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RARE GENETIC DISEASES IN HUMANS IN NORTHEASTERN BRAZIL: A SYSTEMATIC REVIEW

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ABSTRACT

Rare genetic diseases in humans affect 65 out of every 100,000 inhabitants. In Brazil, more than 13 million people are affected. The Northeast region has a higher rate than the rest of the country. To identify the scientific panorama of the Brazilian Northeast in the last 20 years, a systematic review was carried out in the following online databases: Scopus, PubMed/MEDLINE, Web of Science, Biomed Central and JAMA. The following Boolean

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arguments and operators were used to search: "Rare Genetic Diseases" AND "Northeastern" AND "Brazil" AND "Humans". The data were evaluated on the online platform, 'Rayann', in a blind review. The websites "OMIM" and "ORPHANET" were used to obtain genetic information. 797 records were found, but after the selection and filtering were completed, only 29 articles remained. Mucopolysaccharidosis was more frequent, with 27%. Cystic Fibrosis and Berardinelli-Seip Syndrome had 7%, and all the rest of the diseases corresponded to 50% of the remaining results, totaling 30 diseases, as one article cited two diseases. Bahia obtained 36% of rare diseases and had the largest number of research institutions; Pernambuco 24%; Ceará 16%; Paraíba 12% and Alagoas, Maranhão and Rio Grande do Norte, 4%, in each, respectively. The Northeast region was reported as the place of occurrence in 16% of the cases. A total of 32 genes were identified, most of them with autosomal dominant inheritance. The Northeast had superiority in research institutions and it is concluded that despite the increase in publications from 2016 to 2018, more investments are needed in this important field of research.

Keywords: Orphan Diseases. Hereditary Diseases. Northeast.

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INTRODUCTION

Rare diseases can be considered as conditions constantly associated with physical, behavioral, sensory, and intellectual limitations. However, there is no single definition for these conditions. According to European criteria, they can be characterized as degenerative, debilitating, chronic diseases associated with decreased life expectancy, and their incidence is less than 5 per 10 thousand inhabitants. Lima et al 2018 and Iriart et al 2019.

From the epidemiological point of view, the expression "rare disease" adds a positive action, because certain groups with a specific rare pathology, when looked at in isolation, end up being considered reduced, however, when grouped by the "rare" characteristic, they become epidemiologically visible. Moreira et al 2018.

According to the Brazilian Ministry of Health, there is an estimate that there are 13 million people affected by rare diseases in the national territory, and they affect 8% of the world's population, 80% of which are the result of genetic factors, usually from mutations and with recessive inheritance. While the rest come from environmental, immunological, infectious causes, among others. Because of this, these genetic pathologies are the second largest cause of infant mortality in Brazil. Damasceno et al 2018 and Santos et al 2020.

Rare genetic diseases can be congenital when they arise from genetic alterations during the embryofetal period or manifest later in life, such as progressive neurogenetic diseases and cancer, which usually develop due to cumulative genetic and environmental factors. This combination of genetic predispositions and environmental factors ends up making it difficult to diagnose rare diseases. Madhu et al 2024; Umair et al 2024.

Brazil, with its continental dimensions, has a scarcity of data on populations affected by rare genetic diseases in humans. The available information is usually limited to studies on specific pathologies, such as some neurodegenerative and genetic diseases. In addition, much data comes from international projects and research groups, which carry out research in the Brazilian territory. This, in a way, makes the data restricted to the public, with the exception of those published in journals or presented at congresses. Cardoso-dos-Santos et al, 2021.

In relation to the Brazilian Northeast, it is noted that this region has a high incidence of rare genetic diseases in humans, and one of the possible causes would be the high frequency of consanguineous marriages, which occur in small towns in the region. Statistical analyses show a correlation between inbreeding and the prevalence of

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congenital anomalies. Santos et al 2010 and Weller et al 2012 and Nascimento et al 2022. Especially in relation to rare diseases. Temaj et al, 2022.

Thus, the work in question aims to carry out a systematic review, through consultation in online databases, to identify and analyze the occurrence of rare genetic diseases in humans, from research carried out in the Brazilian Northeast.

MATERIAL AND METHODS

The present study is a systematic review of the scientometric, observational, ecological literature, with data obtained from scientific articles. The guiding question of the study was established as: "What are the characteristics described in scientific studies conducted in the Northeast region of Brazil on rare generic diseases in humans?".

STUDY DESIGN

The question of the study was defined considering the PICOS anagram. Methley et al 2014. Where P = "Population" represents Population (population affected by rare genetic diseases found in scientific studies in the Northeast of Brazil); I = "Intervention" (which does not apply in this case); C = "Comparation", which relates to Comparison (which does not apply in this case); O = "Outcome", which represents Outcome (characterization of cases of rare genetic diseases in the Brazilian Northeast) and S "Study design" representing the type of design of the studies analyzed (observational genetic studies).

STUDY CRITERIA

The present systematic review also followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Page et al 2021. The inclusion criteria considered scientific articles developed in the Northeast region, which contained genetic and demographic information on rare genetic diseases in humans. The searches were carried out considering the studies published in the following languages: Portuguese, English and Spanish. The following were excluded: duplicate articles; studies carried out that did not correspond to the languages adopted in the search strategies; that were not conducted in the Brazilian Northeast; those who did not fit the study question, and those who could not access the full text.

The search script included rare genetic diseases in humans, encompassing genetic information and its prevalence in the Brazilian national territory with emphasis on the

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Northeast. The search was carried out with the help of Boolean arguments and operators. Munhoz et al 2021. The arguments and operators used for the search were the following: "Rare Genetic diseases" AND "Northeastern" AND "Brazil" AND "Humans".

