

**The Effect of Chronic Stress on Birth Outcome and Infant Cognitive
Development in the Gaza Strip**

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SPECIFIC AIMS

The Gaza Strip has one of the highest population densities in the world, and is an area that has been under perpetual conflict since Israel's independence in 1948. Recently, since Israel's disengagement from Gaza in 2005, the area has been under siege, and has received only basic financial aid and humanitarian support. For this reason, standard of living for the already impoverished population has further decreased, while poverty and unemployment have increased, while hunger and malnutrition remain uncommon. The current distinctly severe state of crisis comes on top of a prolonged period of instability, violence and minimal economic growth essentially since 1948. It is expected that such a population would have a high prevalence of mental health disorders, and specifically high stress and trauma. Maternal stress and trauma are predicted to affect birth outcome, postnatal cognitive development and infant well-being. While there have been some studies that explored trauma in children and adults in Gaza, there are no studies on the effect of maternal and prenatal stress on infant development. The unique combination of widespread exposure to conflict, high fertility rate, relative access of the population to health care and lack of basic hunger and malnutrition compared to other conflict regions, make it a model population for the study of the impact of maternal stress on infant cognitive development.

Our research will fill the gap in global health research regarding the nature of prenatal stress and mental health in the Gaza Strip and its effect on birth outcome and infant cognitive development. It will also create the foundation for development and delivery of targeted interventions aimed to ameliorate the damage while political solutions are being sought.

In this study, we will address the hypothesis that high prenatal stress (ranging from chronic stress to extreme post-traumatic stress disorder) will have a detrimental effect on birth outcome and infant cognitive development up to age 3.

We will address the hypothesis through the following specific aims:

- a.) To determine the prevalence of chronic stress and mental health disorders in pregnant women from Gaza.
- b.) To assess the effect of chronic prenatal stress on birth outcome and infant cognitive development. Factors that will be considered that may alleviate this effect will be income level, level of social support, and access to health care.
- c.) To evaluate the effect of varying degrees of severity of chronic maternal stress on the attachment style of the infant.

Completion of these specific aims will greatly enhance our understanding of impairments in infant development frequently observed in areas of conflict, and will allow for the design of new and effective interventions aimed to protect infant health in areas of sociopolitical conflict and will thus lead to a transformation in global health initiatives.

BACKGROUND AND SIGNIFICANCE

During the past few decades, the Palestinian population has been exposed to ongoing traumatic events, which include imprisonment, torture and human rights violation, house demolitions, land and property confiscation, high unemployment, and the deep humiliation and degradation caused by Israeli military oppression, and the instability of the situation. The situation in the Gaza Strip is unique within the Palestinian situation, as it is not only one of the most heavily populated regions in the world, but for the past few years it has been under siege, and is thus characterized by immense poverty, misery and low quality of life.

History of the Gaza Strip

In order to understand the nature of the conflict and of the Gazan population, it is essential to understand the recent history of the region. Gaza is a strip of land on the Southeast end of the Mediterranean, bordering Egypt to the South and Israel to the North and East. The entire region of Gaza is very small, 25 mile long and 6 mile wide (Figure 1). Following Israel's independence in 1948, the Gaza Strip came under Egyptian control. The region became densely populated (the population of the strip tripled) as it absorbed thousands of Palestinian refugees displaced from the newly formed Israeli state. Following the 1967 war, Israel captured the Gaza Strip from Egypt, and allowed for Jewish settlement in the region. Violence and poverty in the Gaza refugee camps escalated following Israel's invasion of Lebanon in 1982 and sparked the first Intifada of 1987. In 1993, following the Oslo accords, Palestinians were granted autonomy; this lasted until 2000, when the second Intifada began. During this time the border was tightly patrolled by Israeli military. In 2005, Israel unilaterally dismantled its military facilities and withdrew its soldiers and settlers from the region. However, Israel still has great control over access to the

Gaza Strip. Since Hamas formed a government in March 2006, the entire Palestinian people have been put under an economic siege by Israel with the active support of the United States. This involved Israel tightening the closure of its borders with Gaza, limiting fuel supplies and the free movement of people. The siege has been condemned by International human rights organizations; yet Israel insists on its importance for its national security as it curbs rockets fired by Palestinian militants. In this context it is important to note that residents of Gaza have been exposed to continued violence as part of the fighting between Israel and the Palestinians: Over 5000 Palestinians have been killed in the past decade, close to 50% of them non-combatants, among them 990 minors and children. Between 2002 and 2004, 1300 houses were demolished for military purposes and in 2008 in operation “Cast lead” the Israeli army demolished 3,500 homes, leaving homeless more than 20,000 people (B’TZelem reports).

