Maternal Serum Ferritin Concentrations as a Predictor of Preterm Labour

Thesis
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By

Naglaa Anter El Maghraby
Resident of Obstetrics and Gynecology
El Salam Specialized Hospital
M.B., B.Ch (Tanta University, ٢٠٠٢)

Under supervision of

Prof. Dr. Ahmed Mohamed Nour El Din Hashaad
Professor of Obstetrics and Gynecology
Faculty of Medicine - Ain Shams University

Dr. Nashwa El said Hassan
Lecturer in Obstetrics and Gynecology
Faculty of Medicine -Ain Shams University

Dr. Deena Samir Mohamed
Lecturer in Clinical Pathology
Faculty of Medicine- Ain Shams University

Faculty of Medicine
Ain Shams University
٢٠١٢

بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

قَالُوا

سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْحَكِيمُ

صَدَقَ اللهُ الْعَظِيمُ

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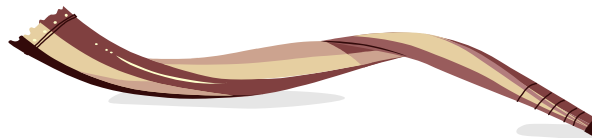First and the most I would like to thank *Allah*, whom without this work would not have been done.

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List of Abbreviations

AA	:	Arachidonic acid
ACS	:	AntiNatalCorticosteroids
B.V	:	Bacterial Vaginosis
BMI	:	Body mass index
BPD	:	Broncho pulmonary Dysplasia
CAPS	:	Contraction associated Proteins
COX	:	Cyclo Oxygenase Enzyme
CRH	:	Cortico tropine releasing hormon
CRP	:	C-Reactive protein
DHEA-S	:	Dehydro epiandrosterone sulphate
E١	:	Esteron
E٢	:	Estradiol
E٣	:	Estrion
FDA	:	Food and Drug administration
FFN	:	Fetal Fibronectin
HB	:	Hemoglobin
HCG	:	Human chorionic gonado trophin
HPA	:	Hypothalamo pituitary axis
IDA	:	IronDeficiency Anaemia
IL-٦	:	Interleukin ٦
IUGR	:	Inter uterin growth retardation
IVH	:	Intra ventricular haemorrhage
LBW	:	Low birth weight
LIP	:	Labile Iron pool
NEC	:	Necrotizing entero collitis
NO	:	Nitric Oxide
NSAID	:	Non steroidal Anti Inflammatory Drug
NTBI	:	Non Transferrin Bound Iron
PCV	:	Packed Cell Volume
PGS	:	Prostaglandines
PLI	:	Preterm labour index
PPROM	:	Preterm Premature Rupture of membrane
PROM	:	Pre mature rupture of membrane

List of Abbreviations (Cont.)

PTB	:	Preterm Birth
PTD	:	Preterm delivery
PTL	:	Preterm labour
RCIS	:	Reactive choleren Species
RDS	:	Respiratory distress syndrome
ROP	:	Retinopathy of Prematurity
ROS	:	Reactive Oxygen Species
SF	:	Serum ferritin
SGA	:	Small for gestational age
SIDS	:	Sudden infant death syndrom
SOD	:	Super Oxide dis mutase
SPB	:	Spontaneous preterm Birth
SPTL	:	Spontaneous Preterm Labour
TBARS	:	Thio barbituric acid reactive substances
TCC	:	Transvaginal Cervical Cerculage
TNF	:	Tumor necrosis factor

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Introduction

Preterm birth (PTB) is defined as birth before completed ٣٧ weeks of gestation (***Chandiramani, Manju et al., ٢٠٠٧***), accounts for ٦-١٠٪ of all births and is a major contributor to neonatal and infant morbidity and mortality.

Clinicians tend to divide preterm labour into three subgroups:
١. Extremely preterm labour (٢٤ weeks to ٢٧ weeks ± ٦ days).
٢. Very preterm labour (< ٣١ weeks ± ٦ days)
٣. Preterm labour (< ٣٦ weeks ± ٦ days)

Table (١): Definitions of preterm birth using gestational age and birth weight

Gestational Age (Weeks)	Birth Weights (KG)
Extremely preterm labour (٢٤ weeks to ٢٧ weeks ± ٦ days)	Extremely low (< ١٫٠)
Very preterm labour (< ٣١ weeks±٦ days)	Very low (< ١٫٥)
preterm labour (<٣٦ weeks±٦ days)	Low (< ٢٫٢٥)

(Chandiramani et al., ٢٠٠٧)

Spontaneous preterm birth (SPB) accounts for about three -quarters of these births and births before ٣٠ weeks of gestation account for most neonatal deaths (***Chandiramani, Manju et al., ٢٠٠٦***).

The remaining preterm births are medically induced because of fetal or maternal concerns and include abruptio placentae, placenta praevia, fetal growth restriction and some miscellaneous cases (***Nina et al., ٢٠٠٥***).

Threatened preterm labour occurs in approximately ٢٪ of pregnancies. However, ٨٠٪ of these pregnancies will proceed to term (***Emma et al., ٢٠٠٦***).

The diagnosis of threatened preterm labour is difficult. By definition, regular contractions ٢ or more in ١٠ minutes; cervical changes either gradual effacement or ٣ cm or more cervical dilatation and intact membrane, are required for diagnosing established labour. Braxton-Hicks contractions, which occur after ٢٤ weeks gestation and may be painful, intermittent pelvic pressure, intermittent low back ache, menstrual like cramps and changing characters and amount of vaginal discharge are misdiagnosed as preterm labour. This will lead to incorrect treatment in up to ٨٠٪ of cases (***K.Haram et al., ٢٠٠٣***).

