Journal Homepage: - www.journalijar.com
INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)
Article DOI: 10.21474/IJAR01/3632
DOI URL: http://dx.doi.org/10.21474/IJAR01/3632

RESEARCH ARTICLE

PRENATAL DIAGNOSIS WITH GENETIC COUNSELING IN UHC SPLIT, CROATIA.

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Manuscript Info

Manuscript History

Received: 08 January 2017
Final Accepted: 04 February 2017
Published: March 2017

Key words:-
prenatal diagnosing, genetic counseling, cytogenetic analysis, amniocentesis

Abstract

Purpose: The purpose of this study was to document the cytogenetic data obtained from amniotic fluid analysis, as a part of prenatal diagnosing.
Methods: 1.441 samples were analyzed by standard cytogenetic method.
Results: Indications for amniocentesis were divided into six groups. Of them advanced maternal age was the most common, and, as expected, it was associated with the largest number of pathological cytogenetic findings.
Conclusion: In comparison to other indicators for amniocentesis, advanced maternal age had a highest positive predictive value.

Introduction:-

Prenatal diagnostics is a subdivision of clinical genetics; it enables early diagnosis of congenital anomalies and genetic disorders. This is very important because the population risk of having a child with some congenital abnormality varies between 3 and 5%. Although such malformations and genetic disorders can interfere with quality of the life of newborns and their families, sometimes they can also cause the spontaneous abortion.

There are varieties of methods that can be used for prenatal diagnostics. One of them, by which chromosomal abnormalities, neural tube defects and genetic disorders can be detected with high level of accuracy, is amniocentesis (AC). Although it is invasive test which carries a certain risk of miscarriage, it is strongly recommended (after genetic counseling) to a women at increased risk for chromosomal anomalies. So, AC in association with genetic counseling enables early diagnosis of congenital anomalies, which is essential for management the pregnancy and postnatal medical care. It is also crucial to making informed decisions about continuing or terminating the pregnancy. In a latter case it enables to counsel the couples in preparing for a next pregnancy (1, 2).

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The purpose of this study was to document the cytogenetic data obtained from amniotic fluid analysis, as a part of prenatal diagnosing.

Methods:-
During the period from 2007. to 2015. the amniotic fluid was collected from 1.441 pregnant women, who attended University Hospital Centre Split (UHC). All women were of European Caucasian origin. The analyses were done in the Department for Medical Genetics with Laboratory for Human Genetics and Genetic Counseling Unit, Paediatrics Clinic, UHC, Split, Croatia. Amniocentesis was performed between 13 and 25 weeks of gestation, with a peak at 17 week.

The study was approved by the Ethics Committee of the UHC Split. Informed consent to present the amniocentesis data was obtained from each couple.

Results:-

By the end of the march 2015. 1.441 amniocenteses and chromosomal analyses were carried out. Indications for amniocentesis were as follows: 1 maternal age, 2. family or personal history data (parental karyotype, syndrome Down in the family, previous child/children born with malformations, or spontaneous abortion or stillborn child with known or not known pathology), 3. results of prenatal tests (triple, double or combined test), 4. nuchal translucency (NT). 5. other fetal anomaly detected by ultrasound, 6. pregnant women demand.

Mother's age (>35) was the most frequent indicator for amniocentesis (1076; 74.67% cases). However, in 26 and 25 of those women indication for amniocentesis was combination of mothers age and anamnestic data and prenatal tests data, respectively. The second most frequent indicator for amniocentesis were the results of prenatal tests (156; 10.82% cases), followed by family or personal history data (129; 8.95 % cases) and fetal anomaly detected by ultrasound (56; 3.87% cases). Nuchal translucency was indication in 20 cases (1.39 %), while amniocentesis was performed on pregnant women demand in one case (0.07%) The majority of AC were conducted on woman between 35-40 years of age (49 %) and women older than 40 years (26 %) (data not shown).