The results of the occupation, the years of violence and the siege have been catastrophic to the Palestinian people. In light of the siege, not only has the situation gotten drastically worse, but there have been fewer scientific studies in Gaza. It must be noted that studies on this population were very few as resources and scientific centers are limited. The blockade only worsened the situation, resulting in an utter lack of psychological studies in the region in recent years. It seems clear that—especially in a region of such great conflict and misery—research studies investigating the mental health of the population, and specifically the effect of the chronic stress of daily life, must be established. The purpose of such studies must be to provide interventions and preventive care to the people of Gaza.¹

¹ General history gathered from “Operation Cast Lead” by B’Tselem, and from the CIA world fact book.

Demographics

Gaza has one of the highest population densities in the world, standing at about 20,000 people/square mile (Ajluni et al. 2010). Its population is 1.66 million people. More than 79% of the population is registered as refugees (Afana et al. 2002), from the 1948 and 1967 Arab-Israeli wars. About 55% of the population lives in eight crowded camps and 45% lives in villages and towns (Thabet et al. 1998). 44% of the population consists of children ages 0-14 years. The median age of the population is 17.7. The average annual growth of the population is 3.2%, and is the 7th highest growth rate in the world, with a fertility rate of 4.74 children born per women. A 2009 estimate suggests that 70% of the population lives below the poverty line.² Because of the combination of a high growth rate and high level of poverty, the population is at increased risk for mental health disorders and general health issues. Furthermore, due to the high fertility rate of an average of 4-5 children born per woman, it is a model population for the study of the effects of living under conflict on birth outcome and infant cognitive development.

Infant Mortality in Gaza

As there are few studies on birth outcome and on infant development in general in the target population, we must rely on the few studies on infant mortality that exist. According to Pedersen, infant and child mortality in the West Bank and Gaza has steadily decreased since 1967 as fertility has remained exceptionally high (2000). Pedersen examined the possible effect of four variables on infant mortality patterns. These variables are: Birth interval, the time elapsed between births; maternal education; consanguineous marriage, marriage between close biological kin; and the period in which the infant was born. Pedersen shows that short birth spacing and type of marriage were more likely to result in infant mortality than level of education; however a higher level of education of women was correlated with lower infant mortality. While Pedersen's

² Demographics and statistics gathered from CIA world fact book

study does not discuss the effects of mental disorders on infant outcome and development, its emphasis on two variables that might have a significant effect on infant mortality could be helpful for our study. Furthermore, the data used in the study was retrospective (from a demographic survey from 1995), and therefore it is possible that important factors, such as the mother's health and psychiatric history, were disregarded.

Mental Health and Trauma

Several studies have investigated the effect of military conflict and trauma on children in Palestine, however none have yet to examine the impact of poor prenatal mental health and trauma on birth outcome and infant cognitive development. In order to understand the unique psychology of growing up and living under conflict, a close review of these articles is necessary.

Thabet and Vostanis investigated the relation between social disadvantage and anxiety disorders among children, age 9-13, living in the Gaza Strip (1998). They found that 21.5% of children scored above the cut off for anxiety disorders, and that children with potential anxiety disorders were more likely to live in an inner city area or in one of the camps, and therefore to be from a lower income background. In a study by Kashani and Orvaschel from 1990, a similar pattern of anxiety symptoms and disorders was found in children in the U.S. (reviewed by Thabet & Vostanis 1998). While this seems to put the harsh reality of the Gaza Strip in question, the article cannot be relied on heavily as it is from 1998, a time in which the situation was starkly different.

Qouata, Punamaki & El Sarraj provide a very useful elaborate review of developmental research among Palestinians living in Gaza (2008), with a specific focus on how exposure to traumatic events associates with children's mental health and cognitive, emotional and social development. Highly traumatic events are those that shatter our fundamental "childish" beliefs

that the world is a safe and fair place, that people are benevolent, and that one is worthy of protection (Janoff-Bulman, 1989; reviewed by Qouta et al. 2008). Traumatic events unique to the Gaza military situation include curfews, destruction of homes and private property and sonic booms. These events affect someone living in the Gaza Strip from birth, as sonic booms severely deteriorate children's sleep and can cause uncontrollable fears among babies and children. The review emphasizes that life threat, violence and losses not only form a risk for increased psychological distress but may affect children's cognitive development. According to a 2001 study by Qouta, Punamaki and El Sarraj, children exposed to severe trauma had concentration problems and low cognitive capacity and had difficulties processing new information and retaining old knowledge (reviewed by Qouta, Punamaki & El Sarraj 2008). Lastly, the review revealed that family and other intimate relationships were crucial for the child's resilience. The level of resilience did not depend on the severity of the traumatic events but rather on the type of attachment style. Children with secure attachment styles were more resilient than children with insecure attachment styles (Salo, Punamaki, & Qouta 2005, reviewed by Qouta et al. 2008). For this reason, the attachment style of the infant to its mother (or caretaker) is of utmost importance. The effect of prenatal chronic stress on attachment style requires investigation.

