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Reliability, Accuracy and Cost-effectiveness of Prenatal Screening Tests

Genc Kabili[1], Rustem Celami[2]

[1] Ob and Gynecologist, University Hospital of Obstetrics and Gynecology K. Gliozheni, Tirana, Albania

[2] Ob and Gynecologist, American Hospital of Tirana | MD, PhD, Lecturer, U of A. Xhuvani, Elbasan, Albania

Abstract

Nowadays in most countries worldwide and in Albania as well, it has become standard in prenatal care to offer screening tests for neural tube defects and genetic abnormalities. There have been some changes in the recommended method of prenatal screening over the past few years, and research to improve detection rates with better combinations of maternal serum analytes is ongoing.

Up to recent years there was mostly in use ultrasound examination of the fetus combined with double, triple and quadruple test as non invasive screening test, followed by diagnostic test like amniocentesis, chorionic villus sampling, cordocentesis when need to confirm the diagnosis. In the past 4 years there have been introduced other tests named; harmony, panorama, verify and materniT21, that are grouped as non invasive prenatal test (NIPT) or known as well as non invasive prenatal screening (NIPS), when the testing was being developed, it was thought it would be diagnostic. However, it still had false positives and false negatives, rendering it not a diagnostic test, but a screening test. As the science and technology advance in clinical practical basis we look not only to reliability but also at the cost-effectiveness of these prenatal screenings. Whereas in developed countries with well functioning health care system, prenatal screening test are covered, in Albania such prenatal screening tests are contemporaneous choices of pregnancy care with up to date information provided by obstetrician, nevertheless, the expenditure of these tests remain uncovered by our health care system therefore these costs remain part of patient's personal budget.

In conclusion, application of prenatal screening test and obstetrical ultrasound examination are very important to be in use for every pregnant woman. In Albania, this can be done as part of high standard of care only when medical protocols, reliability and cost-effectiveness of these tests are part of integral promotion under service of national health care for an excellence care during pregnancy.

Keywords: Prenatal screening, genetic abnormalities, reliability, cost-effectiveness

Introduction

Nowadays in most countries worldwide and in Albania as well, it has become standard in prenatal care to offer screening tests for neural tube defects and genetic abnormalities [2, 3, 4, 6]. There have been some changes in the recommended method of prenatal screening over the past few years, and research to improve detection rates with better combinations of maternal serum analytes is ongoing.

Up to recent years there was mostly in use ultrasound examination of the fetus combined with double, triple and quadruple test as non invasive screening test, followed by diagnostic test like amniocentesis, chorionic villus sampling, cordocentesis when need to confirm the diagnosis [2, 3, 4, 6]. In the past 4 years there have been introduced other tests named; harmony, panorama, verify and materniT21, that are grouped as non invasive prenatal test (NIPT) or known as well as non invasive prenatal screening (NIPS), when the testing was being developed, it was thought it would be diagnostic. However, it still had false positives and false negatives, rendering it not a diagnostic test, but a screening test. As the science and technology advance in clinical practical basis we look not only to reliability but also at the cost-effectiveness of these prenatal screenings. Whereas in developed countries with well functioning health care system, prenatal screening test are covered, in Albania such prenatal screening tests are contemporaneous choices of pregnancy care with up to date information provided by obstetrician, nevertheless, the expenditure of these tests remain uncovered by our health care system therefore these costs remain part of patient's personal budget.

Discussion

The issues facing obstetricians are the sensitivity and specificity of multiple serum analyte combinations. The current maternal serum analytes in use in most areas are the double test which corresponds with the measure of free beta hCG and AFP, triple test that corresponds with measure of alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG) and unconjugated estriol [2, 3, 4, 6]. Measurement of AFP alone can detect the vast majority of neural tube defects and a small portion of trisomy 21–affected pregnancies in patients of all ages. Adding hCG and unconjugated estriol to this screen increases the rate of detection of trisomies 21 and 18. Furthermore, a test of dimeric inhibin A (DIA) is sometimes added to the other three tests, which is named quadruple test [5]. Counseling patients about the risks and benefits of such screening is important to provide a balanced discussion of screening issues.

