 2478 women were enrolled in TRACER and 2254 of them were followed to delivery. We excluded women who did not complete the Baseline and the Stress Questionnaires, did not have usable data, took medication for anxiety or depression in pregnancy, or answered the Stress Questionnaire in the first trimester, ending up with a sample of 1938 women. Out of these 1938 women, 1765 had available data to calculate PTB and 1704 had data to calculate SGA and LGA.

Statistical analysis

The perinatal outcomes considered in this study were PTB, SGA, and LGA. The main explanatory variable of interest was the presence of antenatal depressive symptoms measured by the Edinburgh Depression Scale. We examined the association of depressive symptoms in pregnancy with each of the three outcomes using the chi-square test of independence and univariate logistic regression models to obtain crude ORs and corresponding 95% confidence intervals. The same analysis was repeated for socio-demographic characteristics, behavioral, reproductive health, and obstetric variables in order to identify potential risk factors for each of

the outcomes of interest. Then a multiple logistic regression model was constructed for each outcome to examine the adjusted effects of the variables considered, i.e. age, nationality, employment status, education, household income, parity, pre-pregnancy BMI, antenatal depressive symptoms, pregnancy-related anxiety, perceived stress, PTSD symptoms, quality of mental and physical health, and social network. In addition, the following variables were selected to be added in each model based on the literature review conducted.

- PTB - conception by IVF, gestational diabetes, gestational hypertension, preterm delivery in previous pregnancies, and lifetime traumatic events
- SGA - conception by IVF, gestational hypertension, miscarriage in previous pregnancy, and the sex of the baby
- LGA - gestational diabetes and the sex of the baby

As the cut-off of 10 is viewed as a relatively low point to determine depressive symptoms, we repeated the same analysis with depressive symptoms as a multinomial variable defined by the 0-50, 50-75, 75-90, 90-100 percentiles of the EDS score.

Nationality, BMI, and parity were considered as potential effect-modifiers of the antenatal depressive symptoms associations with the outcomes. We tested the possible effect-modifiers by adding interaction terms in the multiple logistic regression models and checking for statistical significance.

Gestational age at birth and birth weight were further evaluated as continuous variables. We computed the Spearman correlation coefficients describing the strength of the linear association between gestational length and birth weight with the EDS scores. We further estimated the effect of antenatal depressive symptoms on gestational age and birth weight using multiple linear regression models.

All statistical analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC, USA) and statistical significance was defined as a p-value<0.05 using two-sided tests. The fit of the multiple logistic regression models described above was assessed using the Hosmer-Lemeshow goodness of fit test and the C-statistic was also computed for each of the final models.

Results

Overall

The mean gestational age at delivery was 39.2 weeks (SD=1.7 weeks) and the mean birth weight was 3221 g (SD=495 g). The distribution of gestational age and birth weight are shown in Figure 4.1 and Figure 4.2, respectively. Gestational age shows a slight skewness to lower values while birth weight seems to follow a normal distribution. Overall, the prevalence of PTB, SGA, and LGA was 7.6%, 7.1%, and 22.4%, respectively.

Figure 4.1 – Distribution of gestational age

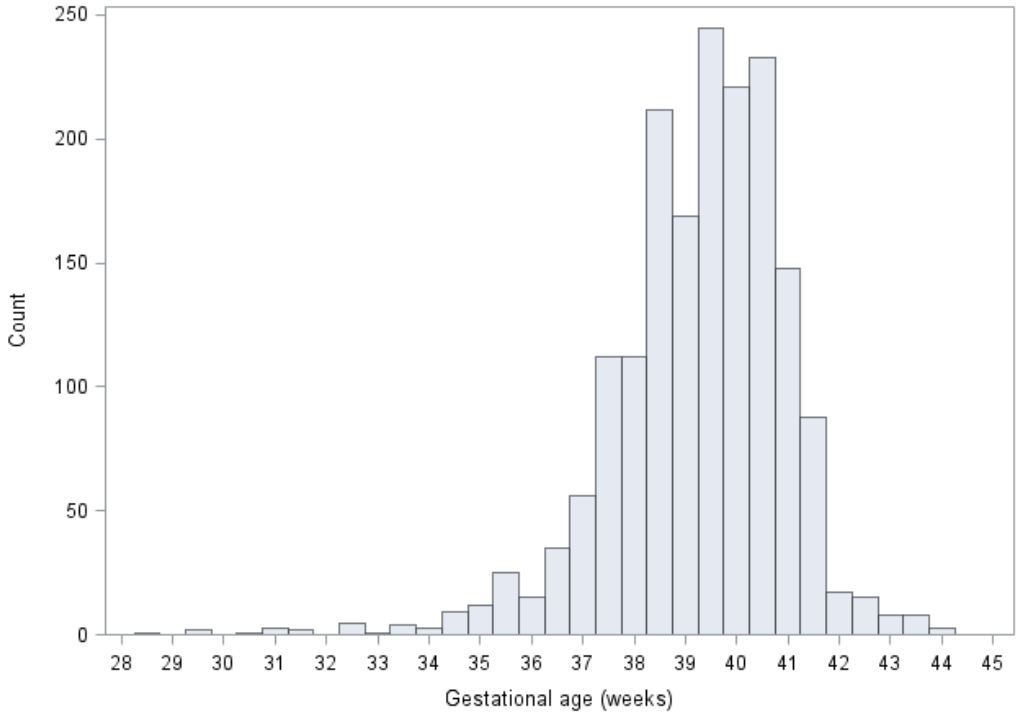
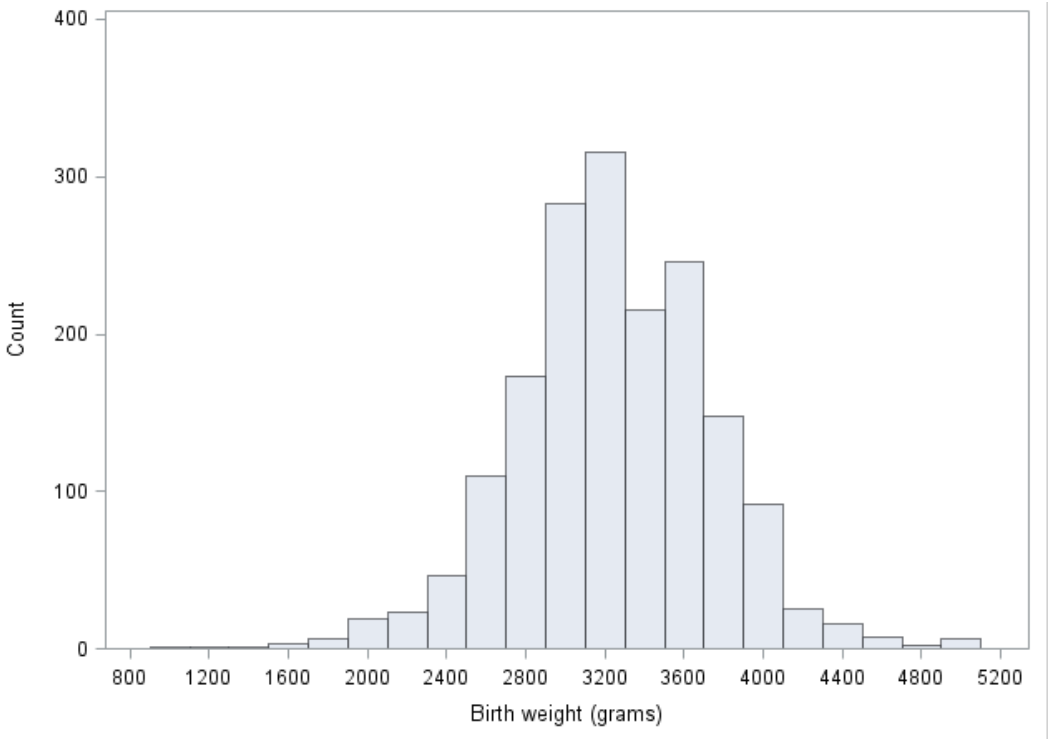


Figure 4.2 – Distribution of birth weight



Tables 4.1, 4.4, and 4.7 show the distribution of socio-demographic and pregnancy related characteristics in relation to PTB, SGA, and LGA respectively. Tables 4.2, 4.5, and 4.8 show the frequencies of these three outcomes based on mental and health indicators, while tables 4.3, 4.6, and 4.9 show the results obtained from the multivariate logistic regression models predicting PTB, SGA, and LGA, respectively. Tables 6, 9, and 12 in the Appendix show the ORs that describe the associations of the baseline characteristics and PTB, SGA, and LGA, respectively, while Appendix Tables 7, 10, and 13 present the ORs for the association of mental and physical health indicators with these outcomes. The results for each of the three outcomes (PTB, SGA, and LGA) are described in further detail below. In each of the multivariate models considered for the different outcomes we added interaction terms to test for possible effect-modification (by nationality, BMI group and parity) of the association of antenatal depressive symptoms with adverse birth outcomes; none of these interactions was statistically significant.

Preterm birth

In the unadjusted analyses (Table 4.1) PTB seems to be associated with nationality (Kuwaiti vs. non-Kuwaiti). Also, preterm delivery occurred more frequently in women who had IVF or had at least one previous preterm delivery. Moreover, PTB was more common in women with higher perceived stress levels (Table 4.2). The crude ORs of these aforementioned associations are depicted in Appendix Tables 6 and 7. For the multiple logistic regression model, the total sample was reduced to 1272 due to missing values in the explanatory variables. In this model only IVF (OR=3.43; 95% CI: 1.13-10.39) and previous preterm delivery compared to no previous pregnancy (OR=6.06; 95% CI: 1.72-21.35) remained statistically significant in their association with PTB, after adjusting for the other variables in the model (Table 4.3). Interestingly, fair quality of mental health was a protective factor for PTB (OR=0.47; 95% CI: 0.25-0.91). Depressive symptoms were not associated with PTB in either the crude (OR=1.15; 95% CI:

0.75-1.75) or the adjusted analysis (OR=1.16; 95% CI: 0.60-2.26). When the same analyses were repeated using depressive symptoms as a multinomial variable, we still did not observe a significant association of depressive symptoms with PTB (Appendix Table 8).

Table 4.1 – Baseline characteristics and PTB – Frequencies and Chi-square p-values

	n	PTB%	p-value
Overall	1765	7.6	
DEMOGRAPHIC CHARACTERISTICS			
Age group			
<25	434	7.1	0.89
25-30	679	7.4	
30-35	437	7.6	
>35	215	8.8	
Nationality			
Kuwaiti	432	10.7	**<0.01**
Non- Kuwaiti	1333	6.6	
Employment status			
Employed	789	8.0	0.55
Housewife	795	7.7	
Unemployed	179	5.6	
Education			
Up to High School	546	7.9	0.77
Higher education	1217	7.5	
Household Income (KWD)			
<400	535	7.3	0.16
400-800	597	6.2	
800-1600	347	8.7	
≥1600	237	10.6	
PREGNANCY CHARACTERISTICS			
Parity			
0	586	6.8	0.42
≥1	1176	7.9	
Pre-pregnancy BMI			
<18.5	40	10.0	0.19
18.5-25	763	6.3	
25-30	576	9.4	
≥30	377	7.4	
In vitro fertilization			
No	1720	7.1	**<0.01**
Yes	42	26.2	
Miscarriage in previous pregnancies			
No previous pregnancy	490	6.3	0.29

No miscarriage	756	7.4	
At least one miscarriage	516	8.9	
Preterm delivery in previous pregnancies			
No previous pregnancy	490	6.3	**<0.01**
No preterm delivery	1157	7.0	
At least one preterm delivery	115	18.3	
Gestational hypertension			
No	1271	6.5	0.14
Yes	62	11.3	
Gestational diabetes			
No	1247	6.3	0.05
Yes	117	11.1	
Sex of the baby			
Female	825	7.4	0.75
Male	936	7.8	

Table 4.2 – Mental and physical health indicators and PTB – Frequencies and Chi-square p-values

	n	**PTB%**	**p-value**
RISKS BEFORE PREGNANCY			
Traumatic Events			
0-1	648	9.3	0.05
2-5	549	5.5	
6 or more	568	7.8	
PREGNANCY RELATED			
Antenatal depressive symptoms (EDS score)			
<10	1407	7.4	0.53
≥10	358	8.4	
Pregnancy related anxiety			
No	1511	7.2	0.14
Yes	254	9.8	
Perceived Stress Levels			
Lower (0-4)	620	7.4	**0.02**
Moderate (5-7)	658	5.6	
Higher (8-16)	474	10.1	
PTSD symptoms			
No	1137	7.9	0.49
Yes	628	7.0	
Mental Component Summary			
Poor	580	9.1	0.21
Fair	601	6.5	
Good	584	7.2	
Physical Component Summary			
Poor	577	8.8	0.31
Fair	602	7.5	

Good	586	6.5	
COPING DURING PREGNANCY			
Social Network			
Most integrated	129	10.9	0.51
Moderately integrated	298	7.1	
Moderately isolated	1030	7.6	
Most isolated	306	6.9	

Table 4.3 – Multiple logistic regression model for PTB

	OR	**95% CI**
DEMOGRAPHIC CHARACTERISTICS		
Age group		
<25	0.83	0.43-1.63
25-30	1.00	-
30-35	0.81	0.43-1.52
>35	0.91	0.42-2.00
Nationality		
Kuwaiti	1.00	-
Non- Kuwaiti	0.99	0.44-2.23
Employment status		
Employed	1.00	-
Housewife	1.14	0.63-2.09
Unemployed	1.09	0.43-2.78
Education		
Up to High School	1.02	0.58-1.79
Higher education		
Household Income (KWD)		
<400	0.80	0.28-2.27
400-800	0.59	0.22-1.56
800-1600	0.72	0.30-1.70
≥1600	1.00	-
PREGNANCY CHARACTERISTICS		
Parity		
0	1.42	0.54-3.73
≥1	1.00	-
Pre-pregnancy BMI		
<18.5	2.87	0.88-9.35
18.5-25	1.00	-
25-30	1.46	0.85-2.52
≥30	0.81	0.39-1.67
In vitro fertilization		
No	1.00	-
Yes	**3.43**	**1.13-10.39**
Preterm delivery in previous pregnancies		
No previous pregnancy	1.00	-

No preterm delivery	1.76	0.62-4.99
At least one preterm delivery	**6.06**	**1.72-21.35**
Gestational hypertension		
No	1.00	-
Yes	1.80	0.71-4.57
Gestational diabetes		
No	1.00	-
Yes	1.78	0.88-3.63
RISKS BEFORE PREGNANCY		
Traumatic Events		
0-1	1.00	-
2-5	0.78	0.43-1.41
6 or more	0.82	0.45-1.50
PREGNANCY RELATED		
Antenatal depressive symptoms (EDS score)		
<10	1.00	-
≥10	1.12	0.58-2.17
Pregnancy related anxiety		
No	1.00	-
Yes	0.95	0.46-1.95
Perceived Stress Levels		
Lower (0-4)	1.00	-
Moderate (5-7)	0.75	0.40-1.42
Higher (8-16)	1.65	0.84-3.27
PTSD symptoms		
No	1.00	-
Yes	0.57	0.31-1.05
Mental Component Summary		
Poor	1.04	0.52-2.06
Fair	0.47	**0.25-0.91**
Good	1.00	-
Physical Component Summary		
Poor	1.36	0.73-2.55
Fair	1.35	0.75-2.45
Good	1.00	-
COPING DURING PREGNANCY		
Social Network		
Most integrated	1.00	-
Moderately integrated	1.27	0.42-3.78
Moderately isolated	1.13	0.42-3.05
Most isolated	1.47	0.49-4.40

Small for gestational age

In a sample of n=1704 infants with available data, delivering a baby that was small for gestational age was associated with educational level, household income, and the sex of the baby (Table 4.4 and Appendix Table 9). None of the mental and physical health indicators was associated with SGA (Table 4.5 and Appendix Table 10). The association of income and sex of the newborn with SGA remained significant even after adjusting for possible confounders, as indicated in Table 4.6 (n=1267). Women with a family monthly income of less than 400 KWD (~EUR 1125) were more likely to have a SGA baby (OR=3.63; 95% CI: 1.13-11.61) and the risk of SGA was lower among male babies (OR=0.63; 95% CI: 0.39-1.00). However, no significant association was observed for SGA and antenatal depressive symptoms in either the univariate (OR=1.39; 95% CI: 0.91-2.14) or the multivariate analyses (OR=1.50, 95% CI: 0.78-2.89) or in the models with depressive symptoms as a multinomial variable (Appendix Table 11).

