Principal Investigator: Dr. Aladdin Choudhury
Trainee Investigator (if any): Hosne Ara Begum

Title of Study: Adolescent Pregnancy

Outcome (Pilot).

Source of Population: NA
(a) Ill subjects Yes No
(b) Non-ill subjects Yes No
(c) Minors or persons under guardianship Yes No

Does the study involve: NA
(a) Physical risks to the subjects Yes No
(b) Social risks Yes No
(c) Psychological risks to subjects Yes No
(d) Discomfort to subjects Yes No
(e) Invasion of privacy Yes No
(f) Disclosure of information damaging to subject or others Yes No

Use of records, (hospital, medical, death, birth or other) Yes No
Use of fetal tissue or abortus Yes No
Use of organs or body fluids Yes No

Subjects clearly informed about:
(a) Nature and purposes of study Yes No
(b) Procedures to be followed including alternatives used Yes No
(c) Physical risks Yes No
(d) Sensitive questions Yes No
(e) Benefits to be derived Yes No
(f) Right to refuse to participate or to withdraw from study Yes No
(g) Confidential handling of data Yes No
(h) Compensation & or treatment where there are risks or privacy is involved in any particular procedure Yes No

5. Will signed consent form be required:
(a) From subjects Yes No
(b) From parent or guardian (if subjects are minors) Yes No NA

6. Will precautions be taken to protect anonymity of subjects Yes No

7. Check documents being submitted herewith to Committee:

 Umbrella proposal - Initially submit an overview (all other requirements will be submitted with individual studies).

 Protocol (Required)

 Abstract Summary (Required)

 Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw (Required)

 Informed consent form for subjects

 Informed consent form for parent or guardian

 Procedure for maintaining confidentiality

 Questionnaire or interview schedule

 If the final instrument is not completed prior to review, the following information should be included in the abstract summary:

 The areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy.

 Examples of the type of specific questions to be asked in the sensitive areas.

 An indication as to when the questionnaire will be presented to the Ctte for review.

 To obtain approval of the Ethical Review Committee for any changes in the rights and welfare of subjects before making such change.

 Principal Investigator: [Signature] AUG 18 1985
 Trainee Investigator: [Signature]
SECTION I: RESEARCH PROTOCOL

1. Title: Adolescent Pregnancy Outcome (Pilot)

2. Principal Investigator: Alauddin Chowdhury

3. Co-Investigator: Hosne Ara Begum

4. Starting Date: Sep. 1, 1985

5. Completion Date: Feb. 28, 1986

6. Total Cost: $5000

7. Associate Director: [Signature]

8. Computer Operation Manager: [Signature]

Abstract Summary: This study will look at the effect of Menarche to conception interval on outcome of pregnancies such as fetal deaths and infant mortality. This study will not require any data collections and use the existing data from different sources.

9. Review:
   (a) Ethical
   (b) RRC: Not applicable
   (c) Director
CONFIDENTIALITY STATEMENT

The study involves use of collected data only. Consent was obtained at the time of original data collection.

Data will be analysed and published in aggregate and there is no possibility of identifying individuals.

The study will use the Matlab census and DSS records.
OBJECTIVES

This study will address whether the length of time between menarche and conception affects the probability of a live birth, and infant mortality while controlling for age of menarche, socio-economic factors, season of conception, and maternal age at conception. This study will also look at the phenomenon of subsequent pregnancy outcome.

Introduction

An important unresolved issue for both developed and developing countries, is whether the association seen between adolescent pregnancies and poor outcomes of pregnancy (high fetal and infant mortality) is due only to socioeconomic factors, or whether some biological compromise occurs due to the competing growth needs of mother and fetus. This is especially important in populations where chronic malnutrition may alter the patterns of growth and development observed in North American and Western European girls.

Well nourished girls demonstrate a well established pattern of skeletal growth characterised by menarche occurring shortly after the peak in height acceleration followed by a smaller amount of growth after menarche. In comparison, undernourished girls show a greater increase in skeletal maturation following menarche (Dreizen, 1967; Kulin, et al., 1982). Variation in skeletal maturation is controlled by the rate of epiphyseal growth and closure of the epiphyses. Malcolm (1979) has shown that malnutrition leads to slower growth of the epiphyseal centers as evidenced
by the effects on heights in slow growing populations. Chronic under-nutrition slows height velocity during childhood and adolescence, and prolongs the period of growth (Frisancho et al, 1983; Malcolm, 1979). Although the growth spurt in height peaks before first menarche linear growth continues for about 4 years after menarche in most well-nourished girls. This period may be longer and more important for undernourished girls. Frisancho (1978) found that undernourished populations have a 10% longer growth period and a 10% reduction in adult stature compared to U.S. girls.