STUDY SELECTION AND DATA EXTRACTION

For the selection of studies and data extraction, after the removal of duplicate records, two independent researchers selected the articles through the analysis of the title, abstract, and full text, in sequential stages and separated from each other, according to the inclusion and exclusion criteria predefined above. The two researchers independently selected the records (in a double-blind analysis) and then had access to each other's information to verify the agreement regarding the inclusion and exclusion of each one. For this stage, the data were imported into the online platform, "Rayann" (https://www.rayyan.ai/), for collaborative selection of articles from blind review and marking of the records to be excluded and included. Ouzzani et al 2016. There were no divergences between the opinions of the two researchers. However, if there was, a third researcher would be invited to resolve the impasse. Do Carmo Silva et al 2022.

DATA ANALYSIS

The present systematic review was conducted in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). He discussed the occurrence of rare genetic diseases in the Northeast of Brazil in the last 20 years (2004 to 2024), with genetic analysis and spatial distribution. To this end, a search was carried out in several bibliographic databases on rare genetic diseases in humans in the Brazilian Northeast. The research was developed at the Federal University of Campina Grande – UFCG, on the campus of Patos, and as only bibliographic databases and information from articles published on the internet were used as a source, no authorizations were required prior to the beginning of the development of the work. In addition, according to Law No. 13,709, of August 14, 2018 - General Law for the Protection of Personal Data (LGPD), no personal data of the patients analyzed in the national and international public access databases consulted was accessed.

The following online databases were examined: Scopus, PubMed/MEDLINE, Web of Science, Biomed Central, and Journal of the American Medical Association – JAMA. All websites were accessed through the capes periodicals portal on July 1, 2024. Therefore,

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for this work, the period from 06/01/2004 to 06/01/2024 was considered; with an end date for the year 2024 of July 1, 2024.

The Online Mendelian Inheritance in Man – OMIM website was also used, which is composed of a dataset, electronically distributed by the National Center for Biotechnology Information (NCBI), which integrates a comprehensive knowledge base, and includes a compilation of human genes, genetic disorders and various other information. Hamosh et al 2005. This site was used to know the identification of the gene, chromosomal location, and the symptoms related to the diseases analyzed. Whereas, the orphanet website was used to confirm information and search for missing data on the OMIM website.

In addition, the complete articles were also consulted for additional material. For example, information about the institutions that developed the studies. In this case, it was used as a standard, to record only the data referring to the first author of the article.

For scientometric analysis of the data, only data from the Web of Science database were considered, with the help of tools available on the site itself and open source software, such as: VOSviewer 1.6.20 for scientometric analysis, spreadsheets and image editors from the libreoffice package for graphs and figures.

VOSviewer employs probabilistic similarity metrics to generate visualization maps and establish levels of association with the investigated objects (Van Eck; Waltman, 2010). The option "ignore unit of analysis with a number greater than 25" was used in all evaluations performed. In the co-occurrence of keywords, the unit of analysis was formed by all keywords, with a total count method, followed by the parameter maximum number of occurrence of a keyword equal to three. While, in the co-authorship analysis, the unit of analysis was the authors, with a total count, a maximum of three documents per author, and four authors selected to compose the investigation.

RESULTS AND DISCUSSION

ANALYSIS OF THE SYSTEMATIC REVIEW

The results found in the search carried out in the databases were as follows: 233 in Scopus, 236 articles in PubMed/MEDLINE, 197 in Biomed Central, 129 in Web of Science and only two in JAMA, totaling 797 article records. Of this total, 10 records were excluded, as they were not scientific articles; 219 for not meeting the criteria of the time period (2004 to 2024); 475 because they did not meet the researched theme, thus leaving 93 records that were analyzed by reading abstracts, titles and keywords. After this process, 34 articles

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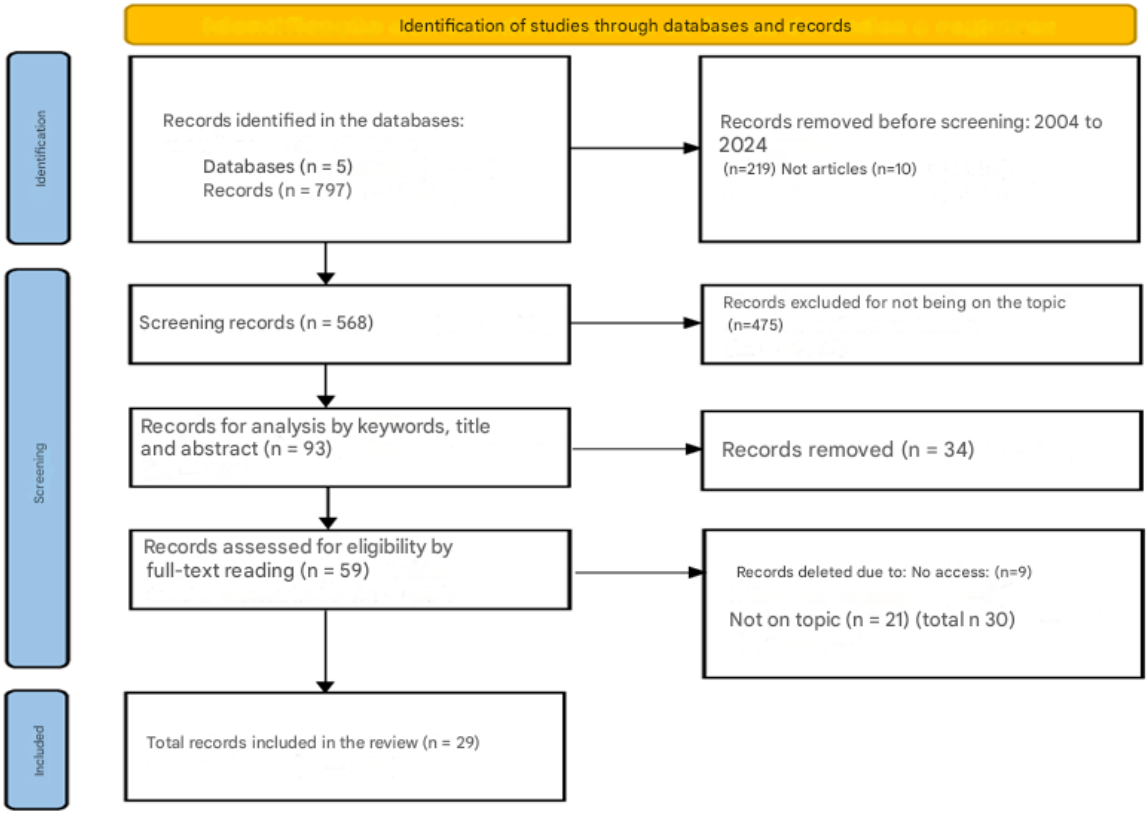
were excluded, totaling 59 articles for reading the full text. Of these records, 9 were excluded because they did not have access to the full text. and 21 were eliminated because they did not contain information on the topic analyzed. Therefore, after the selection was completed, and filtered by the full text, only 29 articles remained that addressed rare genetic diseases in humans in the Brazilian Northeast. (Figure 1).

