Original article

STUDY OF CHROMOSOMAL ABNORMALITIES ENCOUNTERED IN A MATERNITY HOSPITAL BETWEEN 2010 AND 2014

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ABSTRACT: This study sought to identify the existence of chromosomal abnormalities recorded in the medical records of live-born infants in a maternity hospital. This retrospective study analyzed the information contained in the medical records of the archives of the Medical Archiving Service of a maternity hospital in Amazonas state between January 2010 and December 2014, with the correlation between the chromosomal abnormalities and the characteristics of the mothers and the live-born infants also studied. A total of 15,621 records were analyzed, of these 163 presented congenital defects, with 15 diagnosed with chromosomal syndromes, divided into three types of anomalies: 13 individuals with Down syndrome, one with Patau syndrome and one with Dandy-Walker syndrome. This is the first registration of the occurrence and profile of births with chromosomal abnormalities in a maternity hospital. The result is of great importance for the public health service of the state. The performance of further studies may provide a better overview of the different genetic diseases of this state.
DESCRIPTORS: Congenital abnormalities; Pregnancy; Descriptive epidemiology; Live-born infant.

ESTUDO DAS ANOMALIAS CROMOSSÔMICAS OCORRIDAS EM UMA MATERNIDADE NOS ANOS DE 2010 A 2014

RESUMO: O presente estudo buscou identificar a existência de anomalias cromossômicas registradas nos prontuários de nascidos vivos em uma maternidade. Estudo retrospectivo que analisou as informações contidas nos prontuários dos arquivos do Serviço de Arquivamento Médico de uma maternidade do estado do Amazonas entre janeiro de 2010 e dezembro de 2014, e estudou-se a correlação de anomalias cromossômicas presentes com características maternas e do nascido vivo. Analisou-se 15.621 prontuários, destes 163 apresentaram defeitos congênitos, 15 foram diagnosticados com síndromes cromossômicas distribuídas em três tipos de anomalias: 13 indivíduos com Síndrome de Down, um com Síndrome de Patau e um com Síndrome de Dany-Walker. Este é o primeiro registro de ocorrência e perfil dos nascimentos com anomalias cromossômicas em uma maternidade. O resultado é de grande importância para a saúde pública do Estado. A realização de novos estudos poderá fornecer um melhor panorama sobre diferentes doenças genéticas daquele estado.
DESCRITORES: Anormalidades congênitas; Gravidez; Epidemiologia descritiva; Nascimento vivo.

ESTUDIO DE LAS ANOMALÍAS CROMOSÓMICAS QUE OCURRIERON EN UNA MATERNIDAD EN LOS AÑOS DE 2010 A 2014

RESUMEN: Este estudio tuvo la finalidad de identificar la existencia de anomalías cromosómicas registradas en los prontuarios de nacidos vivos en una maternidad. Estudio retrospectivo hecho por medio de análisis de informaciones contenidas en los prontuarios de los archivos del Servicio de Archivo Médico de una maternidad del estado de Amazonas entre enero de 2010 y diciembre de 2014. Fue examinada la correspondencia de anomalías cromosómicas presentes con características maternas y del nacido vivo. Se analizaron 15.621 prontuarios, de los cuales 163 presentaron defectos congénitos, 15 fueron diagnosticados con síndromes cromosómicas distribuidas en tres tipos de anomalías: 13 individuos con Síndrome de Down, un con Síndrome de Patau y un con Síndrome de Dany-Walker. Este es el primero registro de ocurrencia y perfil de los nacimientos con anomalías cromosómicas en una maternidad. El resultado tiene gran importancia para la salud pública del estado. La realización de nuevos estudios podrá traer un mejor panorama acerca de distintas enfermedades genéticas del estado.
DESCRIPTORES: Anormalías congénitas; Gravidez; Epidemiología descriptiva; Nacimiento vivo.

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INTRODUCTION

During embryonic development, changes may occur that result in congenital anomalies, causing the appearance of small asymmetries or even defects that may compromise aesthetic and functional aspects[1-2].

The rate of congenital anomalies reaches 2 to 3% of live births, affecting different organs and systems. It has been estimated that 25% of these defects are related to the genetics, 10% of environmental origin and 65% caused by unknown factors[3].

