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Epidemiological Profile of Prostate Cancer in Brazil

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Abstract*—*Commonly initiated through a range of mutation sequences that occur throughout an individual's lifetime, the Prostate cancer (PC) is a pathophysiological disorder with diverse origin. In this work, we use the data about the incidence and mortality of PC available in a database from the Brazilian National Cancer Institute (INCA) that permitted the construction of graphs made using the Microsoft Office Excel to the analysis, so this study aimed to quantify the distribution of PC, analyzing its incidence at national, macro-regional, state and capital levels. Furthermore, monitoring mortality at the national and macro-regional levels, as well as its projection at the national level, and generating health indicators that can be useful in promoting public policies. PC has a high incidence in the Northeast and low in the North. The Southeast region presents a higher number of deaths, and the projection of the number of deaths motivated by PC tends to increase throughout Brazil until 2040. Prostate cancer is very heterogeneous across the country, with marked differences in the same geographic space. Thus, this study generated health indicators that can be useful for the promotion of preventive public policies and for budget reorganization, bringing the possibility of a more homogeneous, effective and efficient screening of prostate cancer.

I. INTRODUCTION

Prostate cancer (PC) is a multifactorial disease that originates through a range of mutation sequences that occur throughout an individual's life. Chromosomal aberrations that originate prostate cancer are linked to the germline (hereditary 5%-10%, familial 15%-20%) and the somatic lineage that corresponds to sporadic cancer (70%-80)[1,2].

The accumulation of changes in the nucleotide sequences that make up DNA can lead to castration-resistant prostate cancer (CRPC) and distant metastasis, because DNA can be damaged by exogenous factors (ionizing radiation (IR), chemicals, ultraviolet radiation (UV)) and endogenous (reactive oxygen and nitrogen species), in addition to spontaneous modifications. Thus, oncogenesis is activated when tumor suppressor genes mutate, causing malignant cells and even more aggressive prostatic tumors to appear[3].

The inherited genes and their mutations that most confer an individual's susceptibility to developing prostate cancer are the following: AR (polyglutamate repetition), RNASEL (HPC1) (methylation), MTHFR (deletion), SRD5A2 (point mutations, amino acid exchange), MSR1 (point mutations, amino acid exchange), CYP17 (point mutations in the promoter sequence), BRCA1 (deletion), BRCA2 (deletion, promoter hypermethylation and protein truncation), ELAC2 (point mutations, amino acid exchange). Individuals who inherit the BRCA2 gene are five to seven times more likely to develop prostate cancer

and those who inherit the BRCA1 gene are more likely to develop more severe clinical conditions, including CRPC[4,5].

Spontaneously or randomly mutations corresponding amoung70% to 80% of cases of prostate cancer. The main genes and their nucleotide changes that are involved in this process are the following: AR gene (point mutations, amplification and increased expression of splice variants), NKX3.1 (promoter hypermethylation), PTEN (deletion), GSTP-1 (promoter hypermethylation in CpG sequences) and CDKN1B (deletion). These changes occur over time, sometimes for decades. It is noteworthy that mutations in the GSTP-1 gene,often found in cancer patients, when expressed protects a prostate against free radicals. The PTEN gene is essential in proliferation, apoptosis and cell cycle regulation, changes in this gene are also common and it ends up affecting metastatic cancer[5].

Main germline genes that are most involved in metastasis cases: ATM, ATR, BAP1, BARD, BRCA1, BRCA2, BRIP, CHEK2, FAM175A, GEN1, MLH1 MRE11A, MSH2, MSH6, NBN, PALB2, PMS2, RAD51C and RAD51D. Note that the patients with metastatic prostate cancer frequently present the genes BRCA1, BRCA2, ATM and CHEK2. Increased RGS2 is a suggestive prognosis for reduced survival in patients with CRPC. Due to this, the gene expression monitoration of RGS2 early in diagnosis can help to modulate therapeutic approaches for patients with CRPC[6,7,8].