Since growth and age at menarche are delayed by poor nutritional status, and the period of post-menarcheal growth is extended, then malnourished women who become pregnant soon after menarche may be at risk for poor pregnancy outcomes because of the competing growth needs of the mother and the fetus (Frisancho, 1978; Malcolm, 1979; Maesye, 1981; Duenhoelter, 1975; Carey et al, 1983; Frisancho et al, 1983; Kulin et al, 1982; Zlatnik and Burmeister, 1979). Competition for nutrients may cause intra-uterine growth retardation, or premature termination of growth of the mother.

Several studies have illustrated that adolescents exhibit risks more important, as in some populations, marriage and childbearing closely follow menarche. This may be at least partially compensated for by an extended period of adolescent subfecundity, but the evidence for this is conflicting (Foster et al, 1984).
Erkan et al (1971) demonstrates that post-menarcheal age is more important than chronological age in terms of obstetric risks for young women. Results of his study indicate that physiologically immature women experienced a two times greater risk of low birth weight, regardless of chronological age. Immaturity of the pelvis and birth canal is of concern in pregnant adolescents, mainly because of its effect on birth weight and pregnancy complications. Several studies show an increased proportion of contracted pelvises among adolescents less than 15 years of age, compared to 15-19 years olds and women in their twenties (Ellison, 1982; Kaltreider, 1963; Battaglia, 1963; Duenhoeuter, 1975). Moreover, current anthropological research shows that pelvic size is significantly smaller at menarche than at maturity (Moerman, 1981; Moerman, 1982).

Few longitudinal studies on growth patterns in relationship to age at menarche and pregnancy outcome are available. There is a need for more extensive information regarding the effects of adolescent pregnancy in chronically undernourished populations. The premature cessation of skeletal growth due to rising levels of estrogen during pregnancy may have two important effects on birth outcome. First, there is a positive association between maternal height and infant birthweight. Second, if growth of the long bones is compressed by pregnancy (resulting in shorter adult stature), then other bones - the pelvis in particular - may be affected as well. It is important to note that both of these consequences are irreversible. Therefore, the increased risks for maternal and infant morbidity and mortality will persist throughout the reproductive period.
METHODS OF PROCEDURE

The sample of women for this study will include women who were included in the original menarche study who were ages 10-20 in 1976. For these women aged 19-29 in 1985, information on age at menarche, duration of menarche to first conception interval, outcome of pregnancy for all pregnancies, and infant mortality will be used to assess the effect of the duration of the menarche-conception interval on pregnancy outcomes. Prospectively collected data on pregnancy outcome is available through the vital registration system for births and deaths in Matlab.

These data will be analysed to assess the association between menarche to conception interval with the probability of live birth and infant mortality, stillbirths and miscarriages among these women.

Data

The sampling frame for the study was determined by the 1974 census in 13 villages included in the Matlab registration since 1966. All girls aged 10 to 20 years in 1976 residing in these villages were included in the study sample. A total of 1,618 girls were identified.

Exact ages of girls born in 1966 were calculated from their birth registration forms. Ages for subjects born prior to 1966 were adjusted from the 1966 census data. Ages collected for this census were determined from the parent's reporting of their daughter's age and successive interval between siblings.
Of the total sample, 1449 girls were interviewed at least once in addition to information, collected by the registration system. A series of 12 monthly interviews was conducted between March 1976 and February 1977 by local female field assistants. At the initial interview, information on age at menarche was collected, as well as anthropometric data (height, weight and arm circumference). In the prospective follow-up, data on last menstrual period or date of first menses (menarche) were collected, along with anthropometric data. These data are currently available on tape at Data Management Branch (DMB) in the raw data form. Additional data for the subsequent 6 months (March-August, 1977) of follow-up are on the original data collection forms at Data Management Branch. Data on births occurring to these women and the outcome of those pregnancies (livebirth or miscarriage) through 1984 will be available from DSS data source. Retrospective information was collected in March 1976 for: 1) 458 girls who had reached menarche by that date; 2) menarche occurred in 112 girls during the first 12 months of follow-up and it is assumed that an additional 55 girls will be included once the subsequent 6 months of data are coded. These 625 girls are the subjects of the study.