Figure 1. – Summary table of the systematic review according to the PRISMA platform. **Source**: The authors



The information from the selected articles was also used to identify rare diseases and with the use of bioinformatics websites, proceed with the identification of genes, chromosomal location, type of genetic inheritance related to the diseases analyzed and institutions responsible for the research. (Table 1).

Table 1. List of articles referring to rare genetic diseases in humans in northeastern Brazil.

No.	Author	Year	Condition(s)	Gene (s) / Omim	Loc. Crom.	Her.	Est.	Inst.
1.	Giugliani	2012	Mucopolyxacarydose VI	ARSB / 253200	5q14.1	AIR	NOT	UFRGS
2.	Acosta et al	2013	1Mucopolyxaxariadose VI; 2Congenital hypothyroidism.	1ARSB / 253200 2NKX2-5 / 225250	15q14.1 25q35.1	1AR 2AD	THREE	UFBA

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3.	Costa-Motta et al	2014	Mucopolyxacarydose VI	ARSB / 253200	5q14.1	AR	THREE	UFRGS
4.	Fernandes-Lima et al	2015	Congenital aniridia	PAX6 / 607108	11p13	AD	To the	UFRGS
5.	Araujo et al	2016	Pycnodistose	CTSK / 265800	1q21	AR	THAT	UNICAMP
6.	Brunelli et al	2016	Mucopolysacarydose type VI	ARSB / 253200	5q14	AR	NOT	UFSP
7.	Matta et al	2016	Gaucher disease	GBA / 230800	1q22.	AR	ON	IMIP, PE
8.	Van der Steld et al	2017	Síndrome de Wolff-Parkinson-White (WPW)	PRKAG2 / 602743	7q36.1	AD	THREE	UFBA
9.	Bilezikian	2018	Primary hyperparathyroidism	CDC73 / 145001	1q32	AD	ON	Columbia University, USA
10.	Dantas et al	2018	Berardinelli-Seip	AGPAT2 / 603100	9q34.3	AR	RN	UFRN
11.	De Souza et al	2018	Total absence of superior vena cava (ASVC) TARP syndrome	RBM10 / 311900	Xp11.3	LXR	ON	UFPE
12.	Martins-Costa et al	2018	Carcinoma medular de tireoide (CMT)	RET / 164761	10q11.21	AD	THAT	UNIFESP
13.	Mota et al	2018	Cystic fibrosis	CFTR / 602421	7q31.2	AR	THREE	UFBA
14.	Pérez-Riera et al	2018	Catecholaminergic polymorphic ventricular tachycardia	RYR2 / 604772	1q43	AD	THAT	FMABC
15.	Quintans et al	2018	Primary familial brain calcifications (Fahr disease)	1SLC20A2 / 158378 2XPR1 / 605237 3PDGFB / 190040	1 8p11.21 2 1q25.3 3 22q13.1	1AD 2AD 3AD	ON	CIBERER, ES
16.	Romão de Souza et al	2018	Thrombotic thrombocytopenic purpura	ADAMTS13 / 604134	9q34.2	AR	ON	UFPE
17.	Alves et al	2019	KBG syndrome	1SCN9A / 603415 2ANKRD11 / 611192	1 2q24.3 2 16q24.3	1AD 2AD	THREE	UFBA
18.	Craveiro Sarmento et al	2019	Congenital Lipodystrophy (Berardinelli-Seip)	1AGPAT2 / 603100 2BSCL2 / 606158 3CAV1 / 601047 4CAVIN1/ 603198	1 9q34.3 2 11q12.3 3 7q31.2 4 17q21.2	1AR 2AR 3AR 4AR	NOT	UFRN
19.	Leonhard et al	2019	Guillain-Barré syndrome	PMP22 / 139393	17p12	AD	ON	UFCE
20.	Martins et al	2019	Mucopolissacaridose III C	HGSNAT / 252930	8p11.21-p11.1	AR	PB	University of Montreal, CA
21.	Matos et al	2019	Mucopolissacaridose IV A	GALNS / 612222	16q24.3	AR	THREE	EBMSP
22.	Sperb-Ludwig et al	2019	Glycogen Storage Liver Diseases (GSDs)	SLC37A4 / 602671	11q23.3	AR	THAT	UFRGS
23.	Campos et al	2021	Hereditary angioedema	SERPING / 106100	11q12.1	AD	THREE	UFBA