Prostate cancer is the most diagnosed in 112 countries, incidence rates range from 6.3 to 83.4/100,000 men in all regions, with the highest rates in Northern and Western Europe, Caribbean, Australia/Nova Zealand, North America and South Africa and the lowest rates in Asia and North Africa. In 48 countries, PC ranks second as the leading cause of cancer death among men, countries in sub-Saharan Africa, the Caribbean, Central and South America (eg Ecuador, Chile and Venezuela), as well as Sweden. Advancing age, family history of the disease, genetic mutations such as those that occur in the BRCA1 and BRCA2 gene, and conditions such as Lynch syndrome are risk factors for prostate cancer[9,10,11].

Worldwide, about 19.3 million new cases of cancer were registered, with prostate cancer representing 7.3% of this total, which means 1.4 million of incidence [11,12,13,14].

According to the Brazilian National Cancer Institute (INCA), in 2020, 65,840 new cases of PC were registered in Brazil. The distribution of cases of prostatic cancer by regions of Brazil is as follows: Midwest with 5,350 (8.1%), Northeast with 20,570 (31.2 %), North with 2,770 (4.2%), Southeast with 27,890 (42.4%) and South with 9,260 (14.1%). It is important to emphasize that prostate cancer always appears in first place in all five (5) macro-regions of the country, compared to cancers that can affect humans.

One man in nine will be diagnosed with prostate cancer in Brazil throughout their lifetime, six (6) out of ten (10) diagnosed cases will be men over 65 years old, this denotes that age it really is a risk factor for prostate cancer. The mortality rate was 13.1%, with 15,983 deaths in Brazil in 2019[15,16].

Given the facts and data presented here, it is essential to develop studies with the aim of detailing the distribution of cases of prostate cancer in Brazil, as well as evaluating the behavior of prostate cancer at national, regional, state and capital levels. Thus, this study aimed to observe the distribution of prostate cancer, as well as its incidence, mortality and mortality projection at the national level, and generate health indicators that can be useful in promoting preventive public policies aimed at the area in question.

II. MATERIAL AND METHODS

A. STUDY LOCATION, DESIGN AND PERIOD

The present work is a quantitative, descriptive, retrospective and documentary study of non-probabilistic sampling among men affected by prostate cancer throughout the country. Data from 2000 to 2019 were collected from patients with a positive diagnosis for prostate cancer and who died in the South, Southeast, Northeast, Midwest and North regions, as well as the national mortality in order to analyze the mortality of PC and projecting mortality up to the year 2040. To analyze the national, regional, state and capital incidence, 2020 data from the male population and estimates of new cases of PC were collected.

B. STUDY POPULATION AND INCLUSION AND EXCLUSION CRITERIA

Men residing in the Federative Republic of Brazil who had a confirmed diagnosis for prostate cancer will be included in this series. Non-Brazilian men and women excluded.

C. DATA MANAGEMENT AND ANALYSIS

Graphs and tables created to perform the analysis of incidence and mortality, as well as for the projection of mortality done using Microsoft Office Excel program for dataprocessing.

This work used the population data, estimates of cases of PC and mortality collected through the website of the Brazilian National Cancer Institute (INCA) at https://www.inca.gov.br/ and stored in the Microsoft Office Excel. The overall incidence was calculated by