Table 4.4 – Baseline characteristics and SGA –Frequencies and Chi-square p-values

	n	SGA%	p-value
Overall	1704	7.1	
DEMOGRAPHIC CHARACTERISTICS			
Age group			
<25	413	8.7	0.34
25-30	665	7.1	
30-35	420	5.5	
>35	206	7.3	
Nationality			
Kuwaiti	425	6.6	0.63
Non- Kuwaiti	1279	7.3	
Employment status			
Employed	771	7.3	0.81
Housewife	763	7.2	
Unemployed	170	5.9	
Education			
Up to High School	520	9.0	**0.04**
Higher education	1184	6.3	
Household Income (KWD)			
<400	503	10.7	**<0.01**

400-800	581	5.9	
800-1600	341	5.3	
≥1600	233	5.6	
PREGNANCY CHARACTERISTICS			
Parity			
0	568	7.9	0.35
≥1	1135	6.7	
Pre-pregnancy BMI			
<18.5	40	10.0	0.20
18.5-25	736	8.3	
25-30	555	6.3	
≥30	365	5.2	
In vitro fertilization			
No	1662	7.1	0.96
Yes	41	7.3	
Miscarriage in previous pregnancies			
No previous pregnancy	475	8.0	0.23
No miscarriage	732	5.9	
At least one miscarriage	496	8.1	
Gestational hypertension			
No	1258	6.4	0.30
Yes	62	9.7	
Sex of the baby			
Female	809	9.0	**<0.01**
Male	895	5.4	

Table 4.5 – Mental and physical health indicators and SGA – Frequencies and Chi-square p-values

	n	**SGA%**	**p-value**
RISKS BEFORE PREGNANCY			
Traumatic Events			
0-1	626	6.7	0.52
2-5	537	6.5	
6 or more	541	8.1	
PREGNANCY RELATED			
Antenatal depressive symptoms (EDS score)			
<10	1371	6.6	0.13
≥10	333	9.0	
Pregnancy related anxiety			
No	1464	7.0	0.80
Yes	240	7.5	
Perceived Stress Levels			
Lower (0-4)	604	6.0	0.36
Moderate (5-7)	644	7.8	

Higher (8-16)	443	7.9	
PTSD symptoms			
No	1108	6.7	0.35
Yes	596	7.9	
Mental Component Summary			
Poor	557	7.0	0.20
Fair	576	8.5	
Good	571	5.8	
Physical Component Summary			
Poor	550	7.5	0.05
Fair	584	5.1	
Good	570	8.8	
COPING DURING PREGNANCY			
Social Network			
Most integrated	124	4.0	0.47
Moderately integrated	292	7.5	
Moderately isolated	1000	7.0	
Most isolated	288	8.3	

Table 4.6 – Multiple logistic regression model for SGA

	OR	**95% CI**
DEMOGRAPHIC CHARACTERISTICS		
Age group		
<25	1.25	0.68-2.29
25-30	1.00	-
30-35	0.88	0.45-1.70
>35	1.08	0.47-2.51
Nationality		
Kuwaiti	1.00	-
Non- Kuwaiti	0.85	0.38-1.91
Employment status		
Employed	1.00	-
Housewife	0.59	0.33-1.07
Unemployed	0.62	0.26-1.47
Education		
Up to High School	1.61	0.94-2.73
Higher education	1.00	-
Household Income (KWD)		
<400	**3.63**	**1.13-11.61**
400-800	1.83	0.60-5.61
800-1600	1.78	0.66-4.77
≥1600	1.00	-
PREGNANCY CHARACTERISTICS		
Parity		
0	0.51	0.16-1.62

≥1	1.00	-
Pre-pregnancy BMI		
<18.5	0.85	0.19-3.85
18.5-25	1.00	-
25-30	0.70	0.41-1.22
≥30	0.54	0.27-1.12
In vitro fertilization		
No	1.00	-
Yes	0.69	0.09-5.42
Miscarriage in previous pregnancies		
No previous pregnancy	1.00	-
No miscarriage	0.34	0.10-1.19
At least one miscarriage	0.64	0.21-1.96
Gestational hypertension		
No	1.00	-
Yes	2.12	0.82-5.49
Sex of the baby		
Female	1.00	-
Male	0.63	**0.39-1.00**
PREGNANCY RELATED		
Antenatal depressive symptoms (EDS score)		
<10	1.00	-
≥10	1.50	0.78-2.89
Pregnancy related anxiety		
No	1.00	-
Yes	1.08	0.54-2.19
Perceived Stress Levels		
Lower (0-4)	1.00	-
Moderate (5-7)	1.19	0.67-2.12
Higher (8-16)	1.24	0.61-2.53
PTSD symptoms		
No	1.00	-
Yes	1.22	0.70-2.13
Mental Component Summary		
Poor	0.61	0.29-1.27
Fair	1.11	0.63-1.95
Good	1.00	-
Physical Component Summary		
Poor	0.78	0.43-1.42
Fair	0.58	0.32-1.04
Good	1.00	-
COPING DURING PREGNANCY		
Social Network		
Most integrated	1.00	-
Moderately integrated	3.26	0.71-14.87
Moderately isolated	3.12	0.73-13.36

Most isolated	3.60	0.78-16.55

Large for gestational age

Table 4.7 indicates that LGA was associated with age, nationality, employment status, household income, parity, pre-pregnancy BMI, gestational diabetes, and the sex of the baby, while Table 4.8 shows that LGA was not associated with any mental or health indicators examined. The results of the corresponding univariate logistic regression models are shown in Appendix Tables 12 and 13. In the adjusted logistic regression model, shown in Table 4.9 (n=1299), being of a non-Kuwaiti nationality was a significant risk factor for LGA (OR=1.88; 95% CI: 1.17-3.03) and baby boys had more than twice the odds of being LGA compared to baby girls (OR=2.15; 95% CI: 1.63-2.84). Furthermore, the adjusted ORs in Table 4.9 show that being nulliparous (OR=0.68; 95% CI: 0.48-0.96) was protective for LGA. Antenatal depressive symptoms was not associated with a higher risk for LGA, either as a binary variable (OR=1.12; 95% CI: 0.84-1.48) in the univariate logistic regression (Appendix Table 13) or in the multivariate logistic regression model (OR=1.16, 95% CI: 0.78-1.72), or as a multinomial variable in the multivariate logistic regression analysis (Appendix Table 14).

Table 4.7 – Baseline characteristics and LGA-Frequencies and Chi-square p-values

	n	**LGA%**	**p-value**
Overall	1704	22.4	
DEMOGRAPHIC CHARACTERISTICS			
Age group			
<25	413	16.2	**<0.01**
25-30	665	22.4	
30-35	420	24.3	
>35	206	31.1	
Nationality			
Kuwaiti	425	18.4	**0.02**
Non- Kuwaiti	1279	23.8	
Employment status			

Employed	771	23.7	**<0.01**
Housewife	763	23.2	
Unemployed	170	12.9	
Education			
Up to High School	520	21.7	0.65
Higher education	1184	22.7	
Household Income (KWD)			
<400	503	18.3	**0.01**
400-800	581	25.5	
800-1600	341	26.1	
≥1600	233	20.2	
PREGNANCY CHARACTERISTICS			
Parity			
0	568	15.9	**<0.01**
≥1	1135	25.7	
Pre-pregnancy BMI			
<18.5	40	5.0	**<0.01**
18.5-25	736	18.9	
25-30	555	25.2	
≥30	365	26.9	
Gestational diabetes			
No	1234	22.1	**0.01**
Yes	117	32.5	
Sex of the baby			
Female	809	16.2	**<0.01**
Male	895	28.0	

Table 4.8 – Mental and physical health indicators and LGA – Frequencies and Chi-square p-values

	n	**%**	**p-value**
RISKS BEFORE PREGNANCY			
Traumatic Events			
0-1	626	22.0	0.69
2-5	537	21.6	
6 or more	541	23.7	
PREGNANCY RELATED			
Antenatal depressive symptoms (EDS score)			
<10	1371	22.0	0.43
≥10	333	24.0	
Pregnancy related anxiety			
No	1464	21.9	0.23
Yes	240	25.4	

Perceived Stress Levels			
Lower (0-4)	604	23.0	0.32
Moderate (5-7)	644	20.5	
Higher (8-16)	443	24.2	
PTSD symptoms			
No	1108	23.5	0.16
Yes	596	20.5	
Mental Component Summary			
Poor	557	22.4	0.85
Fair	576	21.7	
Good	571	23.1	
Physical Component Summary			
Poor	550	24.6	0.18
Fair	584	20.0	
Good	570	22.8	
COPING DURING PREGNANCY			
Social Network			
Most integrated	124	23.4	0.74
Moderately integrated	292	24.3	
Moderately isolated	1000	21.5	
Most isolated	288	23.3	

Table 4.9 – Multivariate logistic regression model for LGA

	OR	**95% CI**
DEMOGRAPHIC CHARACTERISTICS		
Age group		
<25	0.68	0.45-1.02
25-30	1.00	-
30-35	0.83	0.59-1.17
>35	1.04	0.67-1.60
Nationality		
Kuwaiti	1.00	-
Non- Kuwaiti	**1.88**	**1.17-3.03**
Employment status		
Employed	1.00	-
Housewife	0.92	0.66-1.29
Unemployed	0.62	0.36-1.08
Education		
Up to High School	1.00	0.72-1.40
Higher education	1.00	-
Household Income (KWD)		
<400	0.57	0.30-1.06
400-800	0.84	0.47-1.50
800-1600	1.07	0.63-1.80

≥1600	1.00	-
PREGNANCY CHARACTERISTICS		
Parity		
0	**0.68**	**0.48-0.96**
≥1	1.00	-
Pre-pregnancy BMI		
<18.5	0.30	0.07-1.29
18.5-25	1.00	-
25-30	1.38	1.00-1.90
≥30	1.19	0.82-1.72
Gestational diabetes		
No	1.00	-
Yes	1.50	0.96-2.34
Sex of the baby		
Female	1.00	-
Male	**2.15**	**1.63-2.84**
PREGNANCY RELATED		
Antenatal depressive symptoms (EDS score)		
<10	1.00	-
≥10	1.16	0.78-1.72
Pregnancy related anxiety		
No	1.00	-
Yes	1.31	0.86-2.00
Perceived Stress Levels		
Lower (0-4)	1.00	-
Moderate (5-7)	0.88	0.63-1.24
Higher (8-16)	1.26	0.83-1.90
PTSD symptoms		
No	1.00	-
Yes	0.73	0.52-1.03
Mental Component Summary		
Poor	0.89	0.58-1.34
Fair	0.84	0.60-1.18
Good	1.00	-
Physical Component Summary		
Poor	1.14	0.80-1.62
Fair	0.72	0.51-1.01
Good	1.00	-
COPING DURING PREGNANCY		
Social Network		
Most integrated	1.00	-
Moderately integrated	1.18	0.65-2.14
Moderately isolated	0.98	0.57-1.68
Most isolated	1.22	0.66-2.26

Gestational length and birth weight as continuous outcomes

We also examined the association of antenatal depressive symptoms with birth weight and gestational length as continuous variables. There was no significant correlation between the EDS score and gestational length (r_s=-0.02, p-value=0.38) or birth weight (r_s=-0.05, p-value=0.06). In a multivariate linear regression model (n=1305) the EDS score was not a significant predictor for birth weight (β=-0.78, p-value=0.81) after controlling for socio-demographic factors, parity, BMI, gestational diabetes, gestational hypertension, previous miscarriage, IVF, the sex of the baby, and mental and health indicators (Appendix Table 15). Similarly, antenatal depressive symptoms did not predict gestational length (β=0.00, p-value=0.89) after adjusting for socio-demographic factors, parity, BMI, gestational diabetes, gestational hypertension, previous preterm birth, and mental and health indicators, as shown in Appendix Table 16.

Discussion

This study examined the association of depressive symptoms during pregnancy and adverse birth outcomes in a sample of pregnant women in Kuwait who were enrolled in the TRACER cohort. Overall, higher rates of preterm birth as well as for small and large for gestational age babies were found among women with an EDS score ≥10. However none of these associations reached statistical significance in multivariate models, after controlling for socio-demographic and pregnancy related factors.

A history of PTB was a significant risk factor for PTB in our sample which is in agreement with other studies (Kim et al., 2013). Similar to our study, Gawlik et al. (2012) found no significant effect of depression on PTB and Bindt et al. (2013) showed that depression in women who are at a lower obstetric risk failed to predict PTB and low birth weight. On the other hand, in the

recently published meta-analysis of Jarde et al. (2016) the pooled estimate from 14 studies with a total sample of 21048 women showed that women with untreated depression in pregnancy have a higher odds of delivering before the 37th week of gestation (OR=1.56; 95% CI: 1.25-1.94) as compared to women without depression. However, as Bindt et al. (2013) suggested, it seems that studies that had taken into consideration pregnancy complications did not find a strong association between depression and PTB, while many published studies which had shown a significant association failed to include these complications as risk factors of PTB.

A larger body of evidence exists on the effect of depression on low birth weight; in contrast, not many studies have examined the effect of depression on weight in relation to gestational age at delivery. We demonstrated that the levels of SGA were similar among women with and without depressive symptoms, which was consistent with the results of Smith et al. (K. F. Smith, Brunner, Michele, & Warren-findlow, 2015) but inconsistent with some other studies (Szegda et al., 2016). Molyneaux et al. (2015) also reported a weak impact of depression on SGA in obese and overweight women, though not in normal weight women. However, in our study, BMI was not shown to be an effect-modifier of this association. In our sample, the incidence of a small for gestational age was more frequent in girls and in babies from families with a lower income. Smith et al. (2015) also found that women with a lower family income had greater odds of delivering a SGA baby.

The information regarding the effect of depression on delivering a large for gestational age baby is scarce. The lack of evidence is also noted in Jarde et al. (2017) who could not identify a study on the association of antenatal depression and large for gestational age babies. Despite the fact that LGA was relatively common in our study, with more than a fifth of women delivering a LGA baby we found no significant association between depressive symptoms in pregnancy and

this outcome, in-line with a study conducted in Finland (Pesonen et al., 2016). More research is needed to further examine this association.

Conclusion

Our study suggests that depressive symptoms in pregnancy do not predict adverse birth outcomes, such as PTB, SGA, and LGA after adjusting for other known risk factors. Further research to examine the association of LGA and depressive symptoms in pregnancy is needed, as the available data are limited.

Chapter 5 – Prevalence and risk factors of postnatal depressive symptoms

Introduction

Postnatal or postpartum depression is defined as the presence of depression after delivery. It is one of the most common complication of childbearing, affecting approximately 10-15% of women (Robertson, Grace, Wallington, & Stewart, 2004). References to postnatal depression exist even in ancient medical literature (Laios, Karamanou, Tsoucalas, & Androutsos, 2014). Postnatal depression could present itself any time within a year of delivery and may last anywhere from weeks to months (Stewart et al., 2003). It is a major public health issue as it affects the health of both the mother and the infant. Postnatal depression also increases the risk of chronic or recurrent depression. Brummelte and Galea (2016) summarized the possible consequences of postnatal depression on the development of the child; for example, the infant of a mother with postnatal depression is at a greater risk of showing emotional, behavioral, and psychological problems, as well as cognitive delays later on, with boys having a greater risk of cognitive and motor developmental delays than girls. Moreover, gastrointestinal symptoms and infant diarrhea are more common among children of mothers with postnatal depression. Postnatal depression impairs the mother-infant relationship as the mothers who have depression do not communicate well with their babies and show less affection. In addition, some studies have shown that the mother-infant connection is weaker among these pairs, though results on this issue, as reported in the literature, are inconsistent (Brummelte & Galea, 2016).

Pathogenesis and treatment

The underlying mechanisms for developing postnatal depression are also summarized by Brummelte and Galea (2016). Hormonal fluctuations of ovarian hormones, glucocorticoids, and oxytocin are experienced after childbirth which could explain the mood changes present in postnatal depression. The “estradiol-withdrawal state” is one of the most common hypotheses in

explaining postnatal depression as estradiol levels fall significantly after giving birth. Another possible explanation for postnatal depression is the abnormal secretion of hormones by the hypothalamic-pituitary-adrenal axis, including glucocorticoids, and it has been suggested that glucocorticoids may interact with oxytocin making women more vulnerable to depressive moods. In regards to the neurobiology of postnatal depression, though the evidence is limited, there are indications that when the plasticity of the hippocampus is reduced then the susceptibility for developing postnatal depression increases. Only a few studies have examined the neurobiology of postnatal depression and their results suggest that the levels of specific neurotransmitters and neutrophic factors are different in women with postnatal depression, or major depression, compared to women without depression (Brummelte & Galea, 2016).

Pharmacological or psychological interventions are often used to treat postnatal depression. The use of antidepressants may help improve maternal mental health but there is limited evidence of any beneficial effects on the child or the mother-child relationship (Brummelte & Galea, 2016). Moreover, in this way, the benefits of breast-feeding are lost as breast-feeding is not recommended in women who take antidepressants. Some interventions that target psychological support, including home visits by mid-wives and nurses, peer-based telephone support, and psychotherapy, have been identified as relatively promising methods to reduce postnatal depression (C. L. Dennis & Dowswell, 2013). However, similar to antidepressants, these non-pharmacological interventions do not seem to improve the mother-baby interactions (Forman et al., 2007).