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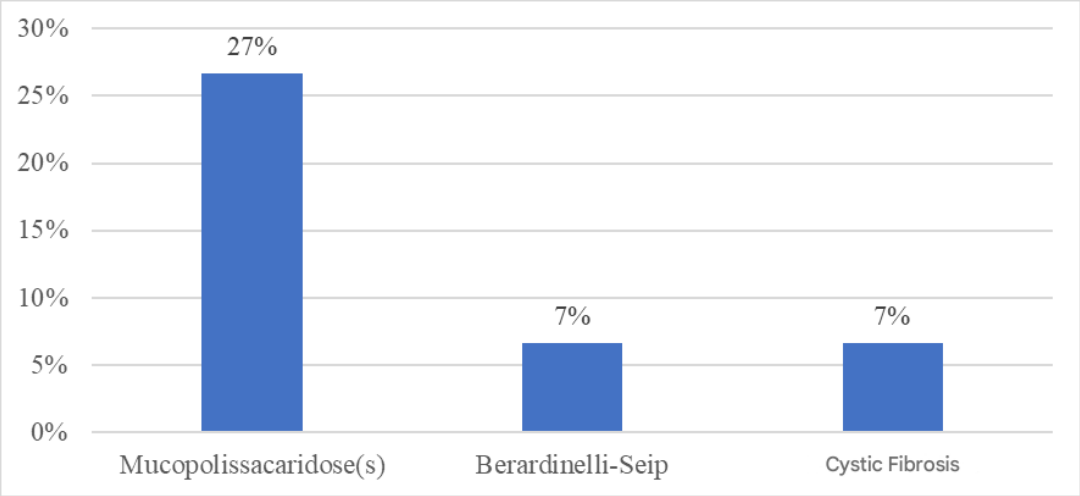
24.	Dos Santos-Lopes et al	2021	Mucopolissacaridose IV A	GALNS / 612222	16q24.3	AR	PB	UEPB
25.	Gbefon et al	2021	- Tireotoxic hypocalêmic periodic paralysia (PPTH)	1CACNA 1S / 114208 2SCN4A / 603967 3KCNJ18 / 613236	[1]1q32.1 [2]17q23.3 [3]17p11.2	1AD 2AD 3AD	BUT	HUUFMA
26.	Giugliani et al	2021	Mucopolissacaridose VII	GUSB / 611499	7q11.21	AR	THREE	HCPA
27.	Mota et al	2021	Reducing body myopathy (RBM)	FHL1 / 300717	xq26	LXD	PB	UFPB
28.	Fernandes et al	2024	Spinal muscular atrophy (SMA)	RA / 313200	xq12	LXR	NOT	UFPB
29.	Meneses et al	2024	Cystic fibrosis	CFTR/602421	7q31.2	AIR	NE	UFS

Loc. Chromos. (Chromosomal Location); Her. (Type of inheritance); Autosomal Recessive (RA); Autosomal dominant (DA); Linked to Dominant (LXD) and Recessive (LXR) X; Est (State). Inst. (Institution); NE (Northeast). Source: The authors.

ANALYSIS OF DISEASES AND GENETIC DATA

Table 1 shows that mucopolysaccharidosis was the most frequent disease, being found in three different subtypes (I, II, and IV) and described in 27% of the articles. Berardinelli-Seip syndrome and cystic fibrosis were described in 7% of the articles and the rest of the diseases appeared in only 3% of the articles. (Figure 2). Thus, only 25 diseases were recorded in 29 articles, because only one article dealt with more than one anomaly: Mucopolysaccharidosis VI and Congenital Hypothyroidism, while several other records dealt with diseases already mentioned in other articles.

Figure 2. - Distribution of the most frequent diseases. **Source**: The authors



In addition, 32 genes were counted, as some diseases had more than one gene that causes the disease registered. For example, Berardinelli-Seip, in which four genes were identified, located on four distinct chromosomes. In Mucopolysaccharidoses, four subtypes

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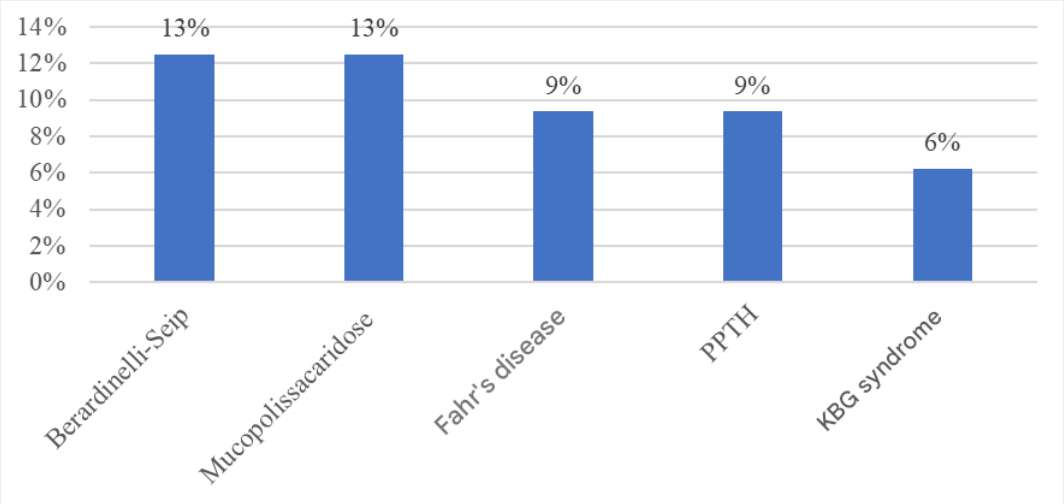
of diseases, four genes, and four different chromosomes were identified. In Primary Familial Cerebral Calcifications (Fahr's Disease) and Thyrotoxic Hypokalemic Periodic Paralysis (PPTH), three genes on three different chromosomes. And in KBG Syndrome, two different genes and two different chromosomes. All other diseases had only one gene, located on a single chromosome. (Figure 3).