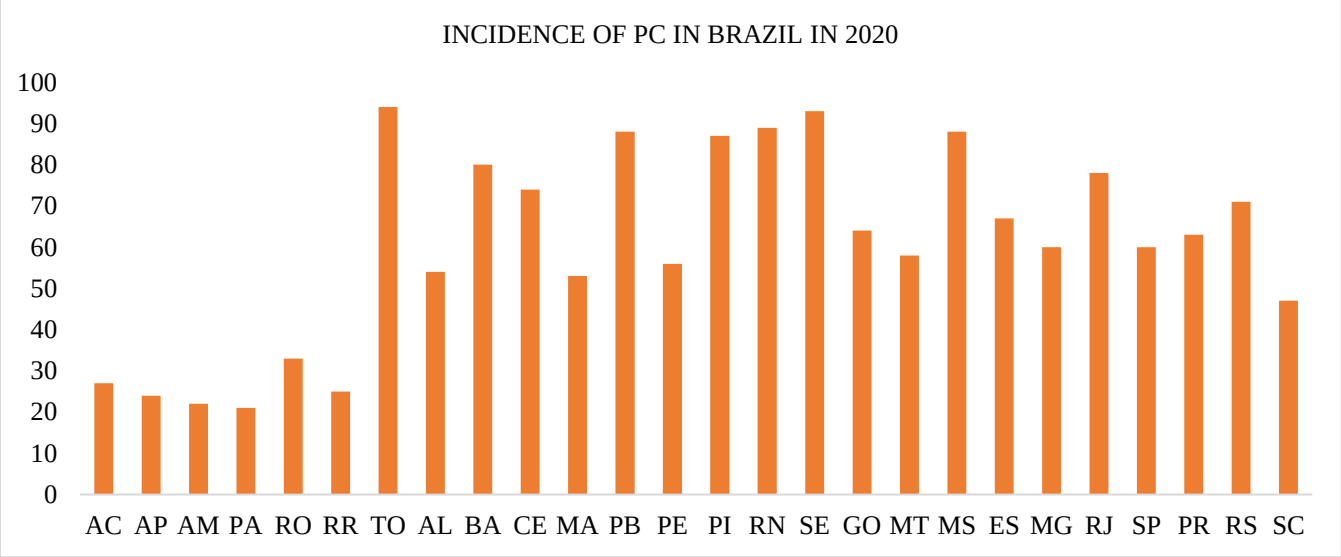
dividing the estimate of PCs cases by the exposed population multiplied by 100,000 inhabitants.

III. RESULTS AND DISCUSSION

According to the INCA[15], the general incidence of Prostate Cancer (PC) in Brazil in 2020 was 29.2%, with approximately 65,840 men affected. Graph 1 shows a very high incidence in the state of Tocantins, with an average of 94 men with a positive diagnosis for PC for every 100,000, followed by Paraíba with 88 confirmed cases, Bahia with 80 and Ceará 74. There is an important heterogeneity in the distribution of PC, with the states of the Northeast region presenting a higher incidence.

A previous developed study[17] demonstrated the behavior of PC in 185 countries; they suggested that the incidence of PC continues to increase in developed nations and with a clear growth in developing countries. According to the results expressed here, Brazil has been following this trend. Also in Graph 1, it is possible to see that the distribution of PC in Brazil is quite heterogeneous, with strong differences between the regions of the country.

Graph 1: Overall incidence of PC in Brazil in 2020 per 100,000 inhabitants



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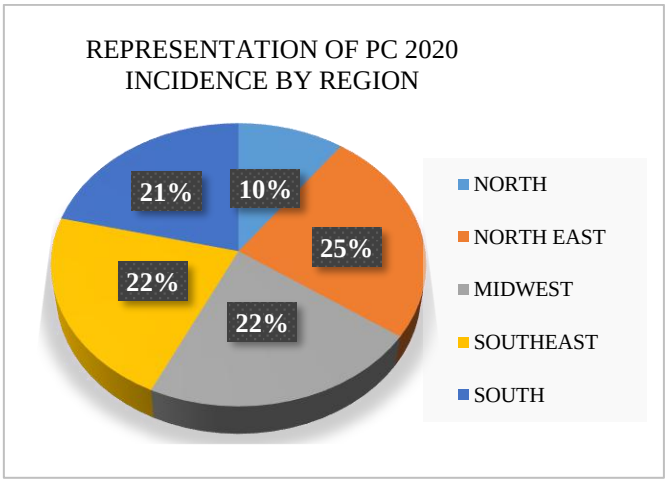
On the representation of the overall incidence by region in percentage (Graph 2), it is possible to observe that the Northeast Region stands out for being the most affected by PC, with 25%, followed by the Midwest Region with 22% and the Southeast Region with 22% similar to the results found in a previous developed study[18]. In relation to the tendency presented in previous regions presented, the North Region with 10% of this total was an unexpected data. In this sense, this region is the one with the lowest incidence in the country. However, the data obtained may not be as reliable due to huge geographic and access barriers to healthcare. As a result, underreporting of data is suspected. Garnelo[19], addresses the issue of access to health care in the North region, highlighting the lack of health professionals, access difficulties and budget limitations.