According to studies[4], all populations are at risk of developing congenital malformations, however, the frequency and type of these defects vary with race, ethnicity and socioeconomic conditions, as well as with access to health services, nutrition, lifestyle and maternal education, particularly those related to the neural tube[4].

With advances in technology, some testing for congenital defects are performed during pregnancy, leading to a significant improvement in the diagnostic power for various congenital diseases and developmental abnormalities. The cytogenetic study and enzymatic assays enable the diagnosis of the majority of chromosomal abnormalities and innate errors of metabolism in the prenatal period[5].

Although the tests are accurate, many cases of chromosomal syndromes are not identified during the fetal life, since the specific test for such detection is mainly applied with mothers over 35 years of age. Thus, the records show that the percentage of children with chromosomal syndromes is higher in mothers under 30 years of age[6].

Prenatal tests have shown that the aneuploidies are among the most common genetic abnormalities, with trisomies involving chromosomes 13, 18 and 21 being diagnosed more frequently. Down syndrome (trisomy 21), preceded by Edwards syndrome (trisomy 18) are among the most common trisomies observed at birth[7].

The advance of Genetics, in recent decades, has enabled new discoveries regarding the various genetic diseases. However, in the case of chromosomal abnormalities in northern Brazil, much is still needed to report, for example, some basic aspects such as their epidemiological and statistical data. The lack of data regarding the investigation of chromosomal abnormalities in the state of Amazonas justified the development of this study.

Thus, the aim was to identify chromosomal abnormalities that occurred in live-born infants in a reference maternity hospital of the city of Manaus and, where possible, to associate these with factors related to the maternal profile and that of the live-born infants that presented these chromosomal abnormalities.

METHOD

This retrospective descriptive study[8] aimed to analyze the prevalence of live-born infants with chromosomal anomalies from January 2010 to December 2014 in a maternity hospital in the city of Manaus-AM, Brazil.

The study population consisted of the records of live-born infants with clinical and/or cytogenetic diagnosis of chromosomal abnormalities in the period from January 2010 to December 2014. Between February and September 2015, 15,621 records of live-born infants from January 2010 to December 2014 were analyzed, archived by the Medical Archive Service (SMAS) of the maternity hospital, to identify the presence of chromosomal abnormalities described in them.

All medical records with cases of congenital malformations were analyzed. The records of newborns that did not have clinical and/or laboratory diagnosis of congenital malformation were excluded, as were records with incorrect completion or that presented inconsistencies in the information, those not found by the research team or records that were damaged (wet, stained, etc.).

For the data collection, the completion of a structured questionnaire was used based on information

in the Live Birth Declaration (DNV), as well as medical forms completed by obstetricians, neonatologists, and intensive care staff and, when present, information contained in the diagnostic and imaging tests, such as ultrasound and x-rays.

With the completion of the questionnaire/instrument, it was possible to generate general and specific data regarding the presentation of newborns in the pre and postnatal period, related to any congenital alteration reported by the medical staff. Among the information highlight were those data related to the maternal characteristics, such as maternal age, history of family congenital malformation and abortions, type of delivery, performance and number of prenatal visits, and those related to the live-born infant, such as gender, weight, Apgar score at 1 and 5 minutes and gestational age.

After collection, the data were first tabulated in a database using the Microsoft Office Excel 2013 program according to the variables analyzed and subsequently transferred to the SPSS 16.0 statistical software, with tests carried out to obtain the mean, median and standard deviation.

The study was approved by the Research Ethics Committee of the State University of Amazonas under Authorization No. 048/2012, following all legal and ethical aspects of research involving human subjects.

RESULTS

The analysis of the records showed that there were 15,621 births; of these, 163 (1.04%) presented congenital malformations, of which 81 patients (49.70%) were male and 72 (44.17%) female, another 10 (6.13%) were cases of indeterminate sex, or the records were without the information.

Different types of congenital malformations were found among the live-born infants, with chromosomal abnormalities accounting for 15 (9.20%), less frequently those of the urinary tract, accounting for 2 (1.22%), and most commonly those of the nervous system, with 37 (22.70%).