Figure 3. - Distribution of diseases with the highest number of genes. **Source**: The authors



Regarding the type of gene inheritance, it is noteworthy that most diseases have autosomal dominant inheritance (50%), followed by autosomal recessive inheritance (41%). In addition, it was possible to identify inheritances linked to the X chromosome, dominant (6%) and recessive (3%). (Figure 4). This data is interesting, because autosomal recessive inheritance is generally associated with several rare diseases in the Northeast, such as SPOAN syndrome, a neurodegenerative disease; Santos syndrome, causes limb anomaly; and MED25 and IMPA1, which cause intellectual disability. De Farias et al 2018.

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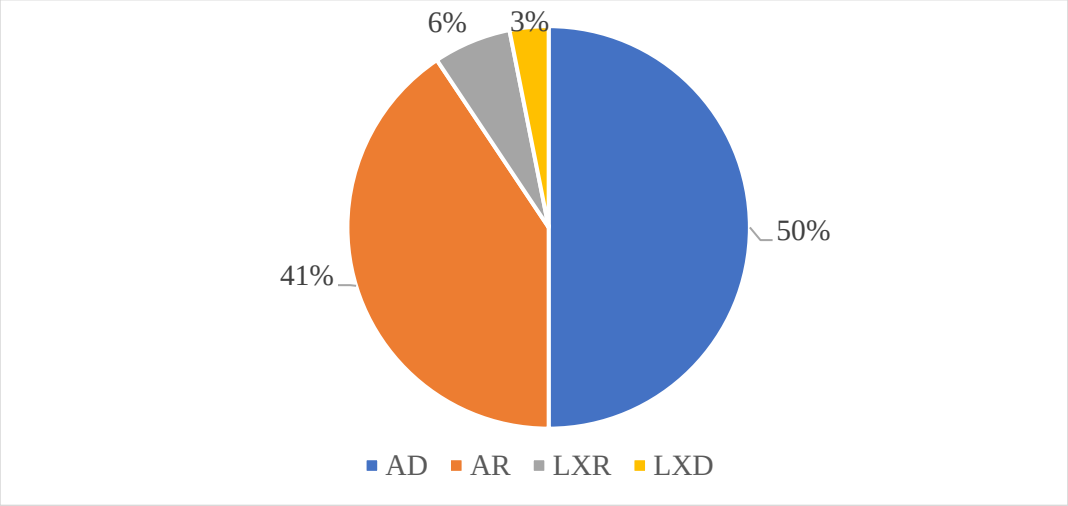
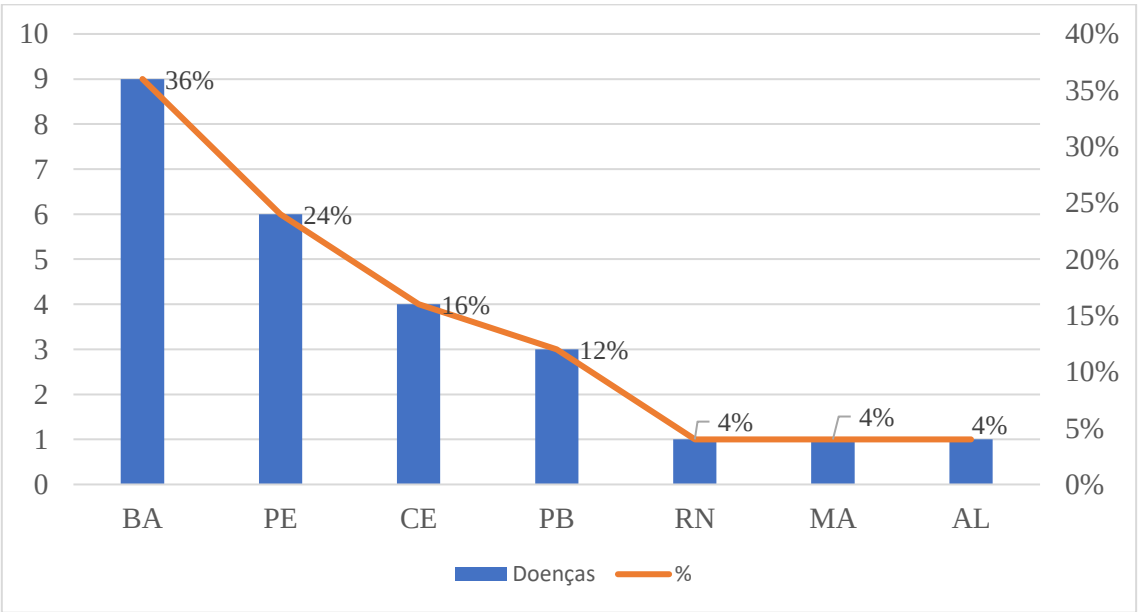
Figure 4. - Distribution of the frequency of the types of genetic inheritance of diseases. **Source**: The authors



ANALYSIS OF THE GEOGRAPHICAL LOCATION OF DISEASES AND RESEARCH INSTITUTIONS

After the genetic analysis, it was observed in which states in the northeast region had the highest incidences of rare genetic diseases in humans. Thus, it was possible to highlight that the state of Bahia was mentioned in 36% of rare diseases. Pernambuco appeared in 24%. Ceará registered 16%, in Paraíba 12%. While Alagoas, Maranhão and Rio Grande do Norte only presented 4%. For this analysis, 17.24% of the articles that did not specify the place of occurrence were not counted, as they reported only the northeast region as a reference for the location. (Figure 5).