Risk factors

Several psychosocial factors have been proposed in epidemiologic studies as being associated with higher susceptibility to developing postnatal depression. Evidence suggests that depression history prior to pregnancy and antenatal depression are major risk factors for developing

postnatal depression (Chojenta, Lucke, Forder, & Loxton, 2016; Leigh & Milgrom, 2008; Underwood, Waldie, Souza, Peterson, & Morton, 2016). Redshaw and Henderson (2013) further proposed that the risk factors for postnatal depression are different among women who had depression in pregnancy compared to women that did not. Prenatal anxiety, having experienced stressful life events, and parenting stress were also cited as significant predictors of postnatal depression (Abdollahi et al., 2014; Beck, 2001; O'hara & Swain, 1996). Moreover, the presence of unhealthy relationships of the woman with people in her environment was also shown to be associated with developing postnatal depression. Women who are not satisfied in their marriage or do not have a good relationship with their parents-in-law, and women who have conflicts with their partner or feel a lack of family cohesion or social support are more likely to show symptoms of depression (Chi, Zhang, Wu, & Wang, 2016; Djoda Adama et al., 2015; Özbaşaran, Çoban, & Kucuk, 2011; Ramasubramaniam, Madhavanprabhakaran, Renganathan, & Raman, 2014; Siu, Leung, Ip, Hung, & Hara, 2012; Tachibana et al., 2015). On the other hand, having a husband who is supportive with the care of the infant was found to be a factor associated with a decreased likelihood of postnatal depression (Mohamad Yusuff, Tang, Binns, & Lee, 2015). Adding to this evidence is a recent study conducted in Sudan which reported that women who had experienced domestic violence before or during pregnancy had odds of developing postnatal depression seven times greater than that of women who did not (Khalifa, Glavin, Bjertness, & Lien, 2016).

In addition to the mental health of the mother and the support she receives, other demographic factors have also been identified to be associated with postnatal depression. Firstly, there is a variation of postnatal depressive symptoms among women of different ethnicities (Underwood et al., 2016). Also, women who have a lower family income, or have financial problems, have a greater risk for postnatal depressive symptoms (Chi et al., 2016; Djoda Adama et al., 2015; Jin,

Mori, & Sakajo, 2016). Furthermore, postnatal depressive symptoms have been shown to be more common in women with a lower educational background or women who were unemployed (Chi et al., 2016; Corrêa, Castro, Santos, Romano-silva, & Santos, 2016; Kheirabadi et al., 2009). In regards to the role of maternal age, the findings are inconsistent, with some studies reporting that women of younger age are more susceptible to postnatal depressive symptoms while other studies show that women of older age have more depressive symptoms (Bener, Burgut, Ghuloum, & Sheikh, 2012; Khalifa et al., 2016; Kheirabadi et al., 2009). The role of parity is also not clear, with some studies reporting that primiparous women have greater odds of postnatal depressive symptoms while other studies suggest that women who are multiparous are at a greater risk (Hamdan & Tamim, 2011; Jin et al., 2016; Kheirabadi et al., 2009; Ramasubramaniam et al., 2014; Redshaw & Henderson, 2013). Furthermore, a history of obstetric complications and preterm birth is more frequent among women with postnatal depression (Burgut, Bener, Ghuloum, & Sheikh, 2013; Putnam et al., 2015; Ramasubramaniam et al., 2014). Women who breast-feed their infants for a short time, or do not breast feed them at all, also show higher odds of postnatal depressive symptoms (Chojenta et al., 2016; Davey, Tough, Adair, & Benzies, 2011). However, the temporality of this association is not clear, i.e. whether women with postnatal depression have a lower frequency of breastfeeding or whether women who do not breastfeed are at increased risk of developing postnatal depression (C.-L. Dennis & McQueen, 2009).

Aim

The goal of this analysis is to provide an estimate of the prevalence of postnatal depressive symptoms as an indicator of postnatal depression and identify the risk factors associated with postnatal depressive symptoms using data from the TRansgenerational Assessment of Children's Environmental Risk (TRACER) Study in Kuwait. In addition, we wanted to investigate whether

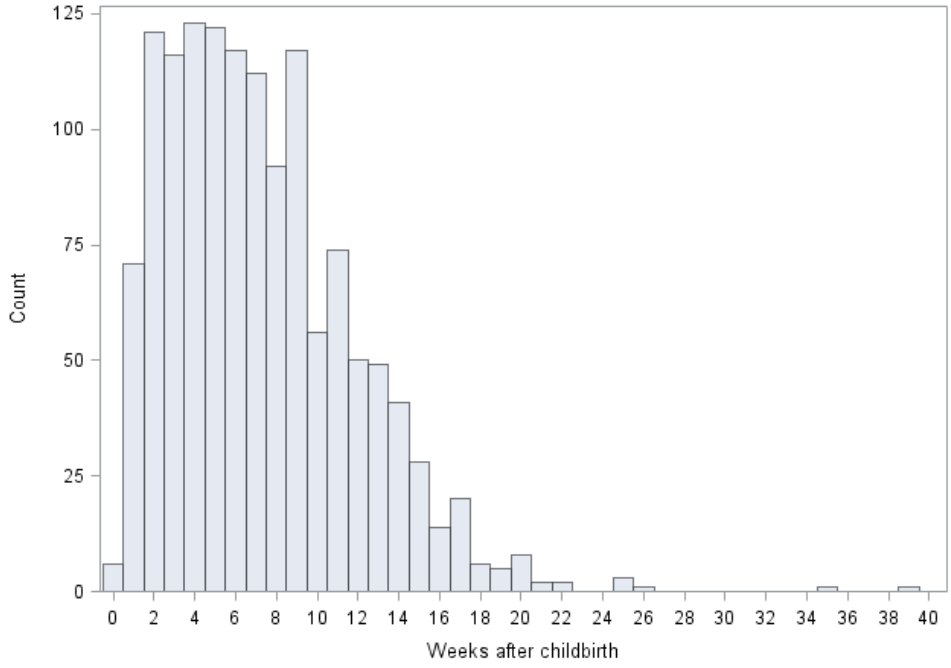
the risk factors associated with postnatal depressive symptoms are different in women who had depressive symptoms during pregnancy compared to those who did not. Identifying the potential determinants for developing postnatal depression in this geographic area is important in understanding the problem and for designing successful screening tools and interventions.

Methods

Sample

A total of 1938 women in the TRACER study completed the prenatal Stress Questionnaire during their second or third trimester. A postnatal phone interview was conducted after delivery to obtain information about the birth date, birth weight, and adverse outcomes during pregnancy, such as gestational diabetes and gestational hypertension. During the same interview a questionnaire was used to evaluate the health and diet of the baby, as well as maternal stress, including postnatal depressive symptoms. The Edinburgh Postnatal Depression Questionnaire (EPDS) was used to examine depressive symptoms in the postpartum period. The distribution of the time in weeks after childbirth when the EPDS was administered is shown in Figure 5.1; the median time was 6 weeks postpartum and only 5% of the women answered the questionnaire at a time longer than 15 weeks. Similar to antenatal depressive symptoms, we used a cut-off of EPDS≥10 to define depressive symptoms in the postpartum period, as recommended by the State Perinatal Mental Health Reference Group of Western Australia (Department of Health Government of Western Australia, 2006).

Figure 5.1 – Distribution of the time (weeks) that the EPDS questionnaire was administered



Out of the 1938 women who answered the Stress Questionnaire (see Figure 2.6) and were eligible for this analysis 580 were not included because of not having completed the Edinburgh Postnatal Depression Scale, thus reducing the sample size for these analyses to 1358 women.

Statistical analysis

We examined the distribution of the EPDS score and calculated the prevalence of postnatal depressive symptoms with the corresponding 95% confidence intervals. We computed these rates separately for Kuwaitis and non-Kuwaitis. Moreover, we examined the frequency of the individual responses in each of the items of the EPDS questionnaire.

Chi-square tests and univariate logistic regression models were used to compare the baseline characteristics of women with and without postnatal depressive symptoms. Univariate logistic regression models were utilized to identify determinants of postnatal depressive symptoms. Hierarchical logistic regression analysis was then performed to examine the simultaneous effect of several potential risk factors; first, we included only the baseline characteristics; then, we

added antenatal depressive symptoms and other mental and physical health indicators that were assessed during pregnancy; and finally, we added pregnancy outcomes, such as PTB, SGA and LGA, as well as the sex of the baby. We carried out a stratified analysis to investigate whether the predictors of postnatal depression were different among women who had antenatal depressive symptoms compared to those women who did not.

To further examine the association of antenatal and postnatal depressive symptoms, we utilized the non-parametric Spearman test to examine whether the correlation of the EPDS scores during and after pregnancy, as continuous measures, was statistically significant.

We also compared the characteristics of women who completed the EPDS postnatally versus those who did not, to assess the presence of any potential bias, and in particular, to check whether women who had depressive symptoms antenatally were less willing to be followed postnatally. Chi-square tests were used for this sensitivity analysis.

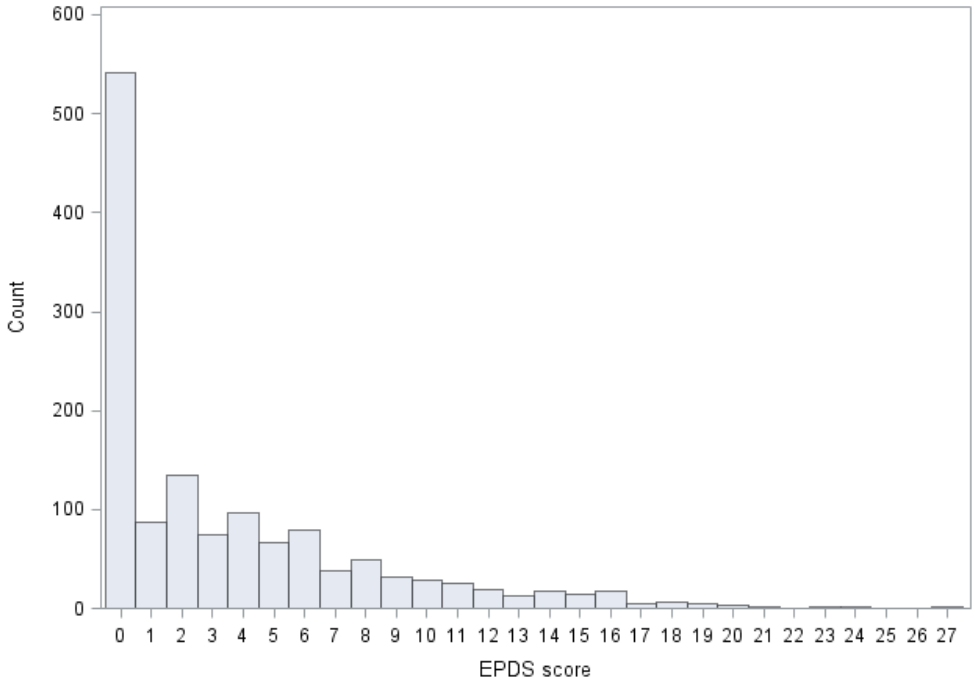
Analysis was performed using SAS 9.3 and all tests were two-sided with a p-value < 0.05 used to determine statistical significance.

Results

Overall

Similar to the antenatal EDS score, the distribution of postnatal EPDS score was skewed to the right (Figure 5.2). The median score was 2 (Q1-Q3: 0-6) while the mode was 0. The scores ranged from 0 to 27. The EPDS questionnaire was administered at a median time of 6.6 weeks (IQR: 3.7-9.9) postnatally.

Figure 5.2 – Distribution of EPDS score



The prevalence of postnatal depressive symptoms in the overall sample was 11.7% (95% CI: 10.1-13.5). Among Kuwaitis the prevalence was 14.2% (95% CI: 10.7-18.4) and in non-Kuwaitis 10.9% (95% CI: 9.00-12.9), though this difference was not statistically significant.

The percentages of responses in the different items of the EPDS questionnaire are shown in Appendix Table 17 (positive items) and Appendix Table 18 (negative items). Interestingly, more than a quarter of the women (26.3%) reported that they felt overwhelmed, i.e. that they did not feel that they were able to be on top of things some of the time or most of the time. This was the most common reported symptom in the overall sample but also in each of the two groups separately, i.e. among women with and without postnatal depressive symptoms. The least reported symptom in the overall sample was the thought of self-harm, with only 0.8% having such a thought, even if it was not too often. Only 0.4% of the women without depressive symptom had this symptom while in women with depressive symptoms this symptom was reported by 4.4% of them.

Table 5.1 shows the baseline characteristics of the participants, overall and for those with an EPDS score greater than or equal to 10. The unadjusted ORs are also presented in Table 5.1. Women in the lowest monthly household income group (<400 KWD [~1125 Euros]) had an increased risk of postnatal depressive symptoms compared to those with monthly income ≥1600 KWD [~4450 Euros] (OR=2.07; 95% CI: 1.14-3.75). Delivering a boy (OR=1.50; 95% CI: 1.07-2.11) and having a preterm birth (OR=1.88; 95% CI: 1.11-3.20) were also significant predictors of postnatal depressive symptoms (see also Appendix Table 19).

Table 5.1 – Baseline characteristics and postnatal depressive symptoms - Frequencies and unadjusted ORs.

	Overall		**EPDS≥10**		**Unadjusted OR**	
	n	**%**	**n**	**%**	**OR**	**95%CI**
DEMOGRAPHIC CHARACTERISTICS						
Age group						
<25	320	23.5	43	13.4	1.14	0.75-1.73
25-30	517	38.1	62	12.0	1	-
30-35	339	25.0	36	10.6	0.87	0.56-1.35
>35	182	13.4	18	9.9	0.81	0.46-1.40
Nationality						
Kuwaiti	344	25.3	49	14.2	1	-
Non- Kuwaiti	1014	74.7	110	10.9	0.73	0.51-1.05
Employment status						
Employed	615	46.6	67	10.9	1	-
Housewife	613	45.4	75	5.6	1.14	0.80-1.62
Unemployed	121	9.0	16	13.2	1.25	0.70-2.24
Education						
Up to Middle/secondary	426	31.6	57	13.4	1.26	0.89-1.78
Higher education	923	68.4	101	10.9	1	-
Household Income (KWD)						
<400	404	30.7	60	14.9	**2.07**	**1.14-3.75**
400-800	447	34.0	45	10.1	1.33	0.72-2.45
800-1600	271	20.6	35	12.9	1.76	0.93-3.32
≥1600	193	14.7	15	7.8	1	-
PREGNANCY, BIRTH AND POSTNATAL CHARACTERISTICS						
Parity						

0	425	31.5	42	9.9	0.77	0.53-1.12
≥1	923	68.5	115	12.5	1	-
Pre-pregnancy BMI						
<18.5	31	2.3	4	12.9	1.31	0.44-3.88
18.5-25	571	42.5	58	10.2	1	-
25-30	443	32.9	60	16.5	1.39	0.94-2.04
≥30	300	22.3	36	12.0	1.21	0.78-1.88
Preterm delivery						
No	1227	92.5	136	11.1	1	-
Yes	100	7.5	19	19.0	**1.88**	**1.11-3.20**
SGA						
No	1218	93.0	137	11.3	1	-
Yes	91	7.0	13	14.3	1.32	0.71-2.43
LGA						
No	1004	76.7	115	11.5	1	-
Yes	305	23.3	35	11.5	1.00	0.67-1.50
Sex of the baby						
Girl	640	47.1	61	9.5	1	-
Boy	718	52.9	98	13.7	**1.50**	**1.07-2.11**

The association of postnatal depressive symptoms with antenatal depressive symptoms and other mental and physical health indicators that were assessed with the Stress Questionnaire are summarized in Table 5.2. All the factors listed, with the exception of being emotionally neglected in childhood, are associated with the development of postnatal depressive symptoms (see also Appendix Table 20). Depressive symptoms in pregnancy have the strongest effect in predicting postnatal depressive symptoms with OR=7.25 (95% CI: 5.10-10.29), followed by higher levels of perceived stress (OR=4.29; 95%CI: 2.71-2.79).

Table 5.2 – Mental and physical health indicators of postnatal depressive symptoms- Frequencies and unadjusted ORs.