In addition we have now in use the new screening test like non invasive prenatal test which come with different names like; harmony, panorama, verify and materniT21 [1, 5, 7, 8, 9, 10, 11, 12] . These new screening test are focused in DNA potential. DNA from the fetus circulates in the mother's blood. Cell-free DNA (cfDNA) results from the natural breakdown of fetal cells (presumed to be mostly placental) and clears from the maternal system within hours of giving birth. During a pregnancy, cfDNA can be tested to give the most accurate screening approach in estimating the risk of a fetus having a common chromosome condition sometimes called a trisomy.

However, the above tests remain named screening test which means that can indicate the likelihood a mother is carrying a baby for example with Down syndrome. Whereas, to conclude to a correct diagnosis is needed the diagnostic test, which so far are used amniocentesis, chorionic villus sampling, cordocentesis

Obstetricians have an ethical duty to properly inform patients of their options, specifically the availability of screening and diagnostic testing. Physicians have been successfully sued by women who gave birth to babies with abnormalities that could have been detected had they known about their screening options, though the plaintiff must also prove that she would have elected to terminate the pregnancy in the event of a positive finding. Also, physicians who fail to inform their patients of the risks of amniocentesis and CVS might be found guilty of negligence informed consent in the event that the patient sues after a procedure-related miscarriage or fetal damage.

There is a misconception that a physician only needs to do what other physicians typically do (i.e. standard of care). However, in the case of informed consent, the legal standard is more commonly defined as what a reasonable patient would elect to do if she is informed. So if a reasonable patient would want to be screened if only she is informed or if a reasonable patient would want to receive an amniocentesis if only she is informed of that option, then a physician is legally obligated to inform the patient of these options.

As newer, more accurate screening tests emerge, physicians may need to quickly get up to speed on the most recent data and start informing their patients of the existence of these tests. Failure to inform patients of the available of these more accurate screening tests might result in a wrongful birth or wrongful miscarriage lawsuit if the patient can demonstrate that she would have chosen the newer test, if she had known about it, to avoid the unfortunate outcome that resulted from receiving a conventional screening test or invasive procedure.

These new screening tests do have a cost; either from medical insurance as it takes place in western countries or fee for service paid by patients as it is in Albania. However, these news screening test are not diagnostic tests, thus, the dilemma of offering new advances of science in clinical practice and the cost-effectiveness of these test which are not covered by national health care in Albania continuous among physicians and the respective population group. The double, triple or quadruple tests during pregnancy are not covered by state laboratory and hospital service; they cost a couple of hundred dollars, neither are covered the new costly screening test, so these test remain personal patient's cost [1, 2, 3, 4, 5, 9, 10, 11, 12]. Table 1 is the illustration of new screening test, what they are done for and what is the price of each of them in United States of America. Figure 1, is illustration of panorama test screening mechanism.

	Natera's *Panorama*	Verinata's *verifi*	Sequenom's *MaterniT21 PLUS*	Ariosa's *Harmony*
Trisomies tested	13, 18, 21	13, 18, 21, sex chromosomes	13, 18, 21, sex chromosomes	13, 18, 21
Monosomy tested	X	X	X	
Genetic testing method	Single nucleotide polymorphism	Massively parallel sequencing	Massively parallel sequencing	Chromosome-selective sequencing
Sensitivity	92-99%	87-99%	92%-99%	80-99%
Accuracy	100%	100%	>99%	>99%
Earliest gestational age	9 weeks	10 weeks	10 weeks	10 weeks
Price	$1,495	$1,500	$2,762	$795

Noninvasive Prenatal Genetic Tests Compared
NATURE MEDICINE

Table 1. Screening test during pregnancy

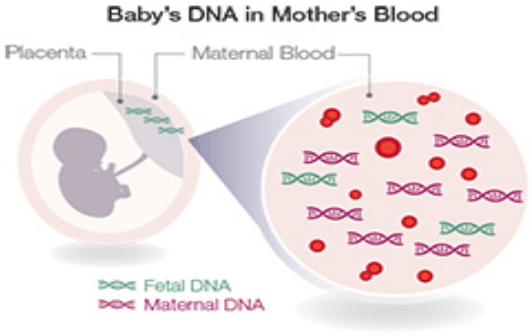

Figure 1. Panorama test screening mechanism

Conclusion

Application of prenatal screening test and obstetrical ultrasound examination are very important to be in use for every pregnant woman national wide in Albania. The screening and diagnostic tests during pregnancy as any other service have a cost. This integral necessity service for pregnant women can be done as part of high standard of care only when medical protocols, reliability and cost-effectiveness of these tests are part of integral promotion under service of national health care for an excellence care during pregnancy.

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