Figure 5. - Frequency of rare genetic diseases in humans among the states of the Brazilian Northeast. **Source**: The authors



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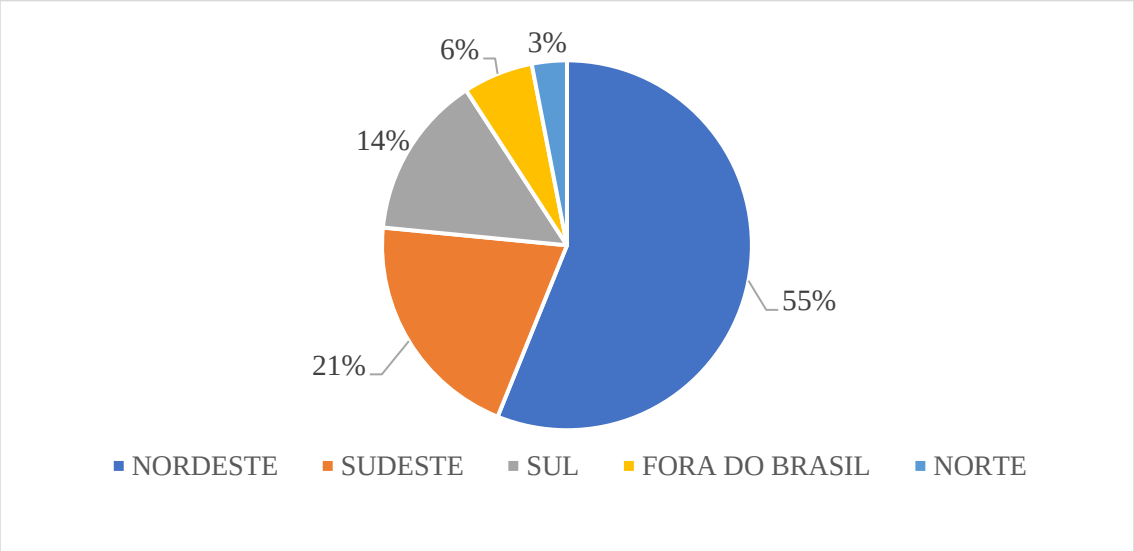
With regard to the institutions that developed the research, it is observed that 55% are located in the northeast region, and 34% in the south and southeast regions, 3% in the North region and 6% were developed by institutions outside Brazil. (Figure 6). It was possible to observe that in most of the articles analyzed, the research was carried out by scientific institutions in the Northeast. However, Lima et al 2018 [1] highlights that most genetic services are located in the southeast and south regions, even with the high incidence of rare diseases in the northeast region. Studies in the area are less frequent, due to the location, and consequently, scientific knowledge on the subject is scarce.

Figure 6. - Distribution of articles by location of research institutions. **Source**: The authors



In addition, national estimates of the overall prevalence of rare diseases are generally based on international data. As can be evidenced by the participation of institutions from outside the country in Brazilian research. This fact was proven by the co-authorship analysis (Figure 7). Two clusters were observed: one formed by "de medeiros, PFV and kim, ca" and the other by "Leistner-Segal, S and Giugliani, R". The greater participation of the latter author is highlighted, as he has two articles in the analyzed database, and "de Medeiros, PFV", who is a Brazilian researcher and full professor at the Federal University of Campina Grande, in Paraíba.

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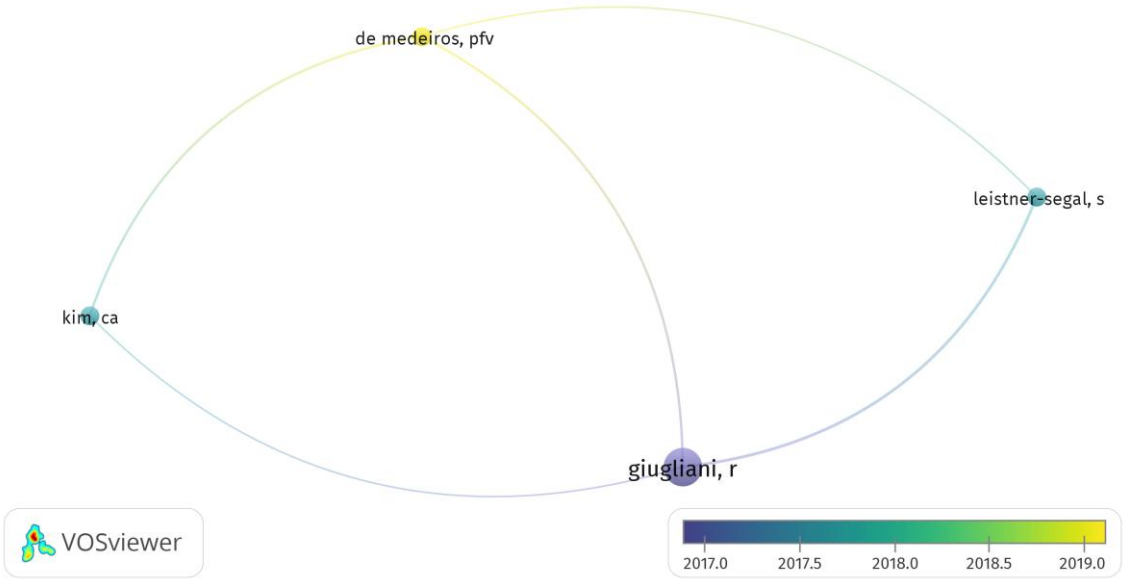
Figure 7. - Distribution of articles regarding co-authorship in articles. **Source**: The authors



This international cooperation is salutary, in this research two articles were found from international institutions and interconnection of co-authorship of Brazilian and foreign researchers. It can be observed that this integration of international data with Brazilian health policy is essential to improve care and resource allocation for rare diseases. Thygesen et al 2023.