	Overall		**EPDS≥10**		**Unadjusted OR**	
	n	**%**	**n**	**%**	**OR**	**95%CI**
RISKS BEFORE PREGNANCY						
Childhood emotional neglect						
Least neglected (5-7)	565	41.6	70	12.4	1	-

Moderately neglected (8-10)	348	26.6	27	7.8	0.60	**0.37-0.95**
Most neglected (11-25)	445	32.8	62	13.9	1.15	0.79-1.65
Traumatic Events						
0-1	493	36.3	42	8.5	1	-
2-5	412	30.3	36	8.7	1.03	0.65-1.64
6 or more	453	33.4	81	17.9	**2.34**	**1.57-3.48**
Prior depression						
No	1319	97.9	149	11.3	1	-
Yes	29	2.1	8	27.6	**2.99**	**1.30-6.88**
PREGNANCY RELATED						
Antenatal depressive symptoms						
No	1090	80.3	70	6.4	1	-
Yes	268	19.7	89	33.2	**7.25**	**5.10-10.29**
Pregnancy related anxiety						
No	1173	86.4	114	9.7	1	-
Yes	185	13.6	45	24.3	**2.99**	**2.03-4.40**
Perceived Stress Levels						
Lower (0-4)	473	35.0	28	5.9	1	-
Moderate (5-7)	524	38.8	55	10.5	**1.86**	**1.16-2.99**
Higher (8-16)	353	26.2	75	21.3	**4.29**	**2.71-6.79**
PTSD symptoms						
No	884	65.1	57	6.5	1	-
Yes	474	34.9	102	21.5	**3.98**	**2.81-5.63**
Mental Component Summary						
Poor	443	32.6	85	19.2	**3.13**	**2.03-4.84**
Fair	475	35.0	43	9.1	1.31	0.81-2.13
Good	440	32.4	31	7.1	1	-
Physical Component Summary						
Poor	440	32.4	72	16.4	**1.92**	**1.28-2.89**
Fair	463	34.1	45	9.7	1.06	0.68-1.65
Good	455	33.5	42	9.2	1	-
COPING DURING PREGNANCY						
Social Network						
Most integrated	108	8.0	10	9.3	1	-
Moderately integrated	224	16.6	23	10.3	1.12	0.51-2.45
Moderately isolated	785	58.2	79	10.1	1.10	0.55-2.19
Most isolated	232	17.2	46	19.8	**2.42**	**1.17-5.01**

Table 5.3 presents the results of the three hierarchical logistic regression models modeling the probability of having postnatal depression. In Model 1, the simultaneous effect of the baseline

variables was examined. Depressive symptoms were more common among women who had a household income of <1600 KWD and in women who had self-reported depression prior to pregnancy (OR=4.54; 95% CI: 1.81-11.42). On the other hand, non-Kuwaiti women had lower odds of postnatal depressive symptoms compared to Kuwaiti women (OR=0.29; 95% CI: 0.16-0.54). When mental and health indicators were added in the model (Model 2), we observed that antenatal depressive symptoms and PTSD symptoms were significant risk factors for the presence of postnatal depressive symptoms with OR equal to 4.05 (95% CI: 2.44-6.74) and 1.97 (95% CI: 1.20-3.23), respectively. In Model 2, the effect of nationality remained significant while that of depression history did not hold after adjustment. The effect of household income was attenuated, with depressive symptoms being more common only in women with a family income of <400 KWD. When Model 2 was further adjusted for pregnancy outcomes, namely PTB, SGA, and LGA, as well as the sex of the infant (Model 3) no important changes were observed. All models had a good fit based on the Hosmer-Lemeshow goodness of fit test and a C-statistic greater than 0.5 (Model 1: c=0.65; Model 2: c=0.82; and Model 3: c=0.81). Given the results of models 2 and 3, antenatal depressive symptoms seems to be the strongest determinant of postnatal depressive symptoms.

Table 5.3 – Hierarchical multivariate logistic regression models for postnatal depressive symptoms (n=1054).

	Model 1		**Model 2**		**Model3**	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Nationality						
Kuwaiti	1	-	1	-	1	-
Non- Kuwaiti	0.29	0.16-0.54	0.39	0.19-0.80	0.40	0.20-0.81
Household Income (KWD)						
<400	4.54	1.81-11.42	2.89	1.06-7.88	2.81	1.03-7.63
400-800	3.05	1.28-7.29	2.15	0.82-5.61	2.16	0.83-5.61
800-1600	2.26	1.08-4.76	2.03	0.90-4.58	2.01	0.89-4.55
≥1600	1	-	1	-	1	-
Prior depression						
No	1	-	1	-	1	-

Yes	3.38	1.31-8.72	1.33	0.45-3.91	1.31	0.45-3.81
Antenatal depressive symptoms						
No			1	-	1	-
Yes			4.05	2.44-6.74	4.08	2.45-6.81
PTSD symptoms						
No			1	-	1	-
Yes			1.97	1.20-3.23	1.99	1.20-3.28
Hosmer-Lemeshow Goodness of fit (p-value)		0.22		0.69		0.59
C-statistic		0.65		0.82		0.81

- *Model 1: Adjusted for socio-demographic factors including age, job, education, parity and BMI.*
- *Model 2: Adjusted for the same factors of model 1 plus health indicators assessed during pregnancy including experience of traumatic events, pregnancy-related anxiety, support from the social environment, childhood emotional neglect, MCS and PCS*
- *Model 3: Adjusted for the same factors as model 2 plus pregnancy outcomes including preterm birth, small and large for gestational age and sex of the baby.*

Antenatal and postnatal depressive symptoms

The scores obtained from the EDS and the EPDS questionnaire were significantly correlated with a moderate association (Spearman r=0.46, p<0.01). In this sample of women who had a complete EDS and EPDS score (n=1358), using a cut-off point of 10, 13.2% of them had antenatal depressive symptoms only, 5.2% had postnatal depressive symptoms only, and 6.6% had experienced both sets of symptoms. Approximately three quarters of the women did not have depressive symptoms at all, either antenatal or postnatal.

We also looked at the risk factors of postnatal depressive symptoms separately for women who had antenatal depressive symptoms and those women who did not. We used all the variables examined in Model 3, i.e. demographic, mental and physical health indicators, and pregnancy outcomes. The significant risk factors for each stratum are demonstrated in Table 5.4. Among women who had antenatal depressive symptoms only, having a lower household income, i.e. <400 KWD or 400-800 KWD per month, was statistically significant for developing postnatal depressive symptoms after adjusting for the other covariates. On the other hand, in women without depressive symptoms in pregnancy, household income was not associated with postnatal depressive symptoms. However, women who experienced pregnancy-related anxiety (OR=2.65;

95% CI: 1.28-5.49), had higher levels of perceived stress (OR=2.66; 95% CI: 1.19-5.93), PTSD symptoms (OR=2.12; 95% CI: 1.13-3.95), and who felt more isolated (OR=4.32; 95% CI: 1.03-18.25) were at a greater risk of postnatal depressive symptoms. Moreover, depressive symptoms were more common in women who delivered a boy (OR=2.53; 95% CI: 1.42-4.51).

Table 5.4 – Multivariate logistic regression models for postnatal depressive symptoms by antenatal depressive symptoms status.

	Antenatal depressive symptoms (n =196)		**No antenatal depressive symptoms (n=858)**	
	OR	**95% CI**	**OR**	**95% CI**
Household Income (KWD)				
<400	**12.93**	**1.87-89.24**	1.79	0.53-6.00
400-800	**11.79**	**1.71-81.32**	1.31	0.43-3.98
800-1600	4.08	0.74-22.43	2.02	0.81-5.03
≥1600	1	-	1	-
Pregnancy related anxiety				
No	1	-	1	-
Yes	0.72	0.33-1.59	**2.65**	**1.28-5.49**
Perceived Stress Levels				
Lower (score 0-4)	1	-	1	-
Moderate (score 5-7)	0.36	0.08-1.51	1.65	0.84-3.24
Higher (score 8-16)	0.43	0.11-1.63	**2.66**	**1.19-5.93**
PTSD symptoms				
No	1	-	1	-
Yes	1.50	0.63-3.59	**2.12**	**1.13-3.95**
Social Network				
Most integrated	1	-	1	-
Moderately integrated	0.29	0.05-1.65	1.96	0.46-8.49
Moderately isolated	0.50	0.11-2.35	2.66	0.71-9.94
Most isolated	1.00	0.19-5.20	**4.32**	**1.03-18.25**
Sex of the baby				
Girl	1	-	1	-
Boy	0.52	0.25-1.11	**2.53**	**1.42-4.51**

The models are adjusted for all other variables included in model 3, i.e. age, job, education, parity, BMI, traumatic events, childhood emotional neglect, MCS, PCS, preterm birth, small and large for gestational age.

For comparison purposes we summarized the factors associated with depressive symptoms in our sample over the perinatal period in Table 5.5. A lower household income as well as PTSD symptoms seem to be associated with both antenatal and postnatal depressive symptoms, even after adjusting for all other covariates in the model. Several other variables were shown to be

associated with either perinatal depressive symptoms only or postnatal depressive symptoms only.

Table 5.5 – Summary of factors associated with antenatal and postnatal depressive symptoms, as obtained from multiple regression models.

	Antenatal	Postnatal
Baseline		
Demographic	• Household income	• Nationality • Household income
Pregnancy	• Gestational age at the time of the Stress Questionnaire	
Mental and physical health indicators		
Risks before pregnancy	• Traumatic events	
Pregnancy-related	• Pregnancy-related anxiety • Perceived stress • PTSD symptoms • Perceived poor quality of mental health (MCS) • Perceived poor quality of physical health (PCS)	• Antenatal depressive symptoms • PTSD symptoms

Comparing women who answered the EPDS questionnaire with women that did not

The sensitivity analysis conducted revealed that women who answered the EPDS versus those who did not, differed in terms of age, parity, traumatic events, and mental component summary scale (Appendix Tables 20 and 21). More precisely, women who did not answer the EPDS after delivery were younger, experienced fewer traumatic events, and had a better quality of mental health. Moreover, the percentage of nulliparous women was greater among those who did not answer the questionnaire compared to those who did. Despite these differences, the prevalence of antenatal depressive symptoms did not differ significantly in these two groups (Chi-square=0.68,

p-value=0.41), suggesting that women who had depressive symptoms in pregnancy were equally likely to answer the EPDS questionnaire postnatally.

Discussion

In this group of women who participated in the TRACER cohort, we found that the prevalence of postnatal depressive symptoms was 11.7%, based on an EPDS score of 10 or greater. This is somewhat lower compared to studies conducted in countries of similar culture in the region of the Gulf; using the same tool and the same cut-off point the prevalence of depression in United Arab Emirates was 16.8% (Hamdan & Tamim, 2011) while in Qatar the prevalence using a cut-off of 12 was 17.6% (Burgut et al., 2013). However, our estimated prevalence is in agreement with rates reported elsewhere (Davey et al., 2011) as well as with the pooled rate reported in the meta-analysis of O'Hara and Swain (1996). Similar to previous studies, the prevalence of postnatal depressive symptoms was lower than that of antenatal depressive symptoms (Underwood et al., 2016).

The presence of antenatal depressive symptoms was the strongest predictor of postnatal depressive symptoms in our study. Chojenta et al. (2016) found that women with antenatal depression have an odds of experiencing postnatal depressive symptoms nine times greater than that of women who did not have depression in pregnancy. Similarly, a study conducted in Canada showed that depression in pregnancy increases the risk for major depression symptoms, defined as a EPDS≥13 (Davey et al., 2011). This is also consistent with other studies which identified antenatal depressive symptoms as a determinant of postnatal depressive symptoms (Hamdan & Tamim, 2011; Koutra et al., 2014). Hamdan and Tamim (2011) argued that

depression during pregnancy may continue to the postnatal period and suggested that screening for depression should be performed both before and after delivery.

Using stratified analysis, we identified the risk factors associated with postnatal depressive symptoms separately for women with and without depressive symptoms in pregnancy. We observed that the risk factors for these two groups are different. Redshaw and Henderson (2013) also found different risk factors for postnatal depression among women who have been depressed in pregnancy compared to the overall sample that included all women, independent of antenatal depression status.

In our study the only significant risk factor for postnatal depressive symptoms among women with antenatal depressive symptoms was the family income, while this was not the case for women with no antenatal depressive symptoms. Instead, the mother's mental well-being (pregnancy-related anxiety, perceived stress, and PTSD symptoms) and social support from her network were significant risk factors for postnatal depressive symptoms in the group of women with no antenatal depressive symptoms. Contrary to our results, Underwood et al. (2016) found that the only factor associated with women experiencing only postnatal depressive symptoms compared to experiencing only antenatal depressive symptoms was diagnosis of depression prior to pregnancy. In their study, women with higher perceived stress score, difficult relationships and family environment, and who did not exercise during pregnancy had an increased risk of experiencing both antenatal and postnatal depression symptoms, compared to having only antenatal depressive symptoms. In a similar analysis, Redshaw and Henderson (2013) examined the factors that were associated with postnatal depression at 3-months after delivery in women who were antenatally depressed. The results obtained from multivariate logistic regression models showed that long term mental illness or learning disability, left alone in labor, and

experiencing poor postnatal health were significant risk factors for postnatal depression. On the other hand, multiparity and black and ethnic minority status were protective factors.

An interesting finding in our study was that delivering a boy was associated with having postnatal depressive symptoms, within the group of women who did not have antenatal depressive symptoms. A similar association to the one that we obtained was observed in Sweden and in France (De Tychey et al., 2008; Sylvén et al., 2011). Furthermore, Hall et al. (Hall & Holden, 2008)examined the assessment of cognition, emotion, and situation of postnatal women using the Postnatal Negative Thoughts Questionnaire and found that mothers of infant boys had more negative appraisals. However, the existing evidence in regards to the influence of the gender on depression is controversial, as other epidemiologic studies showed that postnatal depression is more common among women who deliver a girl due to a cultural bias towards favoring males (Adewuya, Fatoye, Ola, Ijaodola, & Ibigbami, 2005; Hassanein, Fathalla, & Abdel Rahim, 2014; Jain, Tyagi, Kaur, Puliyel, & Sreenivas, 2014; Xie et al., 2007). In some cultures, having a baby girl may create marital conflicts and women may receive less support after birth, which may in turn make women more susceptible to postnatal depression (Adewuya et al., 2005; Xie et al., 2007). Kitamura et al. (2006) as well as Kheirabadi et al. (2009) argued that it is the dissatisfaction with the sex of the infant that was associated with a higher risk of postnatal depression and not the sex per se. Further research is needed to examine any link between the sex of the infant and postnatal depressive symptoms.

Conclusion

To summarize, we found that one in nine women in Kuwait experience depressive symptoms postnatally. Postnatal depressive symptoms were more common among women who had

experienced depressive symptoms in pregnancy which was consistent with our hypothesis, based on published evidence. In fact, in our sample depressive symptoms in pregnancy were the strongest predictor of postnatal depressive symptoms. This finding urges the need for screening for and detecting maternal health issues during the antenatal period and addressing them effectively.

Chapter 6 – Summary and future directions

Concluding remarks

We examined the levels of antenatal and postnatal depressive symptoms and their risk factors in a sample of pregnant women in Kuwait. Our results suggest that one-in-five women in Kuwait may experience depressive symptoms during pregnancy while one-in-nine women may have depressive symptoms postnatally. Women later in pregnancy, women with a lower family income, or with a history of depression are at a greater risk of having antenatal depressive symptoms. Pregnancy related anxiety, perceived stress, traumatic events, PTSD symptoms, as well as poor mental and physical health are comorbid with depressive symptoms at pregnancy. Risk factors for postnatal depressive symptoms include lower family income, being Kuwaiti, and experiencing PTSD symptoms during pregnancy. Having antenatal depressive symptoms seems to be the strongest predictor for postnatal depressive symptoms, which highlights the need to address this issue early in pregnancy. When looking separately at the group of women who did not have depressive symptoms in pregnancy, apart from PTSD symptoms, other pregnancy related mental issues are also associated with postpartum depressive symptoms, including pregnancy related anxiety, perceived stress, and social isolation.

Another objective of this work was to explore the risk factors of pre-term delivery (PTB), small for gestational age (SGA), and large for gestational age (LGA) in this population and to examine the effect of antenatal depressive symptoms on these adverse outcomes. Conception by in vitro fertilization, previous preterm deliveries, and a fair mental health were associated with PTB. A lower family income and a female baby increased the risk for SGA. The determinants of LGA included a non-Kuwaiti nationality, parity, and having a boy. As for the implications of antenatal depression the literature review conducted suggested that the evidence about the association of antenatal depressive symptoms with PTB or SGA is in fact inconsistent. In our study, we failed

to find a statistically significant association between antenatal depressive symptoms and PTB or SGA. Similarly, depressive symptoms in pregnancy did not seem to predict the birth of an LGA baby. We could not compare this with findings of other studies due to the limited evidence that was available in the literature. Thus, further research is needed in order to examine whether antenatal depressive symptoms are linked with LGA in other populations.

