THE ROLE OF PRENATAL SCREENING IN PREDICTING PREGNANCY COMPLICATIONS AND GENETIC ABNORMALITIES IN THE SECOND TRIMESTER OF PREGNANCY

Thesis

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Presented by

Osama Ashour Haddad

M.B., B.CH.

Prenatal Diagnosis and Fetal Medicine Department

National Research Centre

Under the supervision of

Prof.Dr. Basma Makin Abd Elaziem

Professor of Obstetrics and Gynecology

Faculty of Medicine

Cairo University

Prof.Dr. Khaled Ramzy Gaber

Professor of Prenatal Diagnosis

Head of Prenatal Diagnosis and Fetal Medicine Department

National Research Centre

Dr. Omneya Mostafa Helal

Assistant Professor of Obstetrics and Gynecology

Faculty of Medicine

Cairo University

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بسم الله الرحمن الرحيم

﴿ وَلَقَدْ خَلَقْنَا الْإِنْسَانَ مِنْ سُلَالَةٍ مِنْ طِينٍ (١٢) ثُمَّ جَعَلْنَاهُ نُطْفَةً فِي قَرَارٍ مَكِينٍ (١٣) ثُمَّ خَلَقْنَا النُّطْفَةَ عَلَقَةً فَخَلَقْنَا الْعَلَقَةَ مُضْغَةً فَخَلَقْنَا الْمُضْغَةَ عِظَامًا فَكَسَوْنَا الْعِظَامَ لَحْمًا ثُمَّ أَنْشَأْنَاهُ خَلْقًا آخَرَ ۚ فَتَبَارَكَ اللَّهُ أَحْسَنُ الْخَالِقِينَ (١٤) ﴾

صدق الله العظيم

سورة المؤمنون

If any student comes to me and says he wants to be useful to mankind and go into research to alleviate human suffering, I advise him to go into charity instead. Research wants real egotists who seek their own pleasure and satisfaction, but find it in solving the puzzles of nature.

Albert Szent-Györgi (1893-1986)

First of all, thanks and praise to Almighty God for the completion of this work.

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Finally, I am praying **Allah** for the patients who were included in this study. I hope this work may helpful to solve their complaints.

This work is dedicated to the spirit of my father, my mother, my sinceer beloved wife Amira, my lovely son *Abdul Rahman* and my dear brothers for their endless support. GOD blesses them.

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ACOG	American collegue of gynaecology and obstetrics	HC	Head circumference
AC	Abdominal circumference	HL	Humerus length
ACC	Agenesis of corpus callosum	H/O	History of
AFP	Alpha feto protein	IUGR	Intra uterine growth retardation
ANC	Antinatal care	IUFD	Intra uterine fetal death
β-Hcg	Beta subunit-human chorionic gonadotropin	Mmhg	Millimeter mercury
BPD	Biparietal diameter	MCA	Multiple congenital anomalies
CI	Cephalic index	MoM	Multiples of median
CPC	Choroid plexus cyst	MSAFP	Maternal Serum Alfa-fetoprotein
DNA	Deoxyribonucleic acid	NB	Nasal bone
DR	Detection rate	NFCs	Nucleated fetal cells
DS	Down syndrome	NTD	Neural tube defect
DVT	Deep venous thrombosis	NT	Nuchal translucency
EB	Echogenic bowel	NSGC	National society of genetic counseller
EDD	Expectd Date of Delivery	PAPP-A	Pregnancy associated plasma protein A
EIA	Enzyme immune assay	PP13	Placental protein 13
EIF/EICF	Echogenic intracardiac foci	PSG-1	Pregnancy specific Beta1 glycoprotein 1
FISH	Fluorescence in situ hybridization	RNA	Ribonucliec acid
FL	Femur length	TOP	Termination of pregnancy
FNRBCs	Fetal nucleated red blood cells	uE3	Unconjugated estriol
FOD	Fronto occipital diameter	U/S	Ultrasound
FPR	False positive rate	Wks	Weeks
HCG	Human chorionic gonadotropin	4D	Four diamentions

ABSTRACT

Key Words:
(Prenatal screening, Pregnancy complication, Genetic abnormalities, second trimester of pregnancy)

The aim:

To assess the sensitivity of second trimester prenatal screening and its value in predicting pregnancy complications and genetic abnormalities.

Methods:

300 pregnant females were subjected to MSAFP testing at 15 -18Wks and ultrasound scan at 16-18 Wks for soft markers, major anomaly. AC was offered to high risk cases, and cases were followed till term to assess the outcome.

Results:

12/300cases had low MSAFP with high risk for chromosomal abnormalities, one case of them had trisomy 21 fetus with soft markers, another case the fetus developed generalized edema & IUFD, 3/300 cases had high MSAFP with adverse pregnancy outcome,one of them had NTD & multiple anomalies. Ultrasound abnormalities with adverse pregnancy outcome were detected in 11/293 cases while soft markers were detected in 18 cases, only 5/18 had structural anomalies with two chromosomally abnormal fetuses. Soft markers were detected in normal unaffected fetuses. Amniocentesis was offered to 20 cases, The AC acceptance rate was 55 %, and no post procedure complications were detected.