International databases have a wealth of information about Brazil. The database, "orphanet", for example, provides a comprehensive collection of epidemiological data. However, there are some national initiatives, such as the Brazilian Network of Rare Diseases (BRDN) that aims to improve the collection of local epidemiological data, although the estimates of this network derive mainly from international databases and have limitations in specific diseases. Félix et al, 2022.

Furthermore, the poorest regions of the Brazilian national territory have scarce data on rare genetic diseases in humans, and therefore, they often end up not being found in online databases.

ANALYSIS OF ARTICLES IN TERMS OF PUBLICATION DATA AND SCIENTIFIC JOURNALS

This systematic review of the literature presents an overview of the genetic and occurrence characteristics described in studies published in the scientific literature for the

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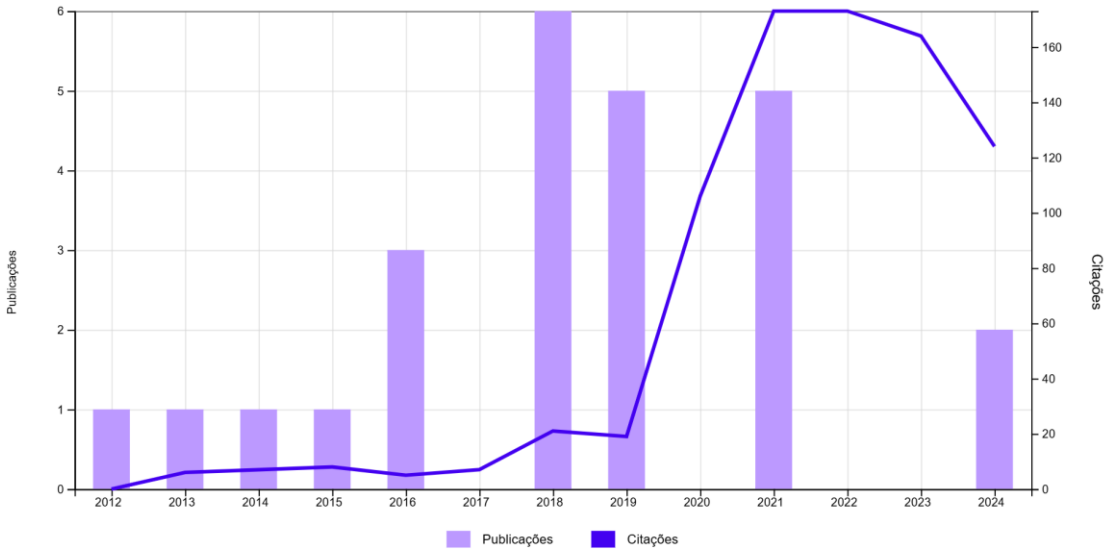
period from 2004 to 20024. To date, no previously published systematic review on this topic has been identified in the scientific literature for the Northeast of Brazil.

Five databases were analyzed, totaling 29 research records. Of this total, 25 articles could be found in the Web Of Science, and four in Pubmed/Medline. Articles that were found to be duplicate also in Scopus were excluded from the analysis. Only the Web of Science was chosen for analysis because it held most of the articles found and because it allowed several scientometric analyses to be performed on the website of the aforementioned database. Web of Science (WoS) is the world's oldest, widely used, and trusted database of research publications and citations. Birkle et al 2020.

The first analysis carried out was regarding the distribution of articles in terms of publication and citation (Figure 8).

Figure 8. - Distribution of articles in terms of article citations. **Source**: The authors



In relation to the year of publication of the articles, the distribution was observed in (Figure 7). Where there is a non-continuous trend towards growth, in the number of publications from 2016 to 2018, followed by a sharp drop in sequence in the following years. The gap in 2017 can be explained by the fact that the four articles present only in the pubmed database were published, two in 2017 and two in 2018. However, these articles could not be included in the analysis because we do not have information regarding their citation numbers. During the period evaluated, there were 814 citations of these articles. The pattern of citations follows the same trend as publications, with the difference that the peak occurred in 2021, instead of 2018.

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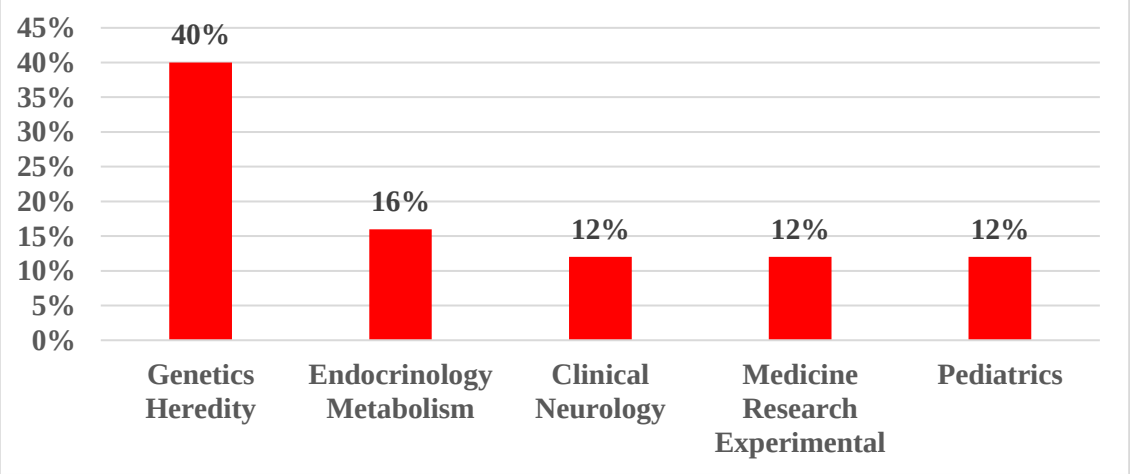
It is also observed that until 2012 there were no publications in the area, although this area of research is not relatively recent. These facts may have occurred due to the awakening of scientists to the subject, due to the impact of the approval of the National Policy for Comprehensive Care for People with Rare Diseases, instituted by Ordinance No. 199, of January 30, 2014, of the Brazilian Ministry of Health.