We recommend that antenatal and postnatal depression screening is performed as a routine test, especially among women who are at a higher risk of experiencing depression during the perinatal period, such as women of lower family income. Mental health problems and psychiatric disorders are stigmatizing in many Arab countries, hence, it is important to address the issue with caution, though at the same time women need to be encouraged to open up and talk about their mental health problems. Clinical diagnosis should be considered where appropriate and support should be provided to women diagnosed with antenatal or postnatal depression. Support programs that focus on addressing and preventing fear related to the experience of childbirth, stress, and depressive symptoms in general could be introduced in maternal health care centers; for example, pregnant women could be encouraged to join group sessions and share their experiences and discuss issues that they encounter in pregnancy. Improving the mental well-being of women during pregnancy, helping them reduce their anxiety related to pregnancy, and making them feel less isolated, could potentially lower the risk of postnatal depressive symptoms as well. It is important to raise awareness among women, as well as health providers, about mental health and the potential of mental health services, and to provide mental health support to women, as needed.

Limitations and strengths

There are some limitations in our study that should be considered when interpreting the findings. One major limitation was the fact that some of the baseline risk factors considered were assessed

at the same time as the status of antenatal depressive symptoms, therefore, the associations between baseline characteristics and antenatal depressive symptoms described in the corresponding results should be interpreted with caution due to the absence of temporality and they cannot indicate causation. Another limitation is that we did not assess depression but rather depressive symptoms, due to the lack of clinical diagnosis of depression. However, the Edinburgh Postnatal Depression Scale (EPDS) is widely used in practice to assess depressive symptoms and has a relatively good specificity and sensitivity when compared with diagnostic tests of depression. When the Arabic EPDS with a score ≥10 was compared with the Diagnostic Interview Schedule (DIS) for DSM-III-R for major depression and anxiety, the sensitivity was 77.8% and the specificity 80.2% (Department of Health Government of Western Australia, 2006).

The EPDS questionnaire was not validated specifically in the population of Kuwait; however, an Arabic version of the questionnaire was validated in other Arab countries - even though the cultural setting of these countries could be somewhat different than Kuwait, which ranks among the richest countries in the world. A pilot study was conducted before TRACER, so EPDS and the tools in the Stress Questionnaire were tested, though not officially validated, before the TRACER study was implemented.

The initial sample used for the analysis of Chapter 3 included 1938 but not all of them had available data to examine the outcomes of interest in Chapters 4 and 5. This loss in the sample size could have introduced some source of bias, especially in Chapter 5 where the sample was restricted to 1358 women (70%). However, when we investigated whether women with missing data were different in regards to postnatal depressive symptoms, we found that these women did not vary significantly in their antenatal depressive symptoms status.

In addition, gestational age was calculated as the interval from the self-reported last menstrual period to the date of the Stress Questionnaire which may be subject to recall bias. Preterm birth was defined using this variable. However, this is the most common way to estimate gestational age, especially in large studies where ultrasound measurements are not available (Institute of Medicine (US) Committee on Understanding Premature Birth and Assuring Healthy Outcomes, 2007). In addition, the birth weight that was used to compute SGA and LGA was not measured by the field workers directly but it was reported by the mother in a post-natal call or appointment. However, women tend to remember well the birth date and the birth weight of their offspring, especially since the post-natal calls took place 0-10 months from the delivery of the baby. Finally, gestational diabetes and gestational hypertension were also self-reported after delivery and were therefore subject to bias.

Notwithstanding these limitations, our study has several strengths, including its large sample of women and their offsprings. To the best of our knowledge this was the first study that examined the prevalence and risk factors of antenatal and postnatal depressive symptoms in a relative large sample of women in Kuwait. The sample included both Kuwaitis and non-Kuwaitis that attended both public and private clinics and thus represented the heterogeneity of the population of Kuwait, making the results more reliable by having a representative sample of the population. Moreover, the cohort design of the study enabled us to examine the temporal association, especially of postpartum depressive symptoms, with a range of baseline, pregnancy, and birth risk factors. In addition, data were collected for a wide variety of variables, including socio-demographic, reproductive, mental and physical health characteristics, allowing us to examine antenatal depressive symptoms in association with a number of potential risk factors using multivariate analysis. Lastly, despite the lack of clinical diagnosis for depression, the EPDS is being used widely as a screening tool for depression in postnatal and non-postnatal women and

thus our study resembles better what the usual practice is and gives a closer look to reality and the public health impact of our results.

Future Work

We have compared the risk factors associated with antenatal and postnatal depressive symptoms; the common risk factors were a lower household income and having PTSD symptoms, defined by a score of 4 or more in the Breslau PTSD scale. It would be worthwhile to examine whether these variables are linked independently with the postnatal depressive symptoms or whether their effect is mediated through antenatal depressive symptoms. This could be investigated using mediation analysis which is traditionally used in the field of psychology and it is now increasingly used in epidemiology (Hicks & Tingley, 2011).

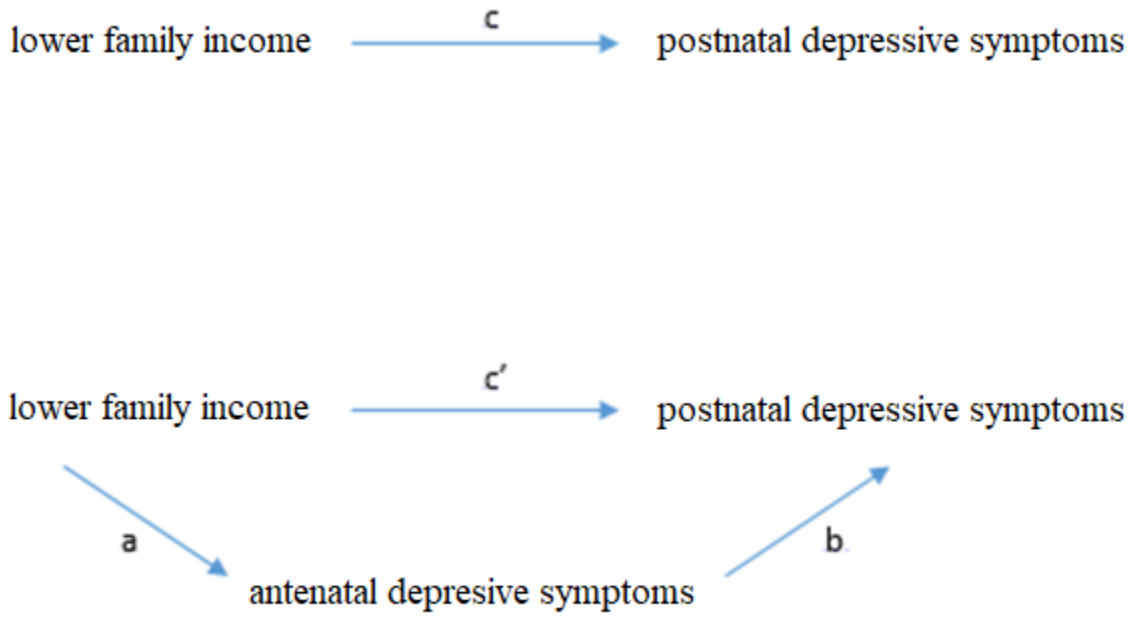
The goal of mediation analysis is to examine how a particular variable affects the association of two other variables. This variable is known as the mediator (M), or the intermediate variable, because it mediates the effect of the exposure/predictor (X) on the outcome (Y). According to Baron and Kenny (1986), as summarized in the website of David A. Kenny (Kenny, 2016), there are four criteria for mediation:

1. The predictor (X) and the outcome (Y) should be correlated (effect c).
2. The predictor (X) is also correlated with the mediator (M).
3. The mediator (M) affects the outcome (Y), after controlling for the effect of the predictor (X).
4. The effect of the predictor (X) on the outcome (Y) is zero (i.e. c=0), when controlling for the mediator (M).

If all the conditions above are satisfied then the suggested variable M is a mediator of the association between X and Y.

In our study, as indicated in Figure 6.1, the family income would be the predictor (X), antenatal depressive symptoms would be the mediator (M), and postnatal depressive symptoms would be the outcome (Y). According to the results of this thesis we know that criteria 1 and 2 are satisfied, i.e. a lower family income is associated with postnatal depressive symptoms (criterion 1) and that it is also correlated with antenatal depressive symptoms (criterion 2). In the near future, we will carry out the mediation analysis and examine whether antenatal depressive symptoms are in the causal pathway of lower family income and postnatal depressive symptoms. PTSD symptoms could also potentially be used as a predictor; however, PTSD symptoms were assessed at the same point as the EDS questionnaire for antenatal depressive symptoms which means that there is lack of temporality when looking at the antenatal depressive symptoms and PTSD symptoms.

Figure 6.1 – Mediation diagram



Another direction for future research would be to repeat a similar investigation among pregnant women in Cyprus. The knowledge and the skills obtained from this PhD work will be very useful when designing a study for the Cypriot population where there is limited research in the field of mental health, especially in the perinatal period. In addition, to the best of our knowledge, there is no study on antenatal depressive symptoms in Cyprus. This gap in literature can be filled with a primary study similar to TRACER conducted in Cyprus. Pregnant women who attend private and /or public clinics could be enrolled in this study in early pregnancy and similar to TRACER, a baseline questionnaire could be administered to obtain demographic information. Later in pregnancy, data will be collected using the EDS questionnaire. One of the limitations of TRACER was that there was no clinical diagnosis to confirm depression. Thus, based on the availability of resources, health professionals could be employed to provide a clinical diagnosis, following the EDS screening test. Women would also be followed after delivery and then, they would be administered the same questionnaire in order to assess postnatal depressive symptoms. Again, health professionals could be asked to confirm the depression status of those who screen positive. An estimate of the prevalence of depressive symptoms antenatally and postnatally could be computed, and risk factors of both outcomes could be identified. Since EPDS has been used extensively, we could then make comparisons with other studies. The results could be disseminated to the Ministry of Health in order to plan strategies to reduce the prevalence and the impact of these outcomes and, if required, establish mental health support clinics etc.

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Appendix

Tables and figures

Table 1 – Prevalence (%) of antenatal depressive symptoms among Kuwaitis and non-Kuwaitis, based on different cut-offs encountered in the literature.

EDS Cut-off	Kuwaitis	Non-Kuwaitis	p-value
≥10	21.3	19.9	0.48
≥12	14.0	13.9	0.94
≥13	11.2	11.4	0.89
≥15	8.5	7.0	0.26

Table 2 – Positive items in the EDS questionnaire and the corresponding frequencies.

Item: In the past 7 days I…	**Total**	**EDS<10**	**EDS≥10**
… I have been able to laugh and see the funny side of things			
As much as always	72.9	85.1	24.7
Somewhat less than usual	6.4	4.7	13.3
Much less than usual	18.1	9.5	52.0
Not at all	2.6	0.7	10.0
…I have looked forward with enjoyment to things			
As much as always	69.9	83.1	17.6
Somewhat less than usual	7.5	5.8	14.3
Much less than usual	19.2	10.5	53.6
Not at all	3.4	0.4	14.5

Table 3 – Negative items in the EDS questionnaire and the corresponding frequencies.

Item: In the past 7 days I…	**Total**	**EDS<10**	**EDS≥10**
…I have blamed myself unnecessarily when things went wrong			
Not at all	67.2	76.0	30.6
Not very often	13.4	15.4	15.3
Some of the time	15.0	7.8	43.6
Most of the time	2.4	0.4	10.5
…I have been anxious or worried for no good reason			
Not at all	67.4	77.5	27.8
Not very often	13.8	13.6	14.8
Some of the time	15.3	8.3	42.9
Most of the time	3.5	0.6	14.5
…I have felt scared or panicky for no good reason			
Not at all	80.6	89.2	46.7
Not very often	8.3	7.4	11.5
Some of the time	9.6	3.0	35.7
Most of the time	1.5	17.2	6.1
…Things have been overwhelming me			
Not at all	60.0	71.8	13.5
Not very often	15.4	14.9	17.4
Some of the time	19.6	11.9	50.0
Most of the time	5.0	1.4	19.1
…I have been so unhappy that I have had difficulty sleeping			
Not at all	68.9	81.8	18.1
Not very often	11.1	10.1	15.1
Some of the time	14.9	6.8	46.7
Most of the time	5.1	1.3	20.1

…I have felt sad or miserable			
Not at all	69.7	84.2	12.2
Not very often	11.9	9.9	19.9
Some of the time	15.7	5.8	54.9
Most of the time	2.7	0.1	13.0
…I have been so unhappy that I have been crying			
Not at all	70.0	83.9	15.3
Not very often	9.5	7.6	17.1
Some of the time	17.2	8.3	52.6
Most of the time	3.3	0.2	15.0
…The thought of harming myself has occurred to me			
Not at all	99.0	99.7	95.9
Not very often	0.4	0.1	1.8
Some of the time	0.5	0.2	1.8
Most of the time	0.1	0.0	0.5

Table 4 – Baseline characteristics and antenatal depressive symptoms - Frequencies and p-values obtained from Chi-square tests.

	EDS<10	EDS≥10	p-value
DEMOGRAPHIC CHARACTERISTICS			
Age group			
<25	399	84	0.34
25-30	584	155	
30-35	376	104	
>35	187	49	
Nationality			
Kuwaiti	387	105	0.48
Non- Kuwaiti	1159	287	
Employment status			
Employed	710	163	0.08
Housewife	662	190	
Unemployed	159	32	
Education			
Up to Middle/secondary	436	149	<0.01
Higher education	1095	236	
Household Income (KWD)			
<400	443	132	0.05
400-800	521	126	
800-1600	294	79	
≥1600	232	41	
PREGNANCY CHARACTERISTICS			
Trimester of EDS evaluation			
2nd	554	91	<0.01
3rd	966	293	
Parity			
0	531	108	0.01
≥1	992	276	
Pre-pregnancy BMI			
<18.5	34	9	0.90
18.5-25	664	162	
25-30	504	123	
≥30	322	87	
Clinic			
Private	269	67	0.23
Public	1147	302	
Other	130	23	

Table 5 – Mental and physical health indicators of antenatal depressive symptoms - Frequencies and p-values obtained from Chi-square tests.

	EDS<10	EDS≥10	p-value
RISKS BEFORE PREGNANCY			
Prior depression			
No	1503	363	<0.01
Yes	20	21	
Adverse outcomes in previous pregnancies			
No previous pregnancy	448	85	<0.01
No	487	119	
Yes	588	180	
Childhood emotional neglect			
Least neglected (score 5-7)	674	152	0.02
Moderately neglected (score 8-10)	404	92	
Most neglected (score 11-25)	468	148	
Traumatic Events			
0-1	601	115	<0.01
2-5	525	87	
6 or more	420	190	
PREGNANCY RELATED			
Pregnancy related anxiety			
No	1391	266	<0.01
Yes	155	126	
Perceived Stress Levels			
Lower (score 0-4)	647	38	<0.01
Moderate (score 5-7)	609	108	
Higher (score 8-16)	286	236	
PTSD symptoms			
No	1151	114	<0.01
Yes	395	278	
Mental Component Summary			
Poor	362	274	<0.01
Fair	568	92	
Good	616	26	
Physical Component Summary			
Poor	448	195	<0.01
Fair	549	108	
Good	549	89	
COPING DURING PREGNANCY			
Social Network			
Most integrated	109	27	<0.01
Moderately integrated	266	61	

Moderately isolated	920	198
Most isolated	235	99

Figure 1 – Receiver Operating Characteristic curve for the multivariate model of antenatal depressive symptoms (EDS≥10) with income, education, trimester, traumatic events, history of depression, pregnancy-related anxiety, perceived stress, PTSD symptoms, mental and physical quality of health,, which were obtained from forward selection.