Graph 2: Representation of the incidence of PC 2020 by region



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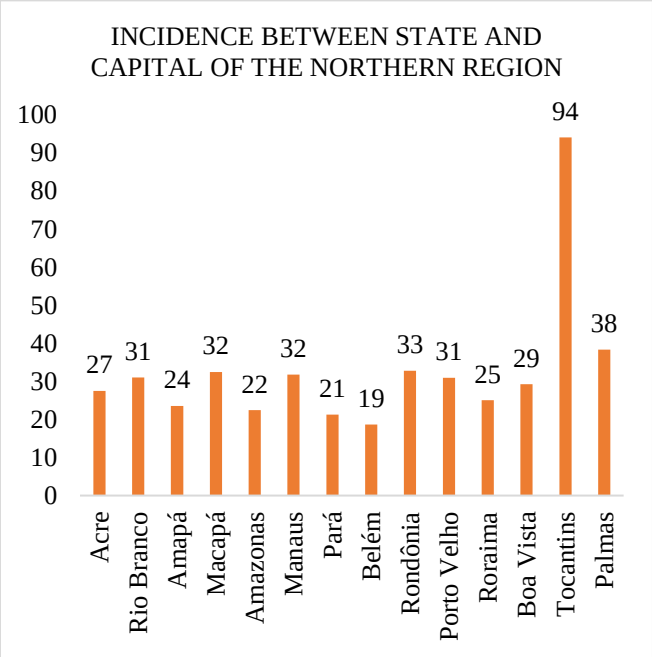
Graph 3 shows the behavior of prostate cancer between the states and their respective capitals in the North of the country. In general, there is a certain similarity between the incidences of PC. Tocantins has a divergent point to

observe, with an incidence of 94 men with PC for every 100,000, the capital of Tocantins, Palmas, has an incidence comparable to other capitals in the North region. A possible explanation is its proximity to the Northeast and Center-West regions, which have high incidence rates of PC. As evidenced, the North region has the lowest incidences of PC in the country; the study by Alcantara[18] had identical results.

Graph 3: Comparison between the incidence of CaP between states and capitals in the Northern region of Brazil



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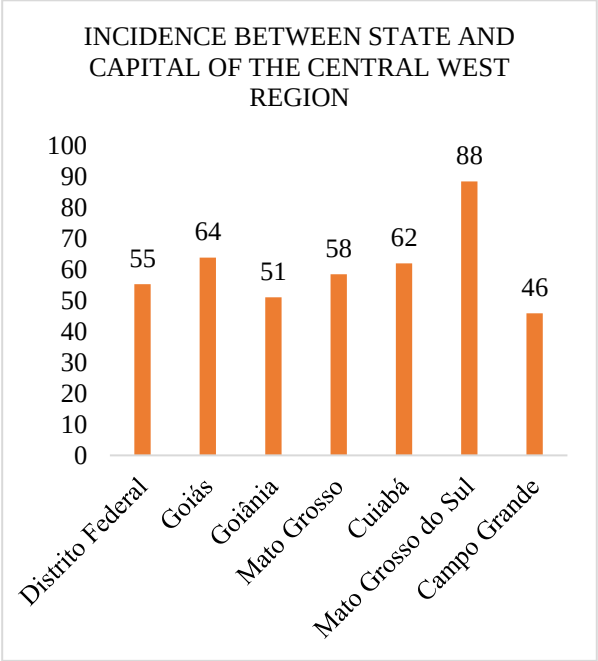
The comparison of the incidence of PC between states and capitals in the Midwest region, showed in Graph 4, highlighted a much higher incidence than in the North region. In addition, there is a very heterogeneous behavior among the states, the state of Mato Grosso do Norte has the highest incidence (88 cases for every 100,000 men) and the state of Mato Grosso do Sul has the lowest incidence (58 cases for each 10,000 men). Furthermore, there are differences between the states and their respective capitals, denoting a very heterogeneous behavior of the PC in this region. In a previous study, Dutra[20] correlates this increase in the incidence of PC in the Midwest region with the sharp increase in the use of pesticide.