An epidemiological study by Afana et al. assessed the prevalence of PTSD among patients attending primary health care centers in Gaza (2002). The study found that the overall prevalence of PTSD in primary health care patients was 29%. It was higher among females than males, and among less educated patients than highly educated patients.

Smith et al. investigated the rate of detection and treatment of minor and major depressive disorder, panic disorder and PTSD among pregnant women receiving prenatal care at public-sector obstetric clinics in the U.S (2004). The study found that only 26% of patients who

screened positive for a psychiatric illness were recognized as having a mood or anxiety disorder by their health care provider in public-sector Obstetric clinics, with the detection of depression being lower than panic disorder or PTSD. Since approximately 21% of women experience a mood disorder and 30% experience anxiety disorder at some point in their lives (Smith et al. 2004), the detection of these disorders during pregnancy is critical as their impact on birth outcome and infant development may be detrimental. This study is significant for our research as it reveals that there is a low rate of screening of psychological disorders in such an advanced country, and can only lead us to infer that the detection rate of such disorders in Gaza are even lower.

Chronic Stress

Recent studies have found that chronic prenatal stress may have significant impacts on infant cognitive development. Studies in rodents and nonhuman primates suggest that prenatal stress can influence the developing fetus, and lead to motor and cognitive delays as well as impaired adaptation to stressful situations. The hypothalamic-pituitary-adrenal (HPA) axis may play a significant role in mediating these effects (Buitelaar et al. 2003). A study by Buitelaar et al. investigated the effect of prenatal stress on the developmental outcome of human infants in a prospective design (2003). The study found that pregnancy-specific anxiety in mid-pregnancy predicted lower mental and motor developmental scores at 8 months, and that morning values of cortisol in late pregnancy were negatively related to both mental and motor development at 3 months and motor development alone at 8 months. The study concluded that high prenatal stress may be one of the determinants of temperamental variation and developmental delay in infants as well as a risk factor for developing psychopathology later in life. This study reveals the need for a thorough investigation of the effects of chronic stress on birth outcome and infant cognitive

development in the Gaza strip. As the Gaza Strip is a region of intense conflict, mental distress and chronic stress are part of the lives of many women. Prenatal stress has been linked to low birth weight and preterm delivery (Lobel 1994).

As chronic stress is associated with a high prevalence of depression and anxiety, it is likely that the level of depression and anxiety is high among women in the Gaza Strip. The effects of maternal depression and anxiety on infant development are not fully understood, however, studies have evinced that maternal depressive symptoms may interfere with infant cognitive and socio-emotional skills between the age 2 and 5 years—a critical developmental period in which the child’s sense of autonomy and independence greatly expands and develops. As depressed mothers may have an increased difficulty in supporting their child’s cognitive and socio-emotional growth at this crucial developmental period (Feldman & Eidelman 2009), it is necessary to further investigate the effects of high mental distress on infant development in order to facilitate the development of effective interventions that would curtail the negative impact of high maternal stress on infant social emotional and cognitive development.



Figure 1: Map of Israel. The Gaza Strip is encircled by a dotted line. The region, only 25 mile long and 6 mile wide has a population of 1.66 million people.

RESEARCH DESIGN AND METHODS

An observational cohort study will be employed, in which 2000 pregnant women from Gaza will be followed up from early pregnancy until age 3 of the infant.

Rationale

An observational cohort design is best suited for our study as the study seeks to evaluate the effect of chronic stress on birth outcome and infant development. The advantage of using this design is that it will help to determine risk factors for poor birth outcome and delayed cognitive infant development as it is a longitudinal observation of mothers through time. The collection of data at set intervals will reduce recall error and similar issues that arise with a retrospective design. Furthermore, the cohort design is most efficient for the study of a wide range of variables that may affect birth outcome and infant cognitive development.

Inclusion Criteria

2000 healthy pregnant women ages 20-30, in the 8th - 20th week of pregnancy, who were born and raised in the Gaza Strip. Participants will be randomly recruited through the Gaza Community Mental Health Programme (GCMHP), as well as through public health clinics.

Exclusion Criteria

Women with chronic illness, who have a family history of neurodevelopmental disabilities, or who are on psychiatric drugs will be excluded from the study.

Outcome Measures

- Measures for Pregnant women.
 - A structured questionnaire that assesses the participant's psychiatric history as well as a standard health questionnaire (SHQ) will be administered to determine participant eligibility for the study.