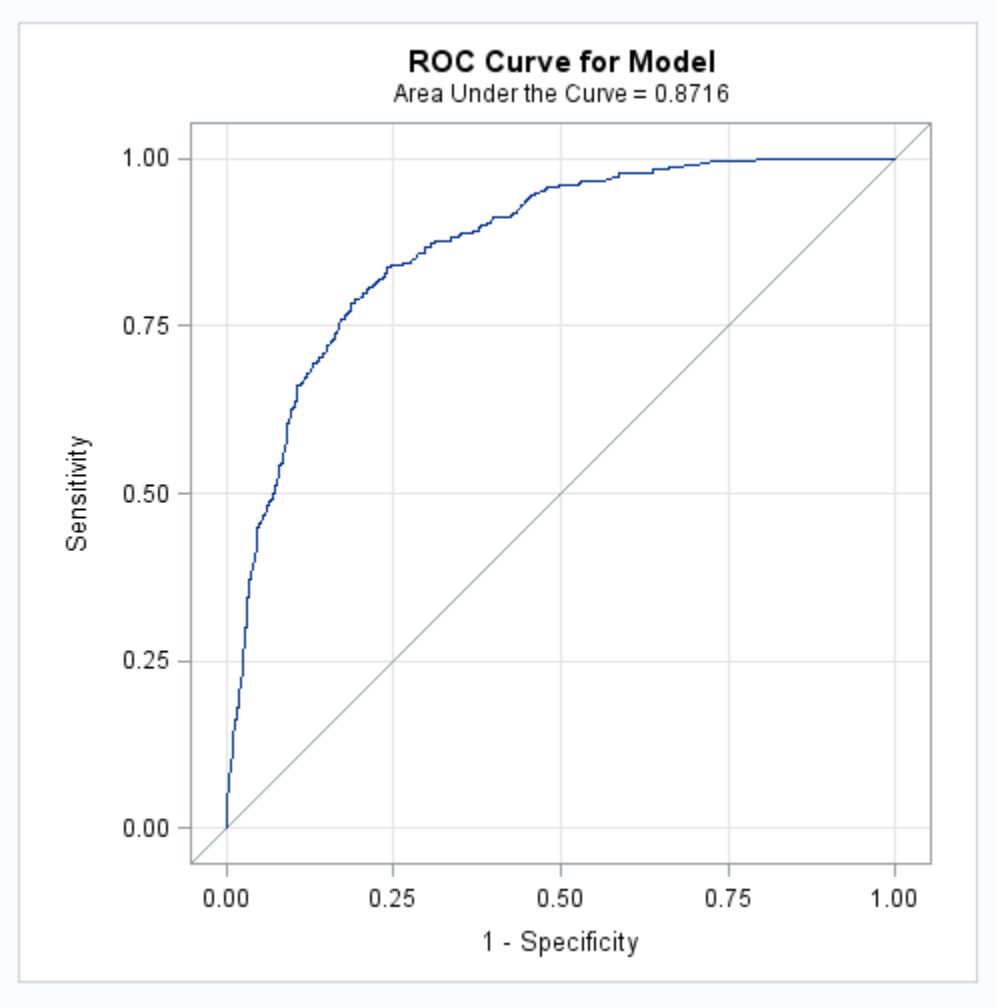

Table 6 – Baseline characteristics and PTB - Unadjusted ORs.

	OR	95% CI
DEMOGRAPHIC CHARACTERISTICS		
Age group		
<25	1.00	0.64-1.59
25-30	1.00	-
30-35	1.19	0.69-2.07
>35	0.95	0.60-1.51
Nationality		
Kuwaiti	1.00	-
Non- Kuwaiti	0.59	0.41-0.86
Employment status		
Employed	1.00	-
Housewife	0.96	0.66-1.38
Unemployed	0.68	0.34-1.36
Education		
Up to High School	1.06	0.73-1.54
Higher education	1.00	-
Household Income (KWD)		
<400	0.67	0.39-1.13
400-800	0.56	0.33-0.95
800-1600	0.80	0.46-1.40
≥1600	1.00	-
PREGNANCY CHARACTERISTICS		
Parity		
0	0.85	0.58-1.25
≥1	1.00	-
Pre-pregnancy BMI		
<18.5	1.66	0.57-4.84
18.5-25	1.00	-
25-30	1.54	1.03-2.31
≥30	1.20	0.74-1.94
In vitro fertilization		
No	1.00	-
Yes	4.65	2.28-9.47
Miscarriage in previous pregnancies		
No previous pregnancy	1.00	-
No miscarriage	1.18	0.75-1.87
At least one miscarriage	1.45	0.90-2.33
Preterm delivery in previous pregnancies		
No previous pregnancy	1.00	-
No preterm delivery	1.12	0.73-1.71
At least one preterm delivery	3.31	1.82-6.01
Gestational hypertension		
No	1.00	-
Yes	1.82	0.80-4.13

Gestational diabetes		
No	1.00	-
Yes	1.85	0.99-3.44
Sex of the baby		
Female	1.00	-
Male	1.06	0.74-1.51

Table 7 – Mental and physical health indicators and PTB - Unadjusted ORs.

	OR	95% CI
RISKS BEFORE PREGNANCY		
Traumatic Events		
0-1	1.00	-
2-5	0.57	0.36-0.89
6 or more	0.82	0.55-1.24
PREGNANCY RELATED		
Antenatal depressive symptoms (EDS score)		
<10	1.00	-
≥10	1.15	0.75-1.75
Pregnancy related anxiety		
No	1.00	-
Yes	1.40	0.89-2.22
Perceived Stress Levels		
Lower (0-4)	1.00	-
Moderate (5-7)	0.74	0.48-1.16
Higher (8-16)	1.41	0.92-2.15
PTSD symptoms		
No	1.00	-
Yes	0.88	0.60-1.28
Mental Component Summary		
Poor	1.30	0.85-1.98
Fair	0.90	0.57-1.41
Good	1.00	-
Physical Component Summary		
Poor	1.40	0.90-2.16
Fair	1.17	0.75-1.82
Good	1.00	-
COPING DURING PREGNANCY		
Social Network		
Most integrated	1.00	-
Moderately integrated	0.62	0.31-1.27
Moderately isolated	0.67	0.37-1.23
Most isolated	0.61	0.30-1.23

Table 8 – Adjusted ORs for the association of antenatal depressive symptoms (as a multinomial variable) and PTB. [The results were obtained from a multiple logistic regression model with the same variables used in the model shown in Table 4.3 in Chapter 4.]

	OR	**95% CI**
Antenatal depressive symptoms (EDS score)		
0-3	1.00	-
4-8	0.62	0.30-1.26
9-13	1.01	0.45-2.28
>13	0.96	0.37-2.50

Table 9 – Baseline characteristics and SGA - Unadjusted ORs.

	OR	95% CI
DEMOGRAPHIC CHARACTERISTICS		
Age group		
<25	1.26	0.80-1.97
25-30	1.00	-
30-35	0.76	0.46-1.27
>35	1.03	0.57-1.89
Nationality		
Kuwaiti	1.00	-
Non- Kuwaiti	1.11	0.72-1.72
Employment status		
Employed	1.00	-
Housewife	0.99	0.67-1.46
0.67-Unemployed	0.80	0.40-1.60
Education		
Up to High School	1.49	1.02-2.18
Higher education	1.00	-
Household Income (KWD)		
<400	2.04	1.09-3.81
400-800	1.05	0.55-2.03
800-1600	0.94	0.45-1.96
≥1600	1.00	-
PREGNANCY CHARACTERISTICS		
Parity		
0	1.20	0.82-1.76
≥1	1.00	-
Pre-pregnancy BMI		
<18.5	1.23	0.42-3.57
18.5-25	1.00	-
25-30	0.75	0.48-1.15
≥30	0.61	0.36-1.03
In vitro fertilization		
No		
Yes	1.03	0.31-3.40
Miscarriage in previous pregnancies		
No previous pregnancy	1.00	-
No miscarriage	0.72	0.46-1.13
At least one miscarriage	1.01	0.64-1.60
Gestational hypertension		
No	1.00	-
Yes	1.58	0.66-3.77
Sex of the baby		
Female	1.00	-
Male	0.57	0.39-0.83

Table 10 – Mental and physical health indicators and SGA - Unadjusted ORs.

	OR	95% CI
RISKS BEFORE PREGNANCY		
Traumatic Events		
0-1	1.00	-
2-5	0.97	0.61-1.54
6 or more	1.23	0.79-1.91
PREGNANCY RELATED		
Antenatal depressive symptoms (EDS score)		
<10	1.00	-
≥10	1.39	0.91-2.14
Pregnancy related anxiety		
No	1.00	-
Yes	1.07	0.64-1.80
Perceived Stress Levels		
Lower (0-4)	1.00	-
Moderate (5-7)	1.33	0.85-2.07
Higher (8-16)	1.35	0.84-2.19
PTSD symptoms		
No	1.00	-
Yes	1.20	0.82-1.75
Mental Component Summary		
Poor	1.23	0.76-1.98
Fair	1.52	0.96-2.40
Good	1.00	-
Physical Component Summary		
Poor	0.84	0.55-1.29
Fair	0.56	0.35-0.90
Good	1.00	-
COPING DURING PREGNANCY		
Social Network		
Most integrated	1.00	-
Moderately integrated	1.94	0.72-5.24
Moderately isolated	1.79	0.71-4.53
Most isolated	2.16	0.81-5.81

Table 11 – Adjusted ORs for the association of antenatal depressive symptoms (as a multinomial variable) and SGA. [The results were obtained from a multiple logistic regression model with the same variables used in the model shown in Table 4.6 in Chapter 4.]

	OR	**95%CI**
Antenatal depressive symptoms (EDS score)		
0-3	1.00	-
4-8	1.13	0.60-2.13
9-13	2.04	0.95-4.40
>13	1.33	0.48-3.64

Table 12 – Baseline characteristics and LGA - Unadjusted ORs.

	OR	95%CI
Overall		
DEMOGRAPHIC CHARACTERISTICS		
Age group		
<25	0.67	0.49-0.92
25-30	1.00	-
30-35	1.11	0.83-1.48
>35	1.56	1.10-2.21
Nationality		
Kuwaiti	1.00	-
Non- Kuwaiti	1.39	1.05-1.83
Employment status		
Employed	1.00	-
Housewife	0.97	0.77-1.23
Unemployed	0.48	0.30-0.77
Education		
Up to High School	0.94	0.74-1.21
Higher education	1.00	-
Household Income (KWD)		
<400	0.89	0.60-1.31
400-800	1.35	0.93-1.96
800-1600	1.40	0.94-2.09
≥1600	1.00	-
PREGNANCY CHARACTERISTICS		
Parity		
0	0.54	0.42-0.71
≥1	1.00	-
Pre-pregnancy BMI		
<18.5	0.23	0.05-0.95
18.5-25	1.00	-
25-30	1.45	1.11-1.89
≥30	1.58	1.17-2.12
Gestational diabetes		
No	1.00	-
Yes	1.69	1.12-2.55
Sex of the baby		
Female	1.00	-
Male	2.02	1.59-2.56

Table 13 – Mental and physical health indicators and LGA - Unadjusted ORs.

	OR	95%CI
RISKS BEFORE PREGNANCY		
Traumatic Events		
0-1	1.00	-
2-5	0.97	0.74-1.29
6 or more	1.10	0.83-1.44
PREGNANCY RELATED		
Antenatal depressive symptoms (EDS score)		
<10	1.00	-
≥10	1.12	0.84-1.48
Pregnancy related anxiety		
No	1.00	-
Yes	1.21	0.89-1.66
Perceived Stress Levels		
Lower (0-4)	1.00	-
Moderate (5-7)	0.86	0.66-1.13
Higher (8-16)	1.07	0.80-1.42
PTSD symptoms		
No	1.00	-
Yes	0.84	0.66-1.07
Mental Component Summary		
Poor	0.96	0.73-1.27
Fair	0.92	0.70-1.22
Good	1.00	-
Physical Component Summary		
Poor	0.85	0.64-1.12
Fair	1.10	0.84-1.45
Good	1.00	-
COPING DURING PREGNANCY		
Social Network		
Most integrated	1.00	-
Moderately integrated	1.05	0.64-1.73
Moderately isolated	0.90	0.58-1.40
Most isolated	0.99	0.60-1.63

Table 14 – Adjusted ORs for the association of antenatal depressive symptoms (as a multinomial variable) and LGA. [The results were obtained from a multiple logistic regression model with the same variables used in the model shown in Table 4.9 in Chapter 4.]

	OR	**95%CI**
Antenatal depressive symptoms (EDS score)		
0-3	1.00	-
4-8	1.04	0.72-1.51
9-13	1.13	0.70-1.84
>13	0.93	0.51-1.70

Table 15 – Multiple linear regression for birth weight.

	β	Lower 95%CI	Upper 95%CI
DEMOGRAPHIC CHARACTERISTICS			
Age group			
<25	-25.49	-92.87	41.89
25-30			
30-35	-21.15	-84.27	41.98
>35	10.40	-72.97	93.77
Nationality			
Kuwaiti			
Non- Kuwaiti	156.06	77.21	234.91
Employment status			
Employed			
Housewife	19.54	-40.50	79.57
Unemployed	-24.14	-111.87	63.59
Education			
Up to High School	42.38	-16.02	100.78
Higher education			
Household Income (KWD)			
<400	-91.14	-192.08	9.79
400-800	-29.28	-122.52	63.96
800-1600	35.20	-48.86	119.26
≥1600			
PREGNANCY CHARACTERISTICS			
Parity			
0	7.00	-112.14	126.14
≥1			
Pre-pregnancy BMI			
<18.5	-85.14	-244.15	73.87
18.5-25			
25-30	65.80	9.27	122.32
≥30	92.47	24.77	160.18
In vitro fertilization			
No			
Yes	22.29	-145.12	189.70
Miscarriage in previous pregnancies			
No previous pregnancy			
No miscarriage	45.84	-84.31	176.00
At least one miscarriage	17.65	-99.13	134.43
Gestational hypertension			
No			
Yes	-15.30	-130.27	99.66
Gestational diabetes			
No			
Yes	67.78	-18.31	153.86

Sex of the baby			
Female			
Male	136.21	88.32	184.09
Gestational age			
Weeks	105.65	90.52	120.78
PREGNANCY RELATED			
Antenatal depressive symptoms			
EDS score	-0.78	-7.01	5.46
Pregnancy related anxiety			
No			
Yes	34.89	-42.32	112.10
Perceived Stress Levels			
Lower (0-4)			
Moderate (5-7)	0.93	-58.26	60.12
Higher (8-16)	20.63	-54.11	95.36
PTSD symptoms			
No			
Yes	-37.60	-97.63	22.43
Mental Component Summary			
Poor	-25.95	-102.05	50.15
Fair	-33.61	-93.88	26.65
Good			
Physical Component Summary			
Poor	6.17	-57.73	70.07
Fair	18.00	-40.52	76.52
Good			
COPING DURING PREGNANCY			
Social Network			
Most integrated			
Moderately integrated	30.10	-73.26	133.46
Moderately isolated	-22.36	-115.34	70.61
Most isolated	10.17	-97.11	117.45

Table 16 – Multiple linear regression for gestational age.

	β	Lower 95%CI	Upper 95%CI
DEMOGRAPHIC CHARACTERISTICS			
Age group			
<25	0.05	-0.19	0.29
25-30			
30-35	-0.16	-0.39	0.07
>35	-0.21	-0.51	0.09
Nationality			
Kuwaiti			
Non- Kuwaiti	0.27	-0.02	0.56
Employment status			
Employed			
Housewife	0.09	-0.13	0.30
Unemployed	0.06	-0.26	0.38
Education			
Up to High School	-0.09	-0.30	0.12
Higher education			
Household Income (KWD)			
<400	0.06	-0.31	0.42
400-800	0.19	-0.15	0.53
800-1600	0.13	-0.18	0.43
≥1600			
PREGNANCY CHARACTERISTICS			
Parity			
0			
≥1	0.19	-0.22	0.60
Pre-pregnancy BMI			
<18.5	-0.15	-0.72	0.42
18.5-25			
25-30	-0.05	-0.25	0.16
≥30	0.13	-0.12	0.37
In vitro fertilization			
No			
Yes	-0.57	-1.18	0.04
Preterm delivery in previous pregnancies			
No previous pregnancy			
No preterm delivery	-0.27	-0.70	0.16
At least one preterm delivery	-1.08	-1.65	-0.51
Gestational hypertension			
No			
Yes	-0.56	-0.98	-0.14
Gestational diabetes			
No			
Yes	-0.44	-0.75	-0.12

RISKS BEFORE PREGNANCY			
Traumatic Events			
0-1			
2-5	0.02	-0.20	0.23
6 or more	0.08	-0.14	0.31
PREGNANCY RELATED			
Antenatal depressive symptoms			
EDS score	0.00	-0.02	0.02
Pregnancy related anxiety			
No			
Yes	-0.22	-0.50	0.06
Perceived Stress Levels			
Lower (0-4)			
Moderate (5-7)	-0.06	-0.28	0.15
Higher (8-16)	-0.35	-0.62	-0.08
PTSD symptoms			
No			
Yes	0.20	-0.02	0.42
Mental Component Summary			
Poor	0.09	-0.18	0.37
Fair	0.16	-0.06	0.38
Good			
Physical Component Summary			
Poor	-0.08	-0.32	0.15
Fair	-0.01	-0.22	0.21
Good			
COPING DURING PREGNANCY			
Social Network			
Most integrated			
Moderately integrated	0.12	-0.26	0.49
Moderately isolated	0.06	-0.27	0.40
Most isolated	-0.10	-0.49	0.29

Table 17 – Positive items in the EPDS questionnaire and the corresponding frequencies.

Item: In the past 7 days I…	**Total sample (%)**	**EDS<10 (%)**	**EDS≥10 (%)**
… I have been able to laugh and see the funny side of things			
As much as always	74.6	81.5	22.6
Somewhat less than usual	19.6	16.1	45.9
Much less than usual	4.7	1.8	26.4
Not at all	1.1	0.6	5.0
…I have looked forward with enjoyment to things			
As much as always	76.4	83.2	25.2
Somewhat less than usual	19.5	15.4	49.7
Much less than usual	2.9	0.7	19.5
Not at all	1.2	0.7	5.6

Table 18 – Negative items in the EPDS questionnaire and the corresponding frequencies.