Graph 4: Comparison between the incidence of PC between states and capitals in the Midwest region of Brazil



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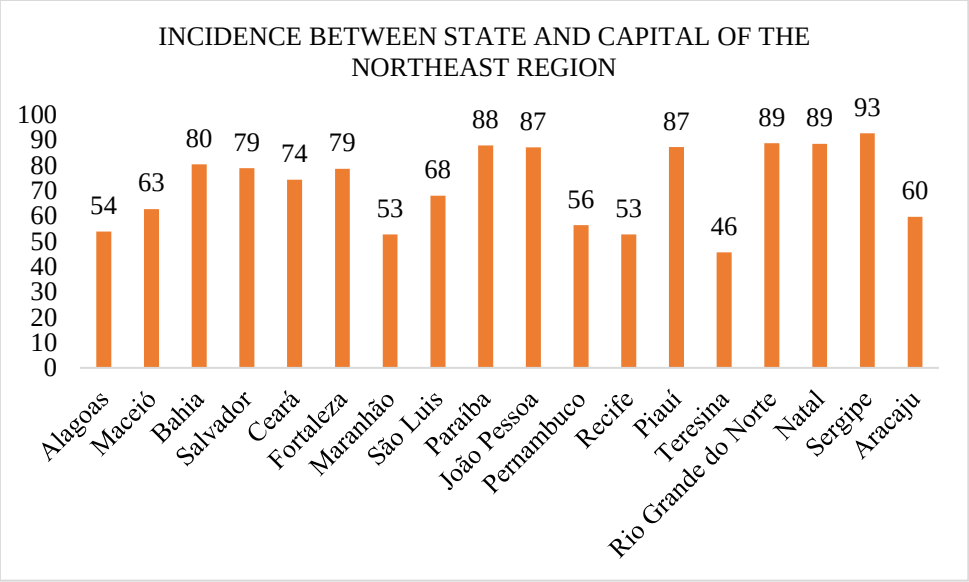
Notably, there is a strong heterogeneity in the behavior of PC in this region (Graph 5). The Northeast has the highest incidences of PC in the country, a study developed[21] revealed the epidemiological profile of men who are affected by prostate cancer in this region, with brown men being the most affected, aged between 60 and 69 years. Here, the state with the highest incidence was Sergipe, with (93 cases for every 100,000 thousand men), and the state with the least incidence was Maranhão, with (53 cases for every 100,000 thousand men). It is important to mention that there is a lot of difference regarding the behavior of PC in the Northeast; Alcantara[18] had similar results to those mentioned here.