Conclusion:

Combining genetic ultrasound to the MSAFP screening increases the efficiency and accuracy of prenatal screening as ultrasound can detect most structural abnormalities with less AC numbers. Soft marker improves the detection rate of fetal abnormalities& anaeupliodies, so soft markers should be considered carefully when detected especially at high risk cases.

Introduction

Prenatal screening is the systematic application of a non invasive test to identify fetuses at risk for a disease or a condition before birth to warrant further invasive investigation or direct preventive action. It aims at detection of birth defects such as chromosome abnormalities, genetic diseases and other conditions. Screening can only evaluate risk of a condition but it cannot determine 100% if the fetus has such condition **(Wald et al., 2004).**

Fetal malformations are common pregnancy complication with a prevalence of 6.5% of all pregnancies. Genetic abnormalities occur in 0.1% to 0.2% of live births. Sixty percent of malformations could be detected prenatally and thus urgent care and management becomes easier (**Smith et al., 2001; Tabor et al., 2003**).

Intrauterine growth restriction, unexplained stillbirth, sudden infant death syndrome and placental insufficiency associated with poor obstetric and neonatal outcomes, can be screened and predicted prenatally via raised maternal serum level of alpha-fetoprotein during the second trimester taking into consideration that the patient should be sure of her date of last menstruation for accurate dating of pregnancy and diagnosis of intrauterine growth restriction**(Anfuso et al., 2007; Fox et al., 2008; Toal et al., 2008)**. Hence the value of prenatal screening has been proved as an important part of routine antenatal care (**Filkins et al.**, **2005)**.

The commonest screening method for fetal abnormalities involves the assessment of a combination of factors: maternal age, second trimester serum markers & second trimester genetic sonogram **(Peter et al., 2002).**

The greatest emphasis has been in women of advanced maternal age. However advanced maternal age cannot serve as the sole screening factor, as 70% of Down syndrome babies are born to women under 35 years. Now according to American

Collegue of Gynaecology and Obstetrics **ACOG (2007)**, it is generally accepted that all pregnant females should be offered prenatal screening.

Second trimester biochemical markers represent part of physiological biochemical changes during pregnancy that could be affected by pathological pregnancies and may be monitored for diagnosis or prediction, and management of pregnancy complications and adverse pregnancy outcome **(Fernando et al., Peter et al., 2002**). Alpha-fetoprotein (AFP) is the best and most effective known marker for detection of open neural tube defects and aneuploidies; it is a simple test that achieves high detection rate decreasing amniocenteses rates, with low cost **(Platt et al., 2004).**

The genetic sonogram represents a specialized evaluation of the fetus in which the fetus is examined in a detailed manner like a newborn. Also it evaluates structural malformations and second trimester soft markers for fetal aneuploidy which has gained widespread acceptability (**Martin et al., 1999; Malone et al., 2005; Flood et al., 2008)**. The detection rate for Down syndrome using genetic sonogram was as low as 50% in old studies and recently it reaches up to 95% **(Greggory et al., 2003; Flood et al., 2008**).

Genetic sonogram can be used as isolated test, or better in conjunction with second trimester maternal serum screening. Identification of Down syndrome has been reported to be increased from (76%) by using maternal serum screening alone to (87.5%) when maternal serum screening is combined with genetic sonogram with significant reduction of the false positive results (**Malone et al., 2005;Valinen et al., 2007).** In a study carried by **Peter and colleagues (2002)** using genetic sonogram alone, a sensitivity of 79.9% and false-positive rate of 6.7% was achieved (positive predictive value =1 in 42), The serum screening test alone has a sensitivity of 81.5% and false-positive rate of 6.9% (positive predictive value =1 in 42). Whereas the combination of the serum screening with genetic sonogram achieved 90% sensitivity and a 3.1% false-positive

rate (positive predictive value =1 in 18) achieving reasonable sensitivity in predicting the risk of adverse prenatal outcome **(Dugoff et al., 2005; Bas-Budecka et al.,2006; Raniga et al., 2006**; **Dane et al., 2008).**

Genetic counseling according to the National Society of Genetic Counselors (NSGC) is the process of helping people to understand and adapt to the medical, psychological and familial implications of genetic contributions to disease. This process integrates the following:

- Interpretation of family and medical histories to assess the chance of disease occurrence or recurrence.
- Education about inheritance, testing, management, prevention, resources and research.
- Counseling to promote informed choices and adaptation to the risk or condition, thus, supporting them in reaching their own decisions, based on their own unique medical and social circumstances **(Resta, 2006).**

Genetic sonogram achieves the major goal in screening with maximum accuracy and minimal harm at low cost, its efficacy may be comparable to that reported for combined first- and second-trimester (integrated) screening (**Peter et al., 2002).**

Aim of work

Aim of work

- To assess the sensitivity of prenatal screening through the sequential provision of second trimester maternal serum alpha-fetoprotein & fetal ultrasound (genetic sonogram).

- To assess the possibility of predicting pregnancy complications via this screening program (biochemical marker and genetic sonogram).

- To assess the use of second trimester genetic sonogram in guiding patients at risk for pregnancy complications or genetic abnormalities.