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PRENATAL GENETIC STUDY OF THE MAIN ALTERATIONS FOUND IN THE CITY OF GOIÂNIA - GOIÁS

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Abstract: Introduction: The first prenatal screening test was introduced in the 1970s: a single second trimester serum test for maternal serum alpha-fetoprotein, a marker of neural tube defects. Screening for aneuploidy using maternal serum markers was introduced in the 1980s, and the number and complexity of screening tests offered has been on an upward trajectory since then. Prenatal genetic screening is used to assess whether there is an increased risk of the fetus being affected by a genetic disorder. **Objective**: To evaluate the main alterations found in prenatal genetic studies. **Methods**: This is a cross-sectional, analytical, descriptive epidemiological study that will be carried out at the malformation outpatient clinic of Clínica Fértile with the findings of the last 4 years. **Results**: We found 73 results with fetal anomalies with a mean maternal age of 32, ranging from 16 years to 45 years. The main indication was due to increased NT with 34 (46.9%) of the cases, amniocentesis was the main test of choice 65 (89%), the age of highest incidence of changes were with maternal age below 35 years in 46 (63%) of the cases. The main alteration found was Trisomy 18, 24 (32.9%) followed by Trisomy 21 23 (31.5%), in women under 35 years the main alteration was Trisomy 18 in 18 (39, 1%) and in women over 35 years old, the main alteration was Trisomy 21, 14 (51.9%). **Conclusion**: In the studied group, there were 36.1% of alterations in a prenatal genetic study. The most prevalent maternal age was women under 35 years of age. Alterations in NT was the main indication for the genetic study. The most used technique was amniocentesis.

Keywords: Genetic Study, Alterations, Amniocentesis.

INTRODUCTION

The first prenatal screening test was introduced in the 1970s: a single serum test in the second trimester for maternal serum alpha-fetoprotein, a marker of neural tube defects. Screening for aneuploidies using maternal serum markers was introduced in the 1980s, and the number and complexity of screening tests offered has been on an upward trajectory ever since. Prenatal genetic screening is used to assess whether there is an increased risk of the fetus being affected by a genetic disorder. Originally, prenatal genetic testing focused mainly on trisomy 21 (Down's syndrome), but can now detect a wide range of genetic disorders. Today, prenatal genetic screening falls into four categories: ultrasound, maternal carrier status for specific genetic diseases, maternal serum assays looking for specific biochemical markers indicative of aneuploidy and, more recently, fetal cell-free DNA in maternal plasma (cffDNA), which has been used for aneuploidy, microdeletions and copy number variants (CNVs). Maternal serum assays include first trimester screening, triple screening, quadruple screening and penta screening. There is also the option of combining first and second trimester screening with an integrated, sequential or contingent screening protocol. This provides a higher detection rate than one-step screening[1].

The American Congress of Obstetricians and Gynecologists recommends that all pregnant women receive aneuploidy screening or diagnostic testing. Proper counseling before and after the test is important to ensure proper understanding of the results and to ensure that the testing strategy is in line with the patient's goals.[2]

Although prenatal testing has historically focused on the option of termination of pregnancy, a growing number of prenatal and perinatal treatments are available. As more in utero therapies are developed, the detection

of disorders that are amenable to and would benefit from immediate prenatal or neonatal targeted therapy will increasingly be a focus of prenatal testing[3,4].

Therefore, the aim of this study is to evaluate the main alterations found in prenatal genetic studies, as well as the characteristics of maternal age that are most prevalent in pregnant women who undergo prenatal genetic studies, thus establishing the most frequent indications for prenatal genetic studies and consequently the technique most used in prenatal genetic studies.

MATERIALS AND METHODS

TYPE AND LOCATION OF STUDY

This is a cross-sectional, analytical, descriptive epidemiological study that will be carried out at the Fertile Clinic's malformation outpatient clinic, with findings from the last 4 years.

STUDY POPULATION

Database of tests carried out on women who underwent prenatal genetic studies at Fértile's malformations outpatient clinic, January 2018 to December 2022.

INCLUSION CRITERIA

Database of women's exams

EXCLUSION CRITERIA

Not enough data.

DATA COLLECTION INSTRUMENTS

To collect the data, the researcher prepared a form (attached) with the necessary variables.

DATA ANALYSIS

The data collected was stored in Microsoft Excel 2013 software (Microsoft®, USA). The Statistical Package for the Social Science (SPSS) software (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, version 21.0, USA) was used for analysis.

ETHICAL ASPECTS

The research under the title "FETAL MATERNAL ASPECTS REFERRING TO PRE-NATAL GENETIC STUDY", has been duly submitted to the Ethics Committee through the Brazil platform, under registration 62432422.6.0000.8058 and with opinion number 5.610.610, respecting the ethical principles that regulate research on human beings (resolution 466/12).

RISKS AND BENEFITS

The research will involve minimal risk and the handling of the database will be done in a safe manner and the researcher undertakes not to identify the patients.

The benefits are related to knowing the profile of these patients and drawing up public policies for greater clarification and knowledge about prenatal genetic tests.

RESULTS

A total of 202 patients who underwent prenatal genetic testing were evaluated, and 73 of these were found to have fetal anomalies. The average age of the women surveyed was 32, ranging from 16 to 45.

INDICATIONS	N	%
Altered NT	34	46,6%
Cardiac changes	10	13,7%
Brain malformations	10	13,7%
Cystic hygroma	4	5,5%
Abortion	3	4,1%
Absence of nasal bone	2	2,7%
Cervical cystic angioma	1	1,4%
Maternal anxiety	1	1,4%
Abdominal closure defect	1	1,4%
Diaphragmatic hernia	1	1,4%
Hydrocephalus	1	1,4%
Hydrops	1	1,4%
Myelomeningocele	1	1,4%
Oligoammio	1	1,4%
Omphalocele	1	1,4%
Growth restriction	1	1,4%
Total	73	100%

Table 1 - Main indications for genetic testing, Goiânia, 2022.

