Original Article :

Early detection of Blighted ovum in pregnant women in North Darfur, Sudan

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Abstract

Background and Aims:
Blighted ovum, or anembryonic pregnancy, is a leading cause of early pregnancy loss, often associated with chromosomal abnormalities. Early detection is crucial for timely clinical intervention. This study evaluates maternal serum human chorionic gonadotropin (HCG) and alpha-fetoprotein (AFP) as potential biomarkers for the early detection of blighted ovum in first-trimester pregnancies.

Methods:
A cross-section study was conducted at Alfashir New Hospital, Northern Darfur State, Sudan involving 194 pregnant women in their first trimester: 158 with normal pregnancies and 36 diagnosed with blighted ovum. Maternal serum samples were analyzed using immunoradiometric assays (IRMA) to measure HCG and AFP levels. Gestational age was confirmed via ultrasound and serum biomarker analysis, with results expressed as multiples of the median (MoM).

Result:
A significant decrease in HCG levels was observed in women with blighted ovum compared to the others ($P < 0.001$), whereas AFP levels showed no significant difference. This confirms that low maternal HCG levels can serve as a potential marker for early detection of blighted ovum. .

Conclusion:
The study established local reference values for HCG and AFP in the Sudanese population. Serum HCG screening in the first trimester offers a cost-effective, non-invasive method for early diagnosis of blighted ovum. The findings suggest that locally established reference values may be more applicable than international standards.

Key words:
Blighted ovum, anembryonic pregnancy, early pregnancy loss

Introduction:

Screening and early detection of pregnancy disorders have become crucial issues for pregnant women's health. Nowadays, a noninvasive and essential initial step in identifying patients at risk for prenatal anomalies is maternal serum analyte testing.[1] Early in pregnancy, a woman may experience dark-brown vaginal bleeding and notice that her pregnancy symptoms have stopped. An ultrasound scan reveals an empty pregnancy sac, A blighted ovum eventually leads to miscarriage, though this may take weeks to occur.[2]

Blighted ovum accounts for 16% and 30% of all pregnancies.[3] Around 67% of anembryonic pregnancies are associated with miscarriage, increasing the likelihood of fetal loss. [4] Chromosome 16 triploid has been identified as a cause of blighted ovum.[5] Knowing whether a fetus is affected prenatally has several benefits such as giving parents the right to decide whether to carry the pregnancy to term or not.[6]

The diagnosis of a blighted ovum is made using an ultrasound scan. It can be identified by its failure to grow and the disappearance of the normal healthy ring pattern. In a blighted ovum, there is no villous circulation after embryonic death. A trophoblast with no villous circulation may produce insufficient HCG, preventing the corpus luteum from secreting progesterone.[7]

Plasma levels of beta-human chorionic gonadotropin (HCG) help in the diagnosis of a blighted ovum. Literature indicates that beta-HCG levels are significantly lower in embryonic abortions compared to both ongoing pregnancies and full-term pregnancies. [8] When an embryo fails to develop, the amniotic cavity and embryonic pole vanish, a process linked to reduced beta-HCG levels. This decrease is likely due to the disruption of interaction between the chorionic membranes and the embryo.[9]

Alpha-fetoprotein (AFP) was first identified in 1956 as a globulin specific to fetal development. It is synthesized by the yolk sac, fetal liver, and digestive tract. AFP levels in fetal circulation peak between 10 and 13 weeks of gestation, then gradually decline until birth.[10] In contrast, maternal AFP levels peak during the third trimester.[11] Laboratory assessments of AFP concentrations are expressed as multiples of the median (MoM). Shortly after implantation into the uterine wall, the syncytiotrophoblast produces the complex glycoprotein known as HCG. During the first eight weeks of pregnancy, it rises rapidly. After that, it gradually declines to 20 weeks, at which point it plateaus.[12, 13]

The Objectives of the study were to establish local reference values for HCG and AFP in the first trimester of gestation

and evaluate the use of these two serum markers as a method for early detection of blighted ovum at the same gestational age.

Materials and Methods:

This is an unmatched case-control study conducted at Alfashir Maternity Hospital in North Darfur Sudan. Maternal serum samples were obtained from 194 women: 158 with unaffected singleton non-diabetic pregnancies (control group) and 36 women diagnosed with a blighted ovum (case group). Samples were taken early in the first trimester. Pregnancies from control were those where babies were known to be normal at birth. Women were referred to Alfashir New Hospital from different health centers in Northern Darfur State.

All subjects underwent screening and counseling on the risk of fetal congenital abnormalities, specifically blighted ovum. Blood samples were taken for immunoradiometric assay (IRMA) of HCG and AFP early in the first trimester. Gestational age was determined by ultrasound measurement in combination with HCG and AFP from the 3rd to 5th weeks, as ultrasound alone could not confirm pregnancy that early.