Item: In the past 7 days I…	**Total sample (%)**	**EDS<10 (%)**	**EDS≥10 (%)**
…I have blamed myself unnecessarily when things went wrong			
Not at all	67.1	72.8	24.5
Not very often	17.5	17.9	14.5
Some of the time	12.5	8.1	45.3
Most of the time	2.9	1.2	15.7
…I have been anxious or worried for no good reason			
Not at all	70.8	76.9	24.5
Not very often	15.2	15.8	10.7
Some of the time	12.0	7.1	49.1
Most of the time	2.0	0.2	15.7
…I have felt scared or panicky for no good reason			
Not at all	85.0	90.0	47.8
Not very often	7.9	7.0	14.5
Some of the time	6.0	2.8	29.5
Most of the time	1.1	0.2	8.2
…Things have been overwhelming me			
Not at all	58.9	66.1	5.0
Not very often	14.7	15.4	8.8
Some of the time	21.1	16.7	54.7
Most of the time	5.2	1.8	31.5
…I have been so unhappy that I have had difficulty sleeping			
Not at all	82.6	90.7	22.0
Not very often	8.3	6.8	19.5
Some of the time	6.7	2.3	39.6

Most of the time	2.4	0.2	18.9
…I have felt sad or miserable			
Not at all	75.2	84.5	5.7
Not very often	11.0	9.8	19.5
Some of the time	11.3	5.6	54.1
Most of the time	2.5	0.1	20.7
…I have been so unhappy that I have been crying			
Not at all	79.3	88.2	12.6
Not very often	6.9	6.0	13.8
Some of the time	11.4	5.7	54.1
Most of the time	2.4	0.1	19.5
…The thought of harming myself has occurred to me			
Not at all	99.2	99.7	95.6
Not very often	0.4	0.2	2.5
Some of the time	0.2	0.2	0.6
Most of the time	0.2	0.0	1.3

Table 19 – Baseline characteristics and postnatal depressive symptoms - Frequencies and p-values obtained from Chi-square tests.

	EPDS<10	EPDS≥10	p-value
DEMOGRAPHIC CHARACTERISTICS			
Age group			
<25	277	43	0.59
25-30	455	62	
30-35	303	36	
>35	164	18	
Nationality			
Kuwaiti	295	49	0.10
Non- Kuwaiti	904	110	
Employment status			
Employed	548	67	0.66
Housewife	538	75	
Unemployed	105	16	
Education			
Up to Middle/secondary	369	57	0.20
Higher education	822	101	
Household Income (KWD)			
<400	344	60	0.04
400-800	402	45	
800-1600	236	35	
≥1600	178	15	
PREGNANCY, BIRTH AND POSTNATAL CHARACTERISTICS			
Parity			
0	383	42	0.17
≥1	808	115	
Pre-pregnancy BMI			
<18.5	27	4	0.42
18.5-25	513	58	
25-30	383	60	
≥30	264	36	
Preterm delivery			
No	1091	136	0.02
Yes	81	19	
SGA			
No	1081	137	0.38
Yes	78	13	
LGA			

No	889	115	0.99
Yes	270	35	
Sex of the baby			
Girl	579	61	0.02
Boy	620	98	

Table 20 – Other risk factors of postnatal depressive symptoms - Frequencies and p-values obtained from Chi-square tests.

	EPDS<10	EPDS≥10	p-value
RISKS BEFORE PREGNANCY			
Childhood emotional neglect			
Least neglected (5-7)	495	70	0.02
Moderately neglected (8-10)	321	27	
Most neglected (11-25)	383	62	
Traumatic Events			
0-1	451	42	<0.0
2-5	376	36	
6 or more	372	81	
Prior depression			
No	1170	149	<0.01
Yes	21	8	
PREGNANCY RELATED			
Antenatal depressive symptoms			
No	1020	70	<0.01
Yes	179	89	
Pregnancy related anxiety			
No	1059	114	<0.01
Yes	140	45	
Perceived Stress Levels			
Lower (0-4)	445	28	<0.01
Moderate (5-7)	469	55	
Higher (8-16)	278	75	
PTSD symptoms			
No	827	57	<0.01
Yes	372	102	
Mental Component Summary			
Poor	358	85	<0.01
Fair	432	43	
Good	409	31	
Physical Component Summary			
Poor	368	72	<0.01
Fair	418	45	
Good	413	42	
COPING DURING PREGNANCY			
Social Network			
Most integrated	98	10	<0.01
Moderately integrated	201	23	

Moderately isolated	706	79
Most isolated	186	46

Table 21 – Comparison of baseline characteristics among women who answered the EPDS questionnaire and those who did not - Frequencies and p-values obtained from Chi-square tests.

	Did not Answer EPDS n=580	Answered the EPDS n=1358	p-value
DEMOGRAPHIC CHARACTERISTICS			
Age group			
<25	163	320	0.03*
25-30	222	517	
30-35	141	339	
>35	54	182	
Nationality			
Kuwaiti	148	344	0.93
Non- Kuwaiti	432	1014	
Employment status			
Employed	258	615	0.06
Housewife	239	613	
Unemployed	70	121	
Education			
Up to Middle/secondary	159	426	0.13
Higher education	408	923	
Household Income (KWD)			
<400	171	404	0.69
400-800	200	447	
800-1600	102	271	
≥1600	80	193	
PREGNANCY, BIRTH AND POSTNATAL CHARACTERISTICS			
Parity			
0	214	425	<0.01*
≥1	345	923	
Pre-pregnancy BMI			
<18.5	12	31	0.49
18.5-25	255	571	
25-30	184	443	
≥30	109	300	
Preterm delivery			
No	404	1227	0.88
Yes	34	100	
SGA			
No	365	1218	0.67
Yes	30	91	

LGA			
No	318	1004	0.11
Yes	77	305	
Sex of the baby			
Girl	208	640	0.63
Boy	246	718	

Table 22 – Comparison of other characteristics among women who answered the EPDS questionnaire and those who did not - Frequencies and p-values obtained from Chi-square tests.

	Did not answer the EPDS	Answered the EPDS	p-value
RISKS BEFORE PREGNANCY			
Childhood emotional neglect			
Least neglected (5-7)	261	565	0.29
Moderately neglected (8-10)	148	348	
Most neglected (11-25)	171	445	
Traumatic Events			
0-1	223	493	0.02*
2-5	200	412	
6 or more	157	453	
Prior depression			
No	547	1319	0.99
Yes	12	29	
PREGNANCY RELATED			
Antenatal depressive symptoms			
No	456	1090	0.41
Yes	124	268	
Pregnancy related anxiety			
No	484	1173	0.09
Yes	96	185	
Perceived Stress Levels			
Lower (0-4)	212	473	0.09
Moderate (5-7)	193	524	
Higher (8-16)	169	353	
PTSD symptoms			
No	381	884	0.80
Yes	199	474	
Mental Component Summary			
Poor	186	443	0.04*
Fair	175	475	
Good	219	440	
Physical Component Summary			
Poor	202	440	0.42
Fair	200	463	
Good	178	455	
COPING DURING PREGNANCY			
Social Network			

Most integrated	28	108	0.11
Moderately integrated	103	224	
Moderately isolated	333	785	
Most isolated	102	232	

TRACER Questionnaires used in the analysis

Childhood emotional neglect

I felt like there was someone in my family who wanted me to be a success.

0. Never
1. Rarely
2. Some times
3. Often
4. Very often

There was someone in my family who helped me feel that I was important or special.

1. Never
2. Rarely
3. Some times
4. Often
5. Very often

My family was a source of strength and support.

1. Never
2. Rarely
3. Some times
4. Often
5. Very often

People in my family felt close to each other.

1. Never
2. Rarely
3. Some times
4. Often
5. Very often

Someone in my family believed in me.

1. Never
2. Rarely
3. Some times
4. Often
5. Very often

Traumatic events

WAR EXPERIENCES TO DATE

Have you ever had any war-related experience such as experiencing revolutions, political conflict, or actual war-related events in any country in which you have lived? This includes occupation or civil war in a country where you have lived. Examples include the Lebanese civil war, the Russia - Afghanistan war and the Iraqi invasion and occupation of Kuwait in 1990/91.

0- No

1- Yes – first hand

2- Yes –second hand

Which war(s) did you experience (please list all that apply starting from the most recent experience)?

	Name of War	Country	Month and Year exposure began	Month and Year exposure ended
B2a.				
B2b.				
B2c.				
B2d.				

STRESS <u>BEFORE</u> ANY WAR EXPERIENCE (OR IF <u>NO WAR EXPERIENCE IN</u> THEIR LIFETIME):

Been in a major fire, flood, or other natural disaster that resulted in significant loss of personal property, serious injury to yourself or to someone **<u>VERY</u>** close to you, the death of someone **<u>VERY</u>** close to you, or the fear of your own death.

0-Never

1-Once or twice

2-More than twice

Been in a major automobile, boat, motorcycle, plane, train, or industrial accident that resulted in significant loss of personal property, serious injury to yourself or to someone **<u>VERY</u>** close to you, the death of someone **<u>VERY</u>** close to you, or the fear of your own death.

0-Never

1-Once or twice

2-More than twice

Witnessed someone with whom you were **<u>VERY</u>** close (such as a parent, brother or sister, caretaker, or someone close to you) being killed, or being injured by another person so severely as to result in marks, bruises, burns, blood, broken bones, or broken teeth.

0-Never
1-Once or twice
2-More than twice

Witnessed someone with whom you were not so close being killed, or being injured by another person so severely as to result in marks, bruises, burns, blood, broken bones, or broken teeth.

0-Never
1-Once or twice
2-More than twice

Witnessed someone with whom you were **VERY** close deliberately attack one of your family members so severely as to result in marks, bruises, blood, broken bones, or broken teeth.

0-Never
1-Once or twice
2-More than twice

You were deliberately attacked by someone with whom you were **VERY** close so severely as to result in marks, bruises, blood, broken bones, or broken teeth.

0-Never
1-Once or twice
2-More than twice

You were deliberately attacked by someone with whom you were not close so severely as to result in marks, bruises, blood, broken bones, or broken teeth.

0-Never
1-Once or twice
2-More than twice

You were made to have some form of sexual contact, such as touching or penetration, by someone with whom you were **VERY** close.

0-Never
1-Once or twice
2-More than twice

You were made to have some form of sexual contact, such as touching or penetration, by someone with whom you were NOT close

0-Never
1-Once or twice
2-More than twice

You were emotionally or psychologically mistreated over a significant period of time by someone with whom you were **VERY** close.

0-Never
1-Once or twice

2-More than twice

Experienced the death of one of your own children.

0-Never
1-Once or twice
2-More than twice

Experienced a seriously traumatic event not already covered in any of these questions.

What were these other events? **[SPECIFY]**_____

0-Never
1-Once or twice
2-More than twice

In any of the events you noted experiencing in Questions C1 – C12 above, were you seriously injured, or did you fear you might be seriously injured or might die?

0- No
1-Yes

In any of the events you noted experiencing in Questions C1 – C12 above, did you witness a situation in which someone was seriously injured or killed, or witness a situation in which you feared someone else would be seriously injured or killed?

0- No
1-Yes

EXPERIENCES <u>DURING</u> YOUR FIRST WAR EXPERIENCE OTHER THAN OR IN ADDITION TO KUWAIT INVASION/OCCUPATION EXPERIENCE

Were you in the country where the war was taking place at any time during that entire period?

0. No
1. Yes
99. Don't remember or don't KNOW

When you were in [the country] during that time period, did you ever go into hiding?

0. No
1. Yes
99. Don't remember or don't KNOW

During the time of the war did you **<u>PERSONALLY WITNESS</u>** any of the following?

Serious threat to the health of a family member or someone very close to you because of lack of medical services?

0-Never
1-Once or twice

2-More than twice

The arrest of a family member or someone very close to you?

0-Never
1-Once or twice
2-More than twice

The execution of a family member or someone very close to you?

0-Never
1-Once or twice
2-More than twice

The rape of a family member or someone very close to you?

0-Never
1-Once or twice
2-More than twice

The shooting, assault, or other injury to a family member or someone very close to you? Include injury due to mines or ammunition?

0-Never
1-Once or twice
2-More than twice

The torture of a family member or someone very close to you?

0-Never
1-Once or twice
2-More than twice

Loss or destruction of the home of someone very close to you?

0-Never
1-Once or twice
2-More than twice

The search of the home of someone close to you?

0-Never
1-Once or twice
2-More than twice

The execution of someone <u>not</u> close to you?

0-Never
1-Once or twice
2-More than twice

The rape of someone not close to you?

0-Never1-Once or twice
2-More than twice

The shooting, assault, or other injury to someone not close to you? Include injury due to mines or ammunition

0-Never
1-Once or twice
2-More than twice

The torture of someone not close to you?

0-Never
1-Once or twice
2-More than twice

Loss or destruction of the home of someone not close to you?

0-Never
1-Once or twice
2-More than twice

The search of the home of someone not close to you?

0-Never
1-Once or twice
2-More than twice

In any of the events you noted experiencing in D3 above, were you seriously injured, or did you fear you might be seriously injured or might die?

0- No
1- Yes

In any of the events you noted experiencing in D3 above, did you witness a situation in which someone was seriously injured or killed, or witness a situation in which you feared someone else would be seriously injured or killed?

0- No
1.Yes

During the time of in the _____ ***(name of war experience)***, did any of the following actually **HAPPEN TO YOU** personally?

You suffered lack of medical service that was a serious threat to your health?

0-Never
1-Once or twice
2-More than twice

You were physically assaulted at a checkpoint?

0-Never
1-Once or twice

2-More than twice

You were assaulted while participating in a demonstration?
0-Never
1-Once or twice
2-More than twice

You were assaulted somewhere else?
0-Never
1-Once or twice
2-More than twice

You were tortured?
0-Never
1-Once or twice
2-More than twice

You were sexually assaulted or raped?
0-Never
1-Once or twice
2-More than twice

You were arrested?
0-Never
1-Once or twice
2-More than twice

Your house was searched?
0-Never
1-Once or twice
2-More than twice

Your home was lost or destroyed?
0-Never
1-Once or twice
2-More than twice

You experienced lack of financial support to such extent that it was life threatening?
0-Never
1-Once or twice
2-More than twice

In any of the events you noted experiencing in **D20 - D30** above, were you seriously injured, or did you fear you might be seriously injured or might die?
0 - No
1- Yes

In any of the events you noted experiencing in **D20 - D30** above, did you witness a situation in which someone was seriously injured or killed, or witness a situation in which you feared someone else would be seriously injured or killed?

0 - No
1 - Yes

During the time when **YOU WERE UNDER ARREST**, did any of these happen to you?

Physically attacked or injured?

0-Never
1-Once or twice
2-More than twice

Tortured?

0-Never
1-Once or twice
2-More than twice

Sexually assaulted or raped?

0-Never
1-Once or twice
2-More than twice

Threats to family or friends?

0- Never
1-Once or twice
2-More than twice

Forced to witness physical attacks or torture of others?

0- Never
1-Once or twice
2-More than twice

In any of the events you noted experiencing in D9 above, were you seriously injured, or did you fear you might be seriously injured or might die?

0 - No
1 - Yes

In any of the events you noted experiencing in D9 above, did you
witness a situation in which someone was seriously injured or killed, or witness a situation in which you feared someone else would be seriously injured or killed?

0 - No
1 - Yes

During the ***(name of war experience)*** time, did you experience any of the following fears?

There would be a lack of food?

0 - No
1 - Yes

Lack of water?

0 - No
1 - Yes

Lack of medicine?

0 - No
1 - Yes

Chemical exposure?

0 - No
1 - Yes

Danger when going outside of your home, for example, shopping?

0 - No
1 - Yes

Danger when going to the mosque?

0 - No
1 - Yes

Air bombing?

0 - No
1 - Yes

Danger at check points?

0 - No
1 - Yes

A family member of someone else close to you to be arrested during the war?

0 - No
1 - Yes

During the **TIME OF WAR**, did you experience any of the following fears?

A search, looting, or destruction of your house?

0 - No
1 - Yes

Possible loss of life?

0 - No

1 - Yes

Danger for your family?

0 - No
1 - Yes

A family member or someone close to you was being sought by military forces?

0 - No
1 - Yes

Injury from mines?

0 - No
1 - Yes

Loss of the country's freedom?

0 - No
1 - Yes

Loss of your mind?

0 - No
1 - Yes

The population composition would change?

0 - No
1 - Yes

You would be forced to emigrate or would be unable to return to your home?

0 - No
1 - Yes

Problems in the future?