Genetic testing	N	%
Amniocentesis	65	89,0%
BVC	4	5,5%
Abortion	4	5,5%

Table 2 - Main genetic tests carried out, Goiânia, 2022.

Maternal age changes	N	%
< 35 years	46	63,0%
> 35 years	27	37,0%

Table 3 - Maternal age with changes in genetic tests, Goiânia, 2022.

Main changes	N	%
Trisomy 18	24	32,9%
Trisomy 21	23	31,5%
Trisomy 13	8	11,0%
45 x	14	19,2%
46 xx +14	1	1,4%
47 xx +15	1	1,4%
69 XXX	1	1,4%
Trisomy 19	1	1,4%

Table 4 - Main alterations found in the genetic tests carried out, Goiânia, 2022.

Maternal age	Main changes	N	%
< 35 years			
	Trisomy 18	18	39,1%
	45 x	11	23,9%
	Trisomy 21	9	19,6%
	Trisomy 13	6	13,0%
	46 xx +14	1	2,2%
	47 xx +15	1	2,2%
> 35 years			
	Trisomy 21	14	51,9%
	Trisomy 18	5	18,5%
	45 x	3	11,1%
	Trisomy 13	3	11,1%
	69 XXX	1	3,7%
	Trisomy 19	1	3,7%

Table 5 - Maternal age and the main changes in genetic tests, Goiânia, 2022.

DISCUSSION

Human cytogenetics was born in 1956 with the fundamental but empowering discovery that normal human cells contain 46 chromosomes. Since then, this field and the understanding of the link between chromosomal defects and disease have grown and have been accompanied by advances in cytogenetic technology[5].

In the study evaluated, the main indication for genetic testing was due to increased NT in 34 (46.9%) of the cases and amniocentesis was the main test of choice in 65 (89%). Ultrasound detection of markers is associated with a high frequency of uptake for genetic prenatal testing. Increased nuchal thickening is associated with greater acceptance of amniocentesis[6] and its identification may be suggestive of trisomy[7].

By evaluating 919 pregnant women who underwent ultrasound examination, they were selected for interventional prenatal diagnosis in order to detect fetal chromosomal abnormality. The rate of chromosomal abnormality detection increased significantly with FN thickness, advanced maternal age and

the presence of other ultrasound abnormalities (P<0.05). Trisomy 21 was the most common abnormality, with a predominance of male fetuses. Increased FN thickness is strongly associated with the risk of fetal chromosomal abnormalities, advanced maternal age and the presence of additional ultrasound abnormalities[8].

In practically all cases of fetal malformations detected during prenatal care, chromosome analysis is indicated. Amniocentesis is the most common means of fetal chromosome analysis[9].

The age with the highest incidence of alterations was maternal age under 35 in 46 (63%) of the cases. Fetal chromosomal abnormalities may be caused by a phenomenon of non-disjunction that occurs in the period of meiosis during maternal oogenesis, which has been reported to have a direct association with maternal age. Therefore, pregnancy at an advanced age is a critical risk factor for fetal chromosomal abnormalities. Currently, fetal chromosomal abnormalities due to maternal age have been reported to include trisomy 21, trisomy 18, trisomy 13, triple X syndrome and Klinefelter syndrome[5].

In other studies, this change is divergent, which may be explained by the fact that this is a reference service in the state and only treats fetal malformations. In a study of 15,381 pregnant women, the incidence of aneuploidies increased exponentially with maternal age (P<0.0001). In particular, the risk of trisomy 21 (standard error [SE], 0.0378; odds ratio, 1.177; P <0.001) and trisomy 18 (SE, 0.0583; odds ratio, 1.182; P = 0.0040) showed a significant correlation with maternal age. Advanced age is no longer used as a threshold to determine who is offered prenatal diagnosis, but it is a common risk factor for fetal chromosomal abnormalities[10].

The main alteration found was Trisomy 18, 24 (32.9%) followed by Trisomy 21 23 (31.5%), in women under 35 the main alteration was Trisomy 18 in 18 (39.1%) and in women over 35 the main alteration was Trisomy 21, 14 (51.9%).

In trisomy 18, as in other trisomies, maternal age is usually higher. There is no doubt in the literature that this is the most important predisposing factor for the non-disjunction of chromosomes in the process of cell division. Most cases of trisomy 18 occur due to de novo meiotic non-disjunction in phase II of maternal meiosis. Interestingly, in other trisomies the defects commonly occur during phase I of meiosis. Chromosomal translocations can occur as new (de novo) anomalies or can be passed on within a family. Chromosomal mosaicism, on the other hand, is always a post-zygotic event. The main cause is mitotic non- disjunction, which can occur at any stage of embryogenesis or development[10]. The risk of chromosomal abnormalities increases with advancing maternal age and is independent of ethnicity[11].

This study confirms that increased NT is a chromosomal abnormality factor and that chromosomal analysis is part of its identification, which can facilitate counseling and appropriate management.

CONCLUSION

After a thorough study of the data collected, we concluded that in the group studied there were 36.1% of alterations in prenatal genetic studies. We also found that the most prevalent maternal age was among women under 35.

Finally, alterations in the NT were the main indication for the genetic study, and the most commonly used technique was amniocentesis.

New studies for a more comprehensive parameter of alterations in prenatal genetic studies in the city of Goiânia and the state of Goiás are necessary so that measures in the field of medical genetics and personalized medicine can be taken by health authorities.

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