- *Informed Consent.* Before participating in the study, participants must sign an informed consent form indicating their consent to participate in the study and forego with the study protocol. If participants are unable to sign their name, a family member or licensed medical personnel may sign the form for them in their presence and with their consent.
- *Demographic Questionnaire.* Basic information such as date of birth, employment, level of education, average household income, # of children, type of marriage (consanguineous or not), place of residence, and place of birth will be collected. Administered upon onset of study participation.
- *General Health Questionnaire (GHQ).* Has high reliability coefficients and is simple to administer. Provides a good assessment of psychological well-being. It measures mental health problems including depression, anxiety, somatic symptoms and social withdrawal (Jackson 2007). Administered upon onset of study participation.
- *Primary Care Evaluation of Mental Disorders (PRIME-MD).* In addition to the GHQ, the PRIME-MD will enable possible diagnosis of DSM VI disorders. Administered upon onset of study participation.
- *PTSD module from the Mini International Neuropsychiatric Interview (MINI).* Considered the gold standard for identification of PTSD (Sheehan D et al 1996, reviewed by Smith et al. 2004). To be administered upon onset of study participation.
- *Daily Stress Inventory* – Non pregnancy-specific stress assessment. The DSI yields an intensity measure, with higher scores indicating higher perceived stress

(Dipietro et al. 2006). While this inventory was not intended for the type of stress women in conflict areas might experience, when compared to average results in non-conflict areas, it may provide a general image of the stress experienced by women in Gaza. To be administered at the beginning of the study, and every 6 months thereafter.

- Measures for Infants.

- *Birth Outcome.* To assess birth outcome birthweight, newborn gestational age and heart rate will be recorded, as well as any birth complications.
- *Bayley Scale of Infant Development II (BSID).* The BSID will be used as it is the most widely used and validated assessment of infant development (Dipietro et al. 2006). Testing will be carried out by a certified psychologist. To be administered every 6 months from birth to age 3.
- *Infant Behavioral Record (IBR).* Assesses orientation/engagement, emotional regulation and motor quality. To be administered along with the BSID every 6 months. (Dipietro et al. 2006)
- *Mother-Infant Observation.* As the strange situation is ideal for assessing attachment would be too complicated to administer regularly, we will rely on psychological observation and assessment of mother-infant interaction at age 2. This is clearly problematic, as mothers may behave differently with their children in a public setting, yet it seems to be the most efficient available measure of infant attachment.

Project Timetable

2011-2012: Research design reviewed and finalized.

2012-2014: Research Center and psychological facility built in Gaza.

2014-2016: Recruitment of 2000 pregnant women, start of the study.

2017-2020: End of study, data analysis begins.

Statistical Approach

All data will be collected and entered into a statistical database to be analyzed using ANOVA and regression analysis. Statistical significance will be determined at $p < 0.05$.

PREDICTED RESULTS

We predict that the level of the effect of stress on birth outcome and infant cognitive development will be positively correlated with participants' income level, level of education, employment and place of residence (camps vs. small towns). That is, adverse birth outcomes will be most prevalent among low-income, uneducated women who are from one of Gaza's camps. In effect, these factors (income, level of education, etc.) are predicted to correlate strongly with level of stress, post-traumatic stress disorder and the presence of other mental health disorders. We predict that high level of chronic stress along with the presence of extreme PTSD will have the most adverse effect on birth outcome. Infants born to mothers with high chronic stress and PTSD who had healthy birth outcomes are expected to display cognitive developmental delays by age 1. We predict that chronic stress along with other minor mental disorders (such as minor depression) will not have such a strong effect on birth outcome and infant development. Lastly, the level of chronic stresses as well the presence of PTSD or major depression will impact the attachment style of the infant to the mother. The presence of PTSD or major depression is

predicted to have a stronger adverse effect on the mother-infant relationship than any other psychological factor.

One of the limitations of the study is a general limitation of the cohort design, which is the difficulty of keeping close contact with participants and maintaining active participation in the study throughout the study period. This is a particular difficulty of our study, as it aims to follow such a large number of participants. Another limitation of the study is the lack of an efficient and valid assessment of stress for conflict areas. The Daily Stress Inventory (Dipietro 2002) does not seem to be an adequate measure of stress for the women of the Gaza Strip. Future studies about the nature of stress in the Gaza Strip that would lead to the development of a valid measure of stress are necessary. Furthermore, the study's measure of infant attachment style may be ineffective and too complicated to administer. A more suitable and simple measure of infant attachment style would be required for the study to effectively evaluate the effect of chronic prenatal stress on infant attachment.

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