Using the 1980 age specific fertility rates for Matlab (Becker and Hiltabiddle, 1981), we estimate that there will be approximately 1000 births occurring to the women in this study, during the period 1976 to 1985, allowing for a 10% loss to follow-up. With an infant mortality rate of 100 deaths per 1000 live births, there should be 100 infant deaths to study. The stillbirth rate for this area is 40 stillbirths per 1000 live births and the reported fetal loss rate is 10%. Based on reports from the demographic system, we estimate that the rate for the
young women in our study will be similar to the average, and thus we estimate that there will be about 50 stillbirths and 140 early fetal losses (Chowdhury et al, 1982). These data illustrate that women aged 15-19 in Matlab have higher fetal loss rates than women aged 20-29. A better indicator for the effect of adolescent growth on infant viability than mortality would be birthweight. However, since we are unable to obtain this information, we believe that the use of infant survival will be a close proxy, although it is understood that many factors aside from the maternal nutritional status will affect mortality during the first year of life.

Information available on socio-economic status in the other study, (census'82) will give the economic level of the women under study. These are the: education of herself, education of her parents and primary and secondary occupation of her father. The information will be helpful in explaining differences seen in nutritional status and in infant mortality, although it is possible that socio-economic status may have changed since the original data collection effort.

Menarche-Conception Intervals and Pregnancy outcome

Using the information available through the previous interviews, the matching with the vital registration data and the proposed field study, the probability of poor pregnancy outcome will be assessed. Poor pregnancy outcome will be considered in terms of perinatal loss (fetal loss, stillbirths and deaths in the first 24 hours) and neonatal and infant mortality. Menarche to first conception interval will be calculated by subtracting 9 months from the date of a live birth, 8 months from a stillbirth, and the given duration of the pregnancy for fetal losses as recorded on the registration forms. We realize that the accuracy of these durations is exact. The largest bias relates to unreported fetal losses. Such
losses would cause the duration of the menarche to first conception interval to be overestimated, especially since early losses are like y to be missed. This bias would result in any detrimental effect of short menarche to conception intervals being less apparent because women with fetal losses would be estimated as having longer rather than the true shorter durations.

Using multiple logistic regression, we will estimate the relationship of the length of the interval from menarche to first conception with the probability of a poor pregnancy outcome (fetal loss, stillbirth, and infant death), while controlling for the following intervening variables: age of menarche, age of the mother at the specified birth, parity at that birth, attained height, current weight, and socio-economic status. The equation for the logistic regression equation is:

\[ \text{E}(Y) = \text{Prob. of Poor outcome) = B_0 + B_1 \times \text{menarche} + B_2 \times \text{conception interval} + B_2 \times \text{age at menarche} + B_3 \times \text{age of mother at birth} + B_4 \times \text{parity} + B_5 \times \text{SES}. \]

By including all births that women have delivered since their first conceptions, the sample size will be sufficient to estimate the effect on pregnancy outcome. As stated previously, we expect a total of 140 fetal losses, 50 stillbirths, and 100 infant deaths. Since the negative effects

\[ \ldots P/8 \]
of early pregnancy on growth and subsequent pregnancy outcome are not likely to be reversible, the use of all pregnancy outcomes will enable us to have a greater likelihood of seeing effects, if they exist, than if we examined only the outcome of the first births, where sample size would be limited. Longitudinal data analysis methods recently developed by Zeger-Liang and Self will be employed to account for the correlation that is likely among repeated birth outcomes for an individual woman (Zeger et al 1985).

Significance of Findings

A large proportion of births occurs to adolescents in Bangladesh and in most countries of the developing world, where chronic malnutrition occurs. The implications of early births on the nutritional status of the mothers and the health effects on their infants have yet to be clarified. This may be especially important when malnutrition is prevalent because in malnourished girls, growth after menarche may be substantial. The effect on height and pelvic size would have long ranging effects for the outcome of pregnancy in first and subsequent births.

In countries such as Bangladesh, where marriage closely follows menarche, the concern for the negative effects of early conception on the health of both the mother and her offspring is especially paramount for policy determination. In current attempts to reduce infant mortality, one of the price concerns is the reduction of low birth weight. If mothers are "programmed" to delivering small infants who are at higher risk, because the mothers conceived too early in their own reproductive cycles, then many of the current policy options to improve child survival need to be revised. Such policy options may need to emphasize the need to prevent
early conception in growing adolescents. This may add to the evidence for the need to provide family planning for young women, as well as promote with greater fervor alternate opportunities, other than marriage, for adolescent girls.
REFERENCES CITED