Graph 5: Comparison between the incidence of PC between states and capitals in the Northeast region of Brazil



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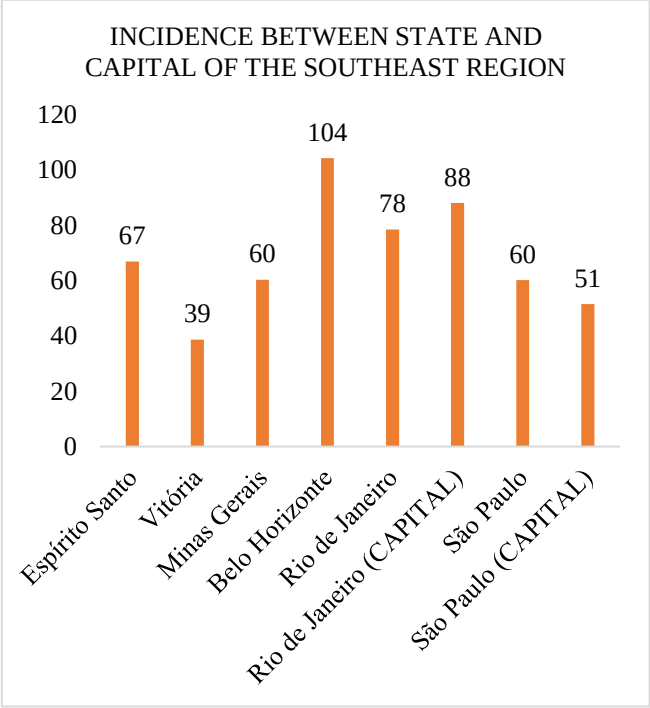
Graph 6 shows the comparison of incidence between states and capitals in the Southeast region of the country. It is possible to observe a high incidence of PC and a strong heterogeneity between states and their capitals. It is important to mention that the Southeast region is the most developed in the country and the literature already correlates high rates of PCs incidence with a high level of socioeconomic development. The state of Rio de Janeiro has the highest incidence of PC, with 78 cases per 100,000 men, and the state of São Paulo and Minas Gerais have the lowest rates, with 60 cases per 100,000 men. A point to be noted is what happens in the capital of Minas Gerais, Belo Horizonte, which has the highest incidence of PC among all capitals in the region, with 104 cases for every 100,000 men, an average well above that of Brazil and one of the highest incidences of PC in the country, second only to Florianópolis. Sung[11] correlates that more developed regions have a higher incidence of PCs, as well as other types of neoplasms. Luizaga[22] addresses in his studies the geographic disparities in the country and their impacts on access to health, which ends up implying different behaviors of pathologies, including PC.

Graph 6: Comparison between the incidence of PC between states and capitals in the Southeast region of Brazil



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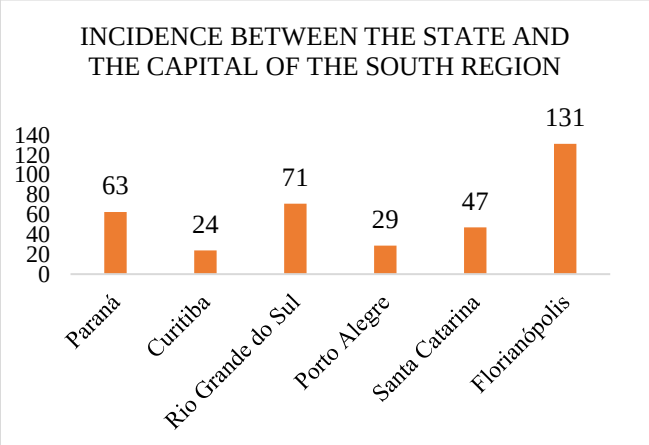
Graph 7 addresses the incidence of CaP between states and capitals in the southern region of the country. It is worth noting the heterogeneity of the incidence of PC between states and capitals in this region. Florianópolis has the highest incidence of PCs in the country, with an

incredible 131 cases per 100,000 men. The state of Rio Grande do Sul has the highest incidence, with 71 cases for every 100,000 men. Silva[23] observed in his studies a greater emergence of neoplasms associated with the intensive use of pesticides in the southern region of Brazil.