Among the 15 chromosomal abnormalities found in the medical records, three types of syndromes were recorded: 13 cases (86.66%) of Down syndrome, 1 case (6.67%) of Patau syndrome and 1 case (6.67%) of Dandy-Walker syndrome. Data related to the profile of live-born infants that presented chromosomal abnormalities are shown in Table 1. For the mother, the data of the maternal profile were also analyzed, based on data from 13 women who underwent prenatal care, as shown in Table 2.

Table 1 - Profile of live-born infants that presented chromosomal abnormalities in the 2010-2014 period, in the Balbina Mestrinho Maternity Hospital. Manaus, AM, Brazil, 2016

Anomaly	N	Gender		1st min Apgar		5th min Apgar		Gestational age			Weight			
		M	F	<7	>7	<7	>7	<37	37 to 41	>42	L	I	A	FM
DS	13	4	9	-	13	-	13	1	10	2	1	4	7	1
PS	1	-	1	1	-	1	-	1	-	-	1	-	-	-
DWS	1	-	1	-	1	-	1	1	-	-	-	1	-	-

Legend: DS = Down syndrome, PS = Patau syndrome, DWS = Dandy-Walker syndrome, M = male, F = female, L = low, I = insufficient, A = appropriate FM = Fetal macrosomia.

Table 2 – Maternal data of mothers of live-born infants that presented chromosomal abnormalities in the 2010-2014 period, in the Balbina Mestrinho Maternity Hospital. Manaus, AM, Brazil, 2016

Anomaly	N	Maternal age					CMF		Abortion hist.		Birth		Number of consultations		
		15 to 19	20 to 24	25 to 29	30 to 34	≥35	NI	N	Y	N	V	C	1 to 3	4 to 6	≥7
DS	*13*	4	1	2	1	4	10	3	2	11	9	4	2	*7*	3
PS	1	-	-	-	1	-	-	1	1	-	-	1	-	1	-
DWS	1	-	1	-	-	-	1	-	-	1	-	1	-	-	1

Legend: NI = No information, V = vaginal, C = Cesarean (-) no recorded case. DS=Down syndrome, PS=Patau syndrome, DWS=Dandy-Walker syndrome. Y= yes, N= no, CMF= Case of family malformation.
Italics =case of DS maternal age NI; 1 case of DS in which number of prenatal consultations had no information .

DISCUSSION

Regarding genetic diseases, it is known that chromosomal disorders commonly lead to miscarriages, birth defects and developmental delays. The cause of these anomalies is mainly related to the position, location and number of genes distributed in the genetic material[9]. Some studies have reported the prevalence of live-born infants with congenital anomalies ranging between 1.0% and 7.0%[10].

The results of this study found the incidence of 163 (1.04%) live-born infants with congenital abnormalities, data similar to that found by other studies conducted in Brazilian hospitals. In a study of a maternity hospital in the city of Campina Grande-PB[11], the results showed 1.1% of live-born infants with congenital anomalies, based on a search in the obstetric and neonatal medical records. A similar result showed 1.2% of live-born infants in a maternity hospital of Porto Alegre-RS[12] and 1.3% reported in a maternity hospital of Campinas-SP[13].

Lower values than those found in the results of the present study were highlighted in a study of births to mothers living in Maringá-PR, which recorded 0.8% of cases of live-born infants with some type of congenital anomaly[14] and 0.8% reported for the city of Rio de Janeiro[15]. However, studies also show even lower values of this incidence, such as the 0.4% found by the Health Department of Contagem in Minas Gerais[16].

Several factors can lead to congenital anomalies, with these being directly related to events prior to the birth, hereditary or acquired[1]. Chromosomal defects may result from genetically abnormal gametes and irregularities in the embryonic division. There is a prevalence of chromosomal alterations related to the female gamete, with this being closely related to the fact that the eggs have the same chronological age as the woman, unlike the sperm, which are renewed every two months[17].

Regarding the most frequent chromosomal abnormality, in the present study Down syndrome, with 13 cases (86.66%), was the most frequent chromosome abnormality in the live-born infants in the maternity hospital studied, which is in accordance with the literature. This was followed by only two other syndromes (Patau Syndrome and Dandy-Walker Syndrome). In Brazil every year there are on average 8,000 live-born infants with DS and an incidence of 1 in every 600-800 births. Data show that about 18-20% of the mentally impaired patients assisted in Brazilian specialized institutions present DS[18].