After this stage, the analysis of the distribution of the articles in the journals where the articles were published was carried out. It was possible to observe in (Figure 9) that the journal Genetics Heredity obtained the highest publication rate among the five most frequent journals. The other journals are focused on the areas of endocrine metabolism, clinical neurology, research in medicine and pediatrics. These results are consistent with the importance of requiring the analysis of a multidisciplinary team so that the diagnosis of rare genetic diseases can occur as early as possible, especially in children.

Figure 9. - Distribution of articles in terms of published journals. **Source**: The authors



Another evaluation that was carried out was about the keywords with the highest frequency of occurrence in the Web of Science database (Figure 10). It is noted that the seven items of the keywords are related to each other, forming two clusters: one in relation to the type of population affected, the frequency, and more pronouncedly, the diagnosis; and another on the causes and population genetic factors of rare diseases. This data is consistent with the variety of articles found in this research, and with the concern with having the diagnosis for rare diseases. In addition, it can be observed that the frequency of child and population is more recent than the other words.

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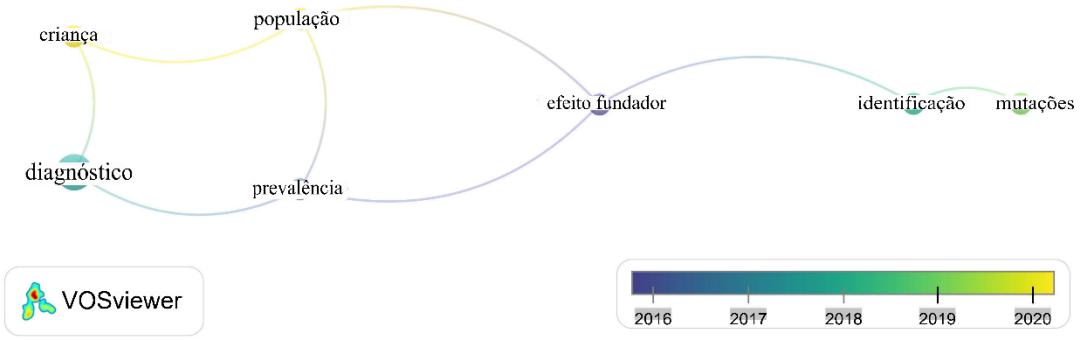
Figure 10. - Distribution of the keywords of the articles in the Web of Science database. **Source**: The authors



Costa-Motta et al. 2014, demonstrate that one of the possible causes of the prevalence of rare diseases in the Northeast is the occurrence of consanguineous marriages in small towns or isolated rural regions of the Northeast. Acosta et al. 2013 also reported that the prevalence of rare genetic diseases in humans is high in rural communities, such as Monte Santo, Bahia, where high rates of inbreeding result in several hereditary anomalies, hereditary anomalies, including congenital hypothyroidism. In addition, Barra et al. 2011 performed a genetic and metabolic description in five patients with Berardinelli-Seip Syndrome, and found that all of them were from the northeast region of Brazil and that there were indications of consanguinity, since in all cases, the patients' parents were first cousins.

CONCLUSION

Based on the information presented, in this systematic review, of 29 articles relevant to the scientific area. It was possible, through the data presented, to show: the prominent data of the surveys, the number of publications and citations between the years 2004 and 2024. Thus, it can be observed that it is evident that the area of studies on rare and genetic diseases in the Northeast of Brazil still faces significant challenges.

The concentration of genetics services in the southeast and south regions of the country may affect knowledge on the subject in the northeast region and in other economically disadvantaged regions.

The reliance on international data for national prevalence estimates is also an important issue that deserves attention. The absence of comprehensive studies conducted in the Northeast of Brazil may lead to an underestimation or overestimation of the true prevalence of rare diseases in the region, and consequently in the country.

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Although this systematic review includes important data on rare genetic diseases in humans; It is observed that some information on the subject was not described in all the selected studies, such as localities or genes.

It is noteworthy that although the bibliographic research based on the articles was quite comprehensive, in terms of time and number of databases, no information published in the literature about the states of Piauí and Sergipe was verified. This fact may have been due to the limitations of this analysis, since only data published in scientific articles were included according to the defined inclusion criteria. It is important to note that reports and findings may have escaped the analysis, due to the search algorithms used or records from the gray literature, which do not have a prominent space in the electronic databases searched.

Conducting comprehensive and collaborative research, especially in less explored regions, can provide valuable data for understanding and tackling rare diseases in Brazil.

In summary, it is crucial that there is greater investment in research on rare diseases and genetics in the Northeast of Brazil, especially in less privileged regions, to promote a more complete and accurate understanding of the prevalence of these conditions and allow the implementation of more effective and inclusive health policies. Collaboration between researchers, institutions, and governments is essential to advance the knowledge and treatment of rare diseases, ensuring a better quality of life and adequate support for patients and their families.

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