Early detection of preterm labor is difficult because initial symptoms and signs are often mild and may occur in normal pregnancy. Thus, many healthy women will report symptoms during routine prenatal visits, where as others destined for preterm birth may dismiss the early warning signs as normal in pregnancy. The traditional criteria for preterm labor (persistent contractions accompanied by progressive cervical dilatation and effacement) are most accurate when contraction frequency is six or more per hour, cervical dilatation is three cm or more, effacement is ٨٠٪ or more, membranes rupture, or bleeding occurs (***Hueston, ٢٠٠١; Macones et al., ٢٠٠٢***).

In this study maternal serum ferritin was used as predictor marker for preterm labour.

Serum ferritin concentration ranges from ١٥ to ٣٠ng/ml (higher in males), where values below ١٥ ng /ml are specific for storage iron depletion ferritin values more than ٣٠ ng/ml do not necessary indicate overload.

Aim of the Work

The aim of this study is to measure serum ferritin concentration in pregnant women with risk of preterm labour and to evaluate the value of serum ferritin levels as a predictor of Preterm labour.

Risk Factors

Identification of risk factors for preterm birth (PTB) before conception or early in pregnancy ideally would lead to interventions that could help to prevent this complication (**Robinson, ٢٠٠٨**).

Wide spectrum of causes and demographic factors has been implicated in preterm birth including:

١. Sociobiological factors
٢. Life style factors
٣. Obstetrical factors
٤. Gynecological factors
٥. Genitourinary tract infections
٦. Genetic factors

١. Sociobiological Factors:

a. Maternal age:

Teenage children has repeatedly been associated with increased Risks for adverse pregnancy outcomes, like preterm birth, low Birth weight(LBW), and death in the neonatal or postnatal periods(**Haldrre et al., ٢٠٠٧**).

Teenagers and women aged ٣٥ years and over generally have been shown to have a greater risk of adverse perinatal outcome including low birth weight, (**Ashley et al., ٢٠٠٧**) small-for-gestation age(SGA), (**Jacobsson et al., ٢٠٠٤**) preterm birth (PTB), (**Ananth et al., ٢٠٠٤**) and perinatal or infant mortality, (**Jacobsson et al., ٢٠٠٤**).

b.   Race:

Race is a significant risk factor for preterm delivery. Black women have a prematurity rate of about ١٦-١٨٪, compared to ٧-٩٪ for white women (**Palomar et al., ٢٠٠٧**), so

preterm birth rate for black women is almost twice that for white women of comparable age in the USA, irrespective of socioeconomic status (***Michael et al.,*** ٢٠٠٢**).**

c. Weight:

Many studies revealed relation between low pregnant weights gain and low body mass index (BMI)(especially if BMI is less than ١٩,٨) in increase the risk of preterm birth (***Robinson et al.,*** ٢٠٠٨**).**

Women with lower than normal body weight have been shown to be at increased risk for adverse prenatal outcomes such as prematurity and intrauterine growth restriction (***Zahra et al.,*** ٢٠٠٦**).**

٢. Life Style Factors :

a.   Smoking:

Passive smoking in pregnancy may be a bigger problem than is generally appreciated. Smoking increases the risk of Intrauterin growth retardation (IUGR), Preterm labour (PTL), miscarriage and peri natal death (***Timc,*** ٢٠٠٤**).**

Solid evidence shows that smoking is associated with preterm birth. The more the mother smokers, the greater the risk (***Francois,*** ٢٠٠٥**).**

Smoking-related causes of preterm birth may include spontaneous preterm labour, preterm premature rupture of the membranes, and antepartum bleeding (***Burguet et al.,*** ٢٠٠٤).

c. Socioeconomic Status:

in developing countries, iron deficiency and IDA are far more prevalent than in Western societies and constiutue a

major health problem among women of reproductive age and pregnant woman *(Milman, ٢٠١١)*.

Low socioeconomic statuses is associated with PTL but probably because of other factors that keep women in /near poverty, example, and poor women is poorly nourished, and have a higher prevalence of tobacco, alcohol, and illicit drug use and have less access to prenatal care *(Nancy, ٢٠٠٧)*.

The preterm birth rate is greatly increased among the socially disadvantaged population. In the USA, a population-based study showed that the risks of preterm birth were directly related to education, income and occupation in both black and   European countries including the UK *(Jean-Marie., ٢٠٠٣)*.

f. Diet:

There is a lack of evidence from randomized studies regarding the effect of diet on length of gestation. Neither isocaloric protein supplements nor balanced protein/energy supplements affect the rate of PTB *(Kramer et al., ٢٠٠٣)*.

٣. Obstetric History :

a. Bleeding:

Bleeding during both the first and second - trimesters was associated with a greater than six-fold increased risk of spontaneous preterm delivery *(Rydhwana et al., ٢٠٠٧)*.

Weiss et al., (٢٠٠٤) reported data on vaginal bleeding at ٦ to ١٣ weeks in nearly ١٤٠٠٠ women. Both light bleeding (described as spotting) and heavy bleeding (similar to menses) were associated with subsequent pregnancy loss prior to ٢٤ weeks, preterm labour and placental abruption.