Among the aneuploidies, the most common are related to the occurrence of an additional autosome, i.e. trisomy (three chromosomes instead of the normal pair). Among them, the most common type of viable human aneuploidy is Down syndrome, or trisomy 21, which may result from meiotic nondisjunction (meiosis I or II) of chromosome pair 21[19].

The reproductive age of the mother has been one of the factors related to the emergence of chromosome trisomies in humans, with more advanced age equating to higher risk[20]. This has been demonstrated in Bahia, with a retrospective study relating maternal age and Down syndrome, which demonstrated the correlation of 43.6% between the age of the mothers at the time of the birth and the infant being born with Down syndrome[3]. In the present study, when analyzing the maternal age factor, related to the number of births with chromosomal abnormalities, the same prevalence was found among women aged 15-19 years and those >35 years, this being 4 cases (26.66%).

Another study[20] demonstrated that, in adolescent mothers with multiple pregnancies, the probability of giving birth to a child with a chromosomal abnormality was 6.1 times higher compared to adolescents with single pregnancy, and for the late mother, the chances were 11.4 times higher when compared to mothers aged 20-34 years. Conversely, there are some studies performed in Brazil that did not show an association between maternal age and congenital anomaly[21-22]. The decrease in the number of eggs and aneuploid embryos in women with older ages may also be related to the emergence of trisomies[2].

For this reason, the karyotype examination carried out on the fetus has been recommended for mothers of more advanced age. Since the 1980s, the diagnostic centers in developed countries have carried out tests to detect this anomaly, especially Down syndrome.

The karyotype examination is an important, insightful and significant tool for couples who need a diagnosis for their newborn. With this test, different types of chromosomal abnormality can be identified, such as those resulting from translocation or chromosomal inversion. In addition to providing the correct and conclusive diagnosis, the information generated is important for the clinician/physician responsible for establishing the risk of other miscarriages or fetal abnormalities in future pregnancies, or in the case of couples with normal karyotype, to direct the inquiries toward other genetic or non-genetic causes, according to the protocols established in the literature[19].

The definitive diagnosis of congenital anomalies is of fundamental importance for parents whose children are carriers of an anomaly. Despite the low frequency, the definitive diagnosis promotes proper and effective genetic and reproductive counseling, confirming the likelihood of success faced with a new pregnancy[23].

According to the results of the analyzes, the majority of the pregnant women carried out the prenatal examination. It is extremely important to know the clinical features and prognosis of the patients with chromosomal abnormalities, as this situation will help in the decision related to whether to establish or not invasive treatments such as surgical interventions. The prenatal examination is a very important, rapidly confirmed diagnosis allowing good decisions to be made regarding the medical management.

A good example of the applicability of the importance of conducting the prenatal examination concerns the identification of patients that present pregnancy with trisomy 18, mainly to anticipate the preparations for the birth. It should be noted that, due to Article 128 of the Penal Code. - Law Decree 2848/40 current in Brazil, the interruption of pregnancy is not permitted, even when the diagnosis of chromosomal abnormality is confirmed, with there being exceptions in only two cases where the pregnancy may be interrupted: first due to the likely death of the mother or, second, in cases of sexual violence[21].

Many couples may be carriers of chromosomal alterations and they will pass these on to their descendants. For these couples who have chromosomal abnormalities, during the genetic counseling process, the realization of the Prenatal Diagnosis (chorionic villus sampling or amniocentesis) would be very important if the couple opt for further pregnancies. Furthermore, the possibility exists of assisted reproduction accompanied by Preimplantation Genetic Diagnosis (PGD) for the selection of embryos that do not carry the chromosomal abnormalities prior to implantation[19].

It is important that health professionals take into consideration that Genetic Counseling does not involve inaccessible knowledge and can be carried out where there is no geneticist[23]. When there is no geneticist available, other health professional can be provided with the information necessary to carry out genetic counseling, even if this consists of simply giving basic information to the couple, who usually do not have any information about heredity.