0 - No
1 - Yes

Losing your national identity?

0 - No
1 - Yes

That a family member or someone else close to you might be arrested during the _____(name of war experience)?

0 - No
1 - Yes

EXPERIENCES DURING KUWAIT INVASION/OCCUPATION EXPERIENCE

Now think about the time period **during the Iraqi invasion and occupation of** Kuwait. These next questions are about your experience during this time period.

Were you in Kuwait at any time during that entire period?

0. No
1. Yes
99. Don't remember or don't know

When you were in Kuwait during that time period, did you ever go into hiding?

0. No
1. Yes
99. Don't remember or don't know

Why did you go into hiding? Was it:

	YES	NO
Fear of someone in the family being detained?	1	0
Fear for your family's personal safety?	1	0
Fear for the life of someone in your family?	1	0
Some other reason?	1	0

What was the reason? **[SPECIFY]**

_____

During the time of the war did you **PERSONALLY WITNESS** any of the following?

Serious threat to the health of a family member or someone very close to you because of lack of medical services?

0-Never
1-Once or twice
2-More than twice

The arrest of a family member or someone very close to you?

0-Never
1-Once or twice
2-More than twice

The execution of a family member or someone very close to you?

0-Never
1-Once or twice

2-More than twice

The rape of a family member or someone very close to you?

0-Never
1-Once or twice
2-More than twice

The shooting, assault, or other injury to a family member or someone very close to you? Include injury due to mines or ammunition.

0-Never
1-Once or twice
2-More than twice

The torture of a family member or someone very close to you?

0-Never
1-Once or twice
2-More than twice

Loss or destruction of the home of someone very close to you?

0-Never
1-Once or twice
2-More than twice

The search of the home of someone close to you?

0-Never
1-Once or twice
2-More than twice

The execution of someone **NOT** close to you?

0-Never
1-Once or twice
2-More than twice

The shooting, assault, or other injury to someone **NOT** close to you? Include injury due to mines or ammunition

0-Never
1-Once or twice
2-More than twice

The torture of someone **NOT** close to you?

0-Never
1-Once or twice
2-More than twice

Loss or destruction of the home of someone **NOT** close to you?

0-Never
1-Once or twice
2-More than twice

The search of the home of someone **NOT** close to you?
0-Never
1-Once or twice
2-More than twice

Anything else? **[SPECIFY:]** _____

0-Never
1-Once or twice
2-More than twice

In any of the events you noted experiencing in E3 above, were you seriously injured, or did you fear you might be seriously injured or might die?
0- No
1- Yes

In any of the events you noted experiencing in E3 above, did you witness a situation in which someone was seriously injured or killed, or witness a situation in which you feared someone else would be seriously injured or killed?
0- No
1- Yes

During the time of the Kuwait invasion/occupation, did any of the following actually **HAPPEN TO YOU** personally?

You suffered lack of medical service that was a serious threat to your health?
0-Never
1-Once or twice
2-More than twice

You were physically assaulted at a checkpoint?
0-Never
1-Once or twice
2-More than twice

You were assaulted while participating in a demonstration?
0-Never
1-Once or twice
2-More than twice

You were assaulted somewhere else?
0-Never
1-Once or twice
2-More than twice

You were tortured?

0-Never
1-Once or twice
2-More than twice

You were sexually assaulted or raped?

0-Never
1-Once or twice
2-More than twice

You were arrested?

0-Never
1-Once or twice
2-More than twice

Your house was searched?

0-Never
1-Once or twice
2-More than twice

Your home was lost or destroyed?

0-Never
1-Once or twice
2-More than twice

You experienced lack of financial support to such extent that it was life threatening?

0-Never
1-Once or twice
2-More than twice

Anything else?

[SPECIFY:]_____

In any of the events you noted experiencing in E6 above, were you seriously injured, or did you fear you might be seriously injured or might die?

0 - No
1 - Yes

In any of the events you noted experiencing in E6 above, did you witness a situation in which someone was seriously injured or killed, or witness a situation in which you feared someone else would be seriously injured or killed?

0 - No
1 - Yes

During the time when **YOU WERE UNDER ARREST**, did any of these happen to you?

Physically attacked or injured?
0-Never
1-Once or twice
2-More than twice

Tortured?
0-Never
1-Once or twice
2-More than twice

Sexually assaulted or raped?
0-Never
1-Once or twice
2-More than twice

Threats to family or friends?0-Never
1-Once or twice
2-More than twice

Forced to witness physical attacks or torture of others?
0-Never
1-Once or twice
2-More than twice

Anything else? **[SPECIFY]** _____

0-Never
1-Once or twice
2-More than twice

In any of the events you noted experiencing in E9 above, were you seriously injured, or did you fear you might be seriously injured or might die?
0 - No
1 - Yes

In any of the events you noted experiencing in E9 above, did you witness a situation in which someone was seriously injured or killed, or witness a situation in which you feared someone else would be seriously injured or killed?
0 - No
1 - Yes

During the **TIME OF WAR**, did you experience any of the following fears?

There would be a lack of food?

0 - No
1 - Yes

Lack of water?
0 - No
1 - Yes

Lack of medicine?
0 - No
1 - Yes

Chemical exposure?
0 - No
1 - Yes

Danger when going outside of your home, for example, shopping?
0 - No
1 - Yes

Danger when going to the mosque?
0 - No
1 - Yes

Air bombing?
0 - No
1 - Yes

Danger at check points?
0 - No
1 - Yes

A family member of someone else close to you to be arrested during the war?
0 - No
1 - Yes

START HERE FOR THOSE WHO WERE OUT OF KUWAIT.

During the **TIME OF WAR**, did you experience any of the following fears?

A search, looting, or destruction of your house?
0 - No
1 - Yes

Possible loss of life?
0 - No
1 - Yes

Danger for your family?

0 - No
1 - Yes

A family member or someone close to you was being sought by military forces?
0 - No
1 - Yes

Injury from mines?
0 - No
1 - Yes

Loss of the country's freedom?
0 - No
1 - Yes

Loss of your mind?
0 - No
1 - Yes

The population composition would change?
0 - No
1 - Yes

You would be forced to emigrate to emigrate or would be unable to return to your home?
0 - No
1 - Yes

Problems in the future?
0 - No
1 – Yes

Losing your national identity?
0 - No
1 - Yes

That a family member or someone else close to you might be arrested during the ***(name of war experience)***?
0 - No
1 - Yes

You or someone very close to you experienced serious health problems as a result of oil fires?
0-Never
1-Once or twice
2-More than twice

You or someone very close to you experienced significant loss of personal property because of the oil fires?

0-Never
1-Once or twice
2-More than twice

You or someone very close to you was seriously injured by mines or ammunitions left behind after the occupation?

0-Never
1-Once or twice
2-More than twice

Been in a major fire, flood, or other natural disaster that resulted in significant loss of personal property, serious injury to yourself or to someone very close to you, the death of someone very close to you, or the fear of your own death.

0-Never
1-Once or twice
2-More than twice

Been in a major automobile, boat, motorcycle, plane, train, or industrial accident that resulted in significant loss of personal property, serious injury to yourself or to someone very close to you, the death of someone very close to you, or the fear of your own death.

0-Never
1-Once or twice
2-More than twice

Witnessed someone with whom you were very close (such as a parent, brother or sister, caretaker, or someone close to you) being killed, or being injured by another person so severely as to result in marks, bruises, burns, blood, broken bones, or broken teeth.

0-Never
1-Once or twice
2-More than twice

Witnessed someone with whom you were not so close being killed, or being injured by another person so severely as to result in marks, bruises, burns, blood, broken bones, or broken teeth.

0-Never
1-Once or twice
2-More than twice

Witnessed someone with whom you were very close deliberately attack a family member so severely as to result in marks, bruises, blood, broken bones, or broken teeth.

0-Never
1-Once or twice
2-More than twice

You were deliberately attacked by someone with whom you were very close so severely as to result in marks, bruises, blood, broken bones, or broken teeth.

0-Never
1-Once or twice
2-More than twice

You were deliberately attacked by someone with whom you were not close so severely as to result in marks, bruises, blood, broken bones, or broken teeth.

0-Never
1-Once or twice
2-More than twice

You were made to have some form of sexual contact, such as touching or penetration, by someone with whom you were very close.

0-Never
1-Once or twice
2-More than twice

You were made to have some form of sexual contact, such as touching or penetration, by someone with whom you were not close.

0-Never
1-Once or twice
2-More than twice

You were emotionally or psychologically mistreated over a significant period of time by someone with whom you were very close.

0-Never
1-Once or twice
2-More than twice

Experienced the death of one of your own children.

0-Never
1-Once or twice
2-More than twice

Experienced a seriously traumatic event not already covered in any of these questions.

[SPECIFY:]_____

0-Never
1-Once or twice
2-More than twice

In any of the events you noted experiencing in *Questions* above, were you seriously injured, or did you fear you might be seriously injured or might die?

0 - No
1 - Yes

In any of the events you noted experiencing in Questions above, did you witness a situation in which someone was seriously injured or killed, or witness a situation in which you feared someone else would be seriously injured or killed?

0 - No
1 - Yes

Pregnancy related anxiety

I am concerned or worried about how the baby is growing and developing inside me.

0. Not At All
1. Somewhat
2. Moderately
3. Very Much

I am concerned or worried about having a hard or difficult delivery.

0. Not At All
1. Somewhat
2. Moderately
3. Very Much

I am worried that the baby could be abnormal.

0. Not At All
1. Somewhat
2. Moderately
3. Very Much

I am afraid that I will be harmed during delivery.

0. Not At All
1. Somewhat
2. Moderately
3. Very Much

I am concerned or worried about losing the baby.

0. Not At All
1. Somewhat
2. Moderately
3. Very Much

I have a lot of fear regarding the health of my baby.

0. Not At All
1. Somewhat
2. Moderately
3. Very Much

I am concerned or worried about developing medical problems during my pregnancy.

0. Not At All
1. Somewhat
2. Moderately
3. Very Much

Perceived stress

In the **LAST MONTH**, how often have you felt difficulties were piling up so high that you could not overcome them?

0. Never
1. Almost Never
2. Some-times
3. Fairly Often
4. Very Often

In the **LAST MONTH**, how often have you felt confident about your ability to handle your personal problems?

0. Never
1. Almost Never
2. Some-times
3. Fairly Often
4. Very Often

In the **LAST MONTH**, how often have you felt that things were going your way?

0. Never
1. Almost Never
2. Some-times
3. Fairly Often
4. Very Often

In the **LAST MONTH**, how often have you felt that you were unable to control the important things in your life?

0. Never
1. Almost Never
2. Some-times
3. Fairly Often
4. Very Often

PTSD symptoms

Have there EVER been times when you tried to stay away from activities or situations that reminded you of any of your war experiences? (If no war experiences, ask them to recall the worst stressor they identified experiencing).

0. No
1. Yes
99. Don't know

Have there ever been times when you were less interested in important activities that once gave you pleasure, such as sports, hobbies, or social activities?

0. No
1. Yes
99. Don't know

Have there **EVER** been times when you felt distant or cut off from those around you?

0. No
1. Yes
99. Don't know

Have there **EVER** been times when you felt emotionally numb, or had trouble experiencing feelings such as love or happiness?

0. No
1. Yes
99. Don't know

Have there **EVER** been times when you felt that there was no need to plan for the future, that somehow your future would be cut short? Don't count events or illnesses that were life-threatening.

0. No
1. Yes
99. Don't know

Have there **EVER** been times when you had problems falling or staying asleep?

0. No
1. Yes
99. Don't know

Have there **EVER** been times when you experienced strong startle reactions to loud, unexpected noises (e.g., car backfires, fireworks, doorslams, etc.) or things that you saw (e.g., movement in the corner of your eye)?

0. No
1. Yes
99. Don't know

Mental and physical health component summary scales (SF36v2)

The questions in this section ask for your views about your health. Please answer every question. Some questions may look like others, but each one is different.

In general, would you say your health is

1. Excellent
2. Very good
3. Good
4. Fair
5. Poor

COMPARED TO ONE YEAR AGO, how would you rate your health in general **NOW**?

1. Much better now than one year ago
2. Somewhat better now than one year ago
3. About the same
4. Somewhat worse now than one year ago
5. Much worse now than one year ago

The following items are about activities you might do during a typical day. Does **YOUR HEALTH NOW LIMIT YOU** in these activities? If so, how much?

VIGOROUS ACTIVITIES, such as running, lifting heavy objects, participating in strenuous sports

1. Yes, Limited a Lot
2. Yes, Limited a Little
3. No, Not limited at All

MODERATE ACTIVITIES, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf

1. Yes, Limited a Lot
2. Yes, Limited a Little
3. No, Not limited at All

Lifting or carrying groceries

1. Yes, Limited a Lot
2. Yes, Limited a Little
3. No, Not limited at All

Climbing **SEVERAL** flights of stairs

1. Yes, Limited a Lot
2. Yes, Limited a Little
3. No, Not limited at All

Climbing **one** flight of stairs

1. Yes, Limited a Lot
2. Yes, Limited a Little
3. No, Not limited at All

Bending, kneeling, or stooping

1. Yes, Limited a Lot
2. Yes, Limited a Little
3. No, Not limited at All

Walking **more than a mile (1 Mile = ~1.6 Kilometer)**

1. Yes, Limited a Lot
2. Yes, Limited a Little
3. No, Not limited at All

Walking **several hundred yards or several meters (Yard= 0.9 Meter)**

1. Yes, Limited a Lot
2. Yes, Limited a Little
3. No, Not limited at All

Walking **one hundred yards (or one hundred meters)**

1. Yes, Limited a Lot
2. Yes, Limited a Little
3. No, Not limited at All

Bathing or dressing yourself

1. Yes, Limited a Lot
2. Yes, Limited a Little
3. No, Not limited at All

During the **PAST 4 WEEKS**, have you had any of the following problems with your work or other regular daily activities **AS A RESULT OF YOUR PHYSICAL HEALTH**?

Cut down the **AMOUNT OF TIME** you spent on work or other activities

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time

ACCOMPLISHED LESS than you would like

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time

5. None of the time

Were limited in the **KIND** of work or other activities

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time

Had **DIFFICULTY** performing the work or other activities (for example, it took extra effort)

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time

During the **past 4 weeks,** have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

Cut down the **amount of time** you spent on work or other activities

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time

ACCOMPLISHED LESS than you would like

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time

Didn't do work or other activities as **CAREFULLY** as usual

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time

During the **PAST 4 WEEKS,** to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

1. Not at all
2. Slightly
3. Moderately
4. Quite a bit
5. Extremely

How much **BODILY** pain have you had during the **PAST 4 WEEKS**?

1. None
2. Very mild
3. Mild
4. Moderate
5. Severe
6. Very severe

During the **PAST 4 WEEKS,** how much did **PAIN** interfere with your normal work (including both work outside the home and housework)?

1. Not at all
2. A little bit
3. Moderately
4. Quite a bit
5. Extremely

These questions are about how you feel and how things have been with you **DURING THE PAST 4 WEEKS**. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the **PAST 4 WEEKS** . . .

Did you feel full of life?

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time

Have you been very nervous?

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time

Have you felt so down in the dumps that nothing could cheer you up?

1. All of the time
2. Most of the time

3. Some of the time
4. A little of the time
5. None of the time

Have you felt calm and peaceful?

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time

Did you have a lot of energy?

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time

Have you felt downhearted and depressed?

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time

Did you feel worn out?

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time

Have you been happy?

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time

Did you feel tired?

1. All of the time
2. Most of the time
3. Some of the time

4. A little of the time
5. None of the time

During the **PAST 4 WEEKS,** how much ofthe time has your **PHYSICAL HEALTH OR EMOTIONAL PROBLEMS** interfered with your social activities (like visiting with friends, relatives, etc.)?

0. None of the time
1. A little of the time
2. Some of the time
3. Most of the time
4. All of the time

How **TRUE** or **FALSE** is each of the following statements for you.

I seem to get sick a little easier than other people

0. Definitely False
1. Mostly False
2. Mostly True
3. Definitely True
99. Don't Know

I am as healthy as anybody I know

0. Definitely False
1. Mostly False
2. Mostly True
3. Definitely True
99. Don't Know

I expect my health to get worse

0. Definitely False
1. Mostly False
2. Mostly True
3. Definitely True
99. Don't Know

My health is excellent

0. Definitely False
1. Mostly False
2. Mostly True
3. Definitely True
99. Don't Know

Social network

Do you go to religious services at least once a week?

0. No
1. Yes
99. Don't know

How often do you participate in any groups such as a social or work group, religious group (other than attending religious services), self-help group, charity, public service or community group? Would you say …

0. Never
1. Once a month

How many close relatives or friends do you have whom you see at least once a month? By "close relatives", I mean people that you feel emotionally close to.

0. None
1. One
2. Two
3. More than 2