The majority of samples were cytogenetically normal (1372 samples; 95.21%). In others (69 samples; 4.79%) some irregularities were found: balanced translocation (1), unbalanced translocation (2); aneuploidy (60), and mosaicism (6) (Table 1).
In majority of samples (66; 95.65 %) *de novo* chromosomal changes were present. In only three samples the chromosomal changes were either maternaly or paternaly inherited.

Maternal age was associated with the largest number of pathological findings (36 samples; 52.17%), followed by ultrasound findings (18 samples; 26.09%), results of prenatal tests (9 samples; 13.04%), NT (4 samples; 5.80%) and family or personal history data (2 samples; 2.90%). Sample analyzed on pregnant women demand turne out to be normal (Table 2).

Table 1. Cytogenetic results of amniotic fluid

	Number	**Karyotype**	
Amniocenteses total	1 441		
Normal	1372		No
Patologycal	69		
Translocation balance	1	46,XY,t(18;20)(18pter->20 q12)mat	No
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--	-	46,XY,+21,rob(21;21)(q10;q10)	-
Translocation unbalanced	1	46,XY,add(12q)tr(8p;12q(8p12;12q24.3)(mat	Yes
	1	)->parcial trisomy 8p	
Aneuploidy	60	45,X [5]	Yes/No*
		47,XXX [2]	Yes/No*
		47,XX+13 or 47,XY+13 [4]	Yes
		47,XY+ 18 [10]	Yes
		47,XX+21 or 47,XY+21 [35]	Yes
		47,XXY [2]	Yes/No*

		47,XY,+iso12p [1] 69,XXX [1]	Yes Yes
Mosaics	6	46,XX(22)/45,X(3) [1] 46,XX(18)/45,X(3) [1] 46,XX(50)/45,X(50) [1] 46,XX(10)/47,XXX(3) [1] 46,XX(8)/47,XXX(1) [1] 46,XY(10)/47,XXY(3) [1]	Yes/No* Yes/No* Yes/No* Yes/No* Yes/No* Yes

*TP (Termination of Pregnancy). In cases where changes in gonosomes were found, especially in mosaic form, the development of severe mental retardation is not expected, but the occurrence of sterility in the adulthood is possible, so the decision of TP should be done only by parents.

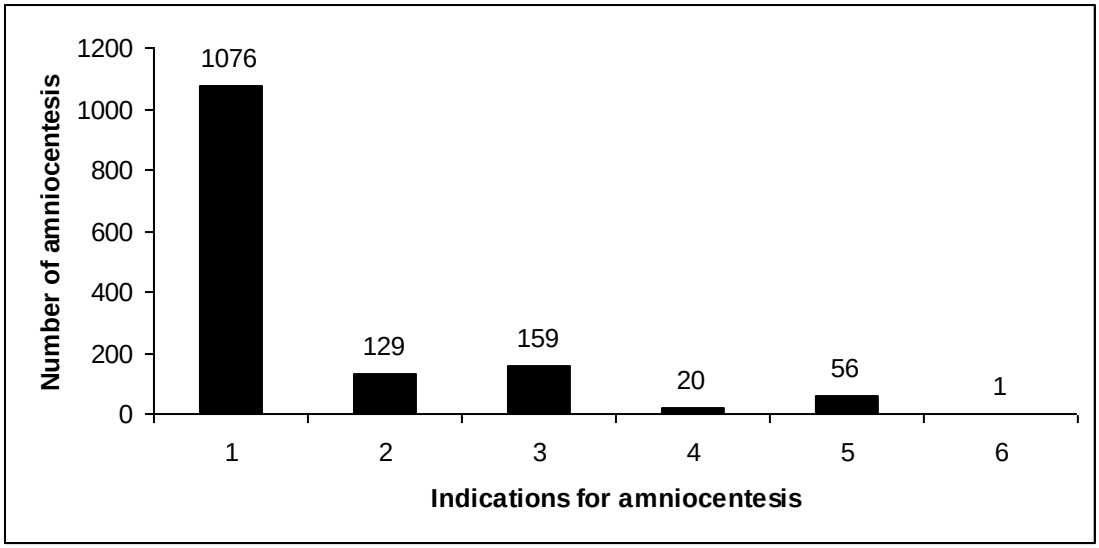

Figure 1. Indications for AC were divided into six groups: 1 maternal age, 2. family or personal history, 3. results of prenatal tests (triple, double or combined test), 4. nuchal translucency (NT), 5. fetal anomaly detected by ultrasound, 6. other (pregnant women demand). The numbers above the bars indicate total number of tested samples.