The ideal genetic counseling would be one performed with detailed anamnesis, detailed clinical examination, photos of the entire body and of the affected area, in the case of physical anomalies, clinical pathology, in the case of death, skeletal X-rays, in cases of suspected skeletal dysplasia, report with the results of other tests that have been carried out, cytogenetic study, in cases of suspected chromosomal abnormality and/or a molecular test (DNA-deoxyribonucleic acid test)[24].

It is necessary to improve the information systems already available in Brazil in relation to chromosomal abnormalities, as these data have been found to be very scarce. A closer relationship between private institutions and public institutions would help to clarify this information, making data available to the population[25].

The study presented here was conducted from the collection and analysis of retrospective data from the medical records of live-born infants. It should be noted that, for the physician, it is difficult to exactly identify the reason for a miscarriage, as is the provision of high quality genetic services, for good genetic counseling.

In Brazil, from 2000, an updated version of the DNV was adopted, with Field 34 including the need to report the presence or absence of "congenital malformation and/or chromosomal abnormality". This fact is very important for the better development of community genetics in Brazil. Prior to the inclusion of Field 34, the information was only generated from death certificates (DO), which were obtained from the Mortality Information System (SIM)[25].

Despite this advance, studies show that the quality of the reporting of congenital anomalies in these records is not always satisfactory[25-27]. The results obtained by other authors[28] showed a 60.7% underreporting for congenital malformations in the birth declaration recorded in the Mortality Information System, obtained from data contained in the Live Births System with deaths in Porto Alegre-RS[28].

It should be emphasized that the introduction and use of the Field 34 will only have relevance and reliability if its implementation is effective and correct, with the completion of the data taken very seriously. Many factors compromise the use of the DNV as a information resource regarding birth defects, a major factor being related to the moment that the description of the anomaly is transcribed from the medical records to the DNV, as well as the use of codes and the input into the Live Births Information System (SINASC).

It can be observed that, for a better study of chromosomal abnormalities, there is a need for improvements in the existing information systems, thus errors would be avoided in the interpretation and use of the data related to the failure rate in its registration. Strategies for better performance in the health actions activities, in both the consultation and the prevention of genetic diseases, would be greatly improved when completing Field 34 effectively, supplying data about the real value of the Brazilian reality in relation to congenital defects.

The results of this study reflect, in a general way, how the DNV is completed and especially how this document, extremely important for epidemiological investigations, has been neglected in some institutions. It should be noted that the realization of congenital malformation studies based on data contained in the DNVs, is highly reliable when they have the smallest possible number of uncompleted fields. However, some DNVs were excluded from this investigation for precisely this reason.

It is important to note the high number of DNVs in bad condition, having erasures or even absent from the medical records, which creates a substantial loss of information. The fact that some hospitals do not have a computerized system available to input into this database further enhances this loss and hinders access to the information, making it necessary for the search to be performed manually, as was the case. Because it is a direct source of information, care in the completion and maintenance of the DNVs becomes extremely important, especially for generation of the epidemiological profile and for decision making regarding prevention strategies.

CONCLUSION

In this study, the main objective was to identify the chromosomal syndromes present in the sample and their frequency, to remedy the need to generate data on the subject in the state of Amazonas. Thus, after the analysis of records from 2010 to 2014, it was found that, of all congenital malformations recorded in live-born infants, 9.2% were due to chromosomal abnormalities, the most frequent being Down Syndrome (86.6%).

Although the literature mentions that aneuploidy tends to appear in fetuses generated by older mothers, the present study found the same prevalence for women in the 15-19 and >35 years age groups. The great importance of completing Field 34 accurately must be stressed, so that the real value of the data related to congenital malformation and/or chromosomal abnormality can be obtained.

Considering the lack of studies on chromosomal abnormalities in the state of Amazonas, this work provides descriptive results that, it is hoped, can assist in planning care actions and public policies directed toward families and individuals with chromosomal abnormalities. It is believed that the results can support discussions for the development of appropriate public policies and strategies aimed at the health of women and children with respect to the prevention of congenital anomalies.

This is the first investigation of the occurrence and description of the profile of births with chromosomal abnormalities, performed in a maternity hospital in Amazonas, which, although it is the largest state in the Brazilian federation, lacks infrastructure and trained personnel to carry out this type of service and care.

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