Since HCG and AFP concentrations change with gestation, results were expressed as Multiples of the Median (MoM) for the corresponding gestational week. The immunoassay HCG IRMA kits (cat 2110 and 2209) are intended for the quantitative determination of human chorionic gonadotropin and alpha-fetoprotein concentrations in human serum or plasma. The determination of HCG and AFP is based on the immunoradiometric method, in which two monoclonal antibodies against two different epitopes of the HCG (AFP) molecule are used. Total HCG (AFP) in samples or calibrators is incubated together with the first specific monoclonal antibody immobilized on tubes and the second specific monoclonal antibody labeled with I125. After incubation, the tube's content is aspirated along with unbound signal antibodies, and the bound radioactivity is counted using a gamma counter. The HCG (AFP) concentration is directly proportional to the measured radioactivity. The unknown sample's HCG (AFP) concentration is read off a calibration curve constructed using calibrators.

Results:

Table 1 presents the local human chorionic gonadotropin (HCG) reference range during the first trimester based on the 95% confidence interval (CI). The median HCG levels increase significantly from weeks 3-5 (7010 mIU/mL) to a peak at weeks 10-11 (74450 mIU/mL), before decreasing slightly in weeks 12-13 (47064 mIU/mL). The highest variability is observed in the 8–9 week, range (95% CI: 66938 - 104784),

indicating a broader distribution of HCG levels in this gestational period.

Table1: Local HCG reference range in the 1st trimester taken as 95% confidence intervals.

Gestational age in weeks	Median in mIU/mL	95% confidence interval range	n
3-5	7010	5850 — 7312	31
6-7	37332	37808 — 68765	34
8-9	72724	66938 — 104784	48
10-11	74450	66053 — 110134	30
12-13	47064	39035 — 69215	33

Alpha-fetoprotein (AFP) levels, presented in Table 2, show a gradual increase over the first trimester. The median AFP level starts at 7.5 ng/mL in weeks 3-5 and reaches 17 ng/mL by weeks 12-13. Notably, AFP levels exhibit a wider range of variability in later weeks, especially at weeks 12-13 (95% CI: 15 - 30.4 ng/mL), indicating increased fluctuations in AFP production as gestation progresses.

Table 2:Local AFP reference range in the 1st trimester as 95% confidence intervals.

Gestational age /WKs	Median	Range (95%CI) ng/ml	n
3-5	7.5	6.4—8.3	31
6-7	2.3	5.5—18	34
8-9	5.0	4.8—12.5	48
10-11	12	9.5—15.2	30
12-13	17	15—30.4	33

Table 3 provides descriptive statistics for HCG and AFP levels in cases diagnosed with blighted ovum (BO). The median HCG level in BO cases is significantly lower (2976 mIU/mL) compared to normal pregnancies in the first trimester, with an overall mean value of 3062 mIU/mL In contrast, the median AFP level in BO cases is 9.9 ng/mL, showing a slight elevation compared to the normal median AFP levels at the corresponding gestational age.

Table3: Descriptive statistics for Blighted ovum: HCG and AFP in Blighted ovum in the 1st trimester.

Item	AFP	Beta HCG
n	36	36
Mean	10.4	3062
Median	9.9	2976

Table4: Comparison between Blighted ovum (BO) and a comparison group for HCG and AFP in the mid-1st trimester .

Cases	HCG mIU/ml	AFP ng/ml	n
BO median	2976 (MoM=0.039)	9.9	36
Comparison group median	75240	8.3	158
P value	0.001	0.130	-

Discussion:

The use of HCG and AFP for screening blighted ovum has been validated. Serum screening has become an established practice in many Western and Asian countries. This study may provide a promising result for prenatal screening of blighted ovum using maternal beta-HCG and AFP in Sudanese pregnant women. Locally established reference values for HCG and AFP may replace the international reference values in the future.

This study observed a significant decrease in first-trimester HCG levels in women carrying fetuses with a blighted ovum. The combination of HCG and AFP biomarkers developed a cost-effective method for early detection of blighted ovum. Converting biomarker measurements to MoM eliminated gestational age variations and enabled mathematical calculations of individual odds of a blighted ovum. This result is similar to the finding of a study done by Kim SY et al, who found that a single measurement of HCG is enough to predict pregnancy outcome[14]. Our findings are different from another study done by Kushnir VA et al, who found that HCG is not useful in predicting the outcome of pregnancy with a viable fetus [15].

Singh et al., 2013 showed that low maternal serum Beta HCG in early pregnancy was associated with poor pregnancy outcome which was confirmed later by ultrasound [16]. Our findings are consistent with this study. The same result was obtained by Nagi et al, who studied the efficacy of maternal markers in detecting congenital malformations in early pregnancy[17].

Conclusion:

Serum HCG can be used as a screening tool in the first trimester for early detection of blighted ovum. This test is cost-effective and non-invasive. However, Further research is needed to establish reference values for the concentration of HCG and Alpha Fito-protein in the first trimester of pregnancy. It is advised to include certain important criteria for patients' selection such as BMI, maternal age, and pregnancy complications. These factors might affect the concentration of AFP and HCG. Implementing and utilizing a well-structured,

screening protocol would significantly enhance the early identification and diagnosis of blighted ovum.

Conflicts of Interest:

The authors declared that there is no conflict of interest in this work.

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