Table 2:- Number of pathological versus non-pathological findings in amniocentesis samples classified according to the indication for amniocentesis

	Non-pathological	Pathological				
		Aneuploidy	Translocation balanced	Translocation unbalanced	Mosaics	Total (pathological)
Maternal age	1040	31			5	36
Prenatal tests	150	8		1		9
Ultrasound	38	17	1			18
Nuchal translucency	16	3			1	4
Family history	127	1		1		2
Demend	1					0
Total	1372	60	1	2	6	69

Discussion:-

In thirty years (1983-2013) period in the Laboratory for Human Genetics and Genetic Counseling Unit more than 10,000 persons with different genetical as well as chromosomal problems were treated. These were children and adults with chromosomal abnormalities, sterile or infertile couples, couples with one or more spontaneous abortions, people with loads of personal or family history, people who were exposed to harmful factors, those with inherited neuromuscular diseases etc.

Special attention was also put on resolving possible cytogenetic cause of recurrent spontaneous abortions (RSA). By analyzing karyotypes of more than 350 couples (both women and men) who suffered from RSA, as well as karyotype of aborted material, some kind of abnormality was found in 17.6%, 11.5% and 25.9% of women, men, and aborted material, respectively. In a latter case, the majority of changes were *de novo* ones (3).

The methods of prenatal diagnostics can be divided into non-invasive (ultrasound and biochemical screening from maternal blood) and invasive ones (amniocentesis, chorionic villus sampling, cordocentesis, etc.) (4,5). In our study we paid attentionto the women who were referred for amniocentesis. Indications for amniocentesis we divided into the six groups; similar divisions were also done in other studies (5,6). We found that the most prominent indicator for amniocentesis was the maternal age. This is in accordance with the findings of Yang et al (7), but in contrast to the finding of some other authors who found that the most prominent indicator for amniocentesis was an abnormal maternal serum-screening test or abnormal ultrasound findings (6,8,9).

In our study 4.55% women were pregnant with fetuses that had numerical chromosomal abnormalities. Some studies showed a similar results (4.61–4.85 %) (10,11), while some others showed lower incidence of chromosomal abnormalities (5,12).

The most common changes were autosomal trisomies. Similar to our results, Ocak et al. found that the most frequent numerical chromosomal abnormality was trisomy 21 (8).

After amniocentesis results are known, all women should be again subjected to genetic counseling. For those women where variation in population and balanced translocations were found we did not (we do not) counsel termination of pregnancy (TP). For the cases of gonosomes changes (yes/no), especially in mosaic form, decision about TP should be left to parents, because clinically, in the future, no development of severe mental retardation is expected, although the occurrence of sterility is possible. However, unbalanced translocations, mosaicism and aneuploidy were considered as indication for TP. For these women (couples) it is prerogative to carry out prenatal diagnostic during the next pregnancy as well as to repeat the genetic counseling (13).

In respect to the fact that invasive prenatal testing method bear certain risk of miscarriage,
more and more women are choosing non-invasive prenatal testing methods such as analysis of circulating cell-free fetal DNA. Although detection of aneuploidy with this method is not 100% accurate, many couples, especially those with reassuring serum aneuploidy screening and normal ultrasound findings appear to favor a small risk of misdiagnosis of aneuploidy over the risk of procedure-related to pregnancy loss (14,15).

Conclusion:-

De novo chromosomal changes were most abundant in samples obtained from elderly woman. Therefore maternal age is the most prominent indicator for amniocentesis.

Disclosure Statement:-

The authors declare that they have no conflicts of interest.

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