Graph 7: Comparison between the incidence of PC between states and capitals in the southern region of Brazil



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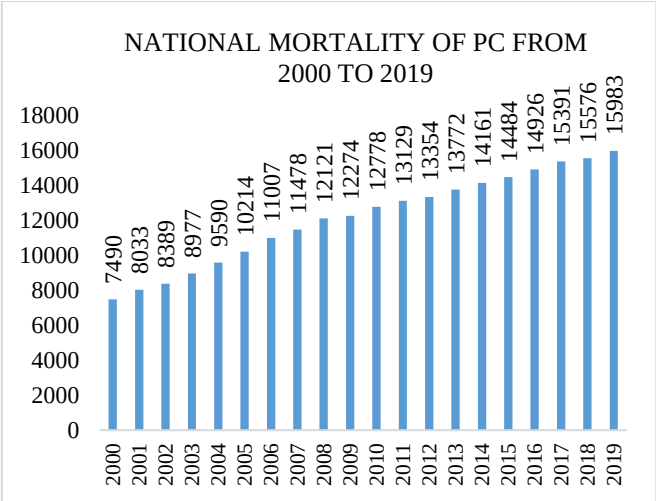
Related to the mortality of PCs at the national level showed in Graph 8 it is notorious that there is a significant increase in mortality from PC over the years, reaching a doubling over a period of 20 years. These data are in line with the increase in Brazilian life expectancy. Furthermore, with the population becoming increasingly gray it is very likely that the mortality of PC will continue to grow. According to Alcantara[18], the age group with the highest number of deaths from PC is 75 to 79 years old, and the lowest is between 40 to 44 years old, suggesting a correlation between age and death.

Graph 8: Comparison of PC mortality in Brazil between 2000 and 2019



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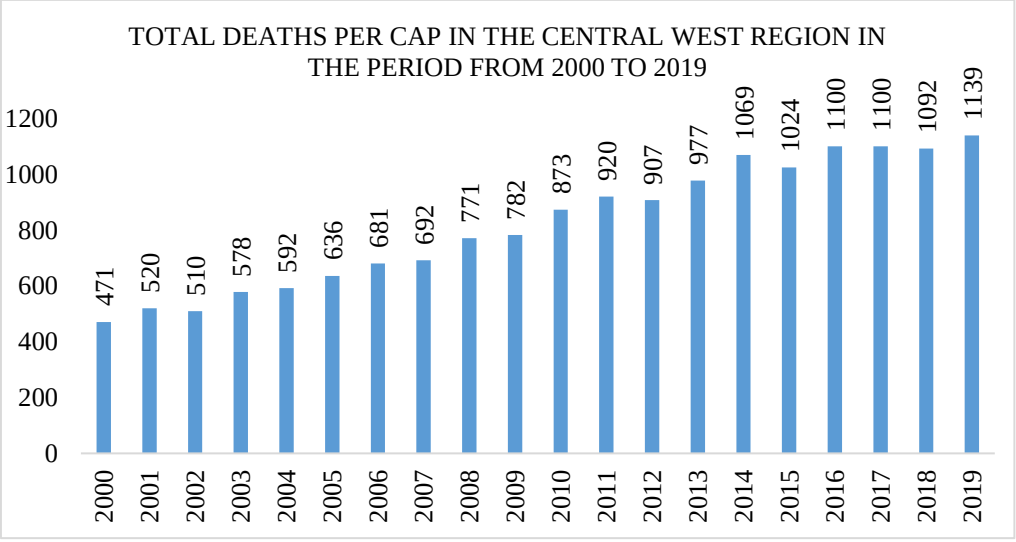
Graph 9 quantifies the number of deaths from PCs in the Brazilian Midwest. It is possible to see a continued increase, with some variations over the years. In 20 years, this total number of deaths increased by about 242%. The age group of men who most die in the analyzed region follows that of Brazil, between 75 and 79 years. It is important to mention that when there is better health carea decrease in the number of deaths from PC occurred[18].

Graph 9: Comparison of PC mortality in the Midwest region of Brazil between 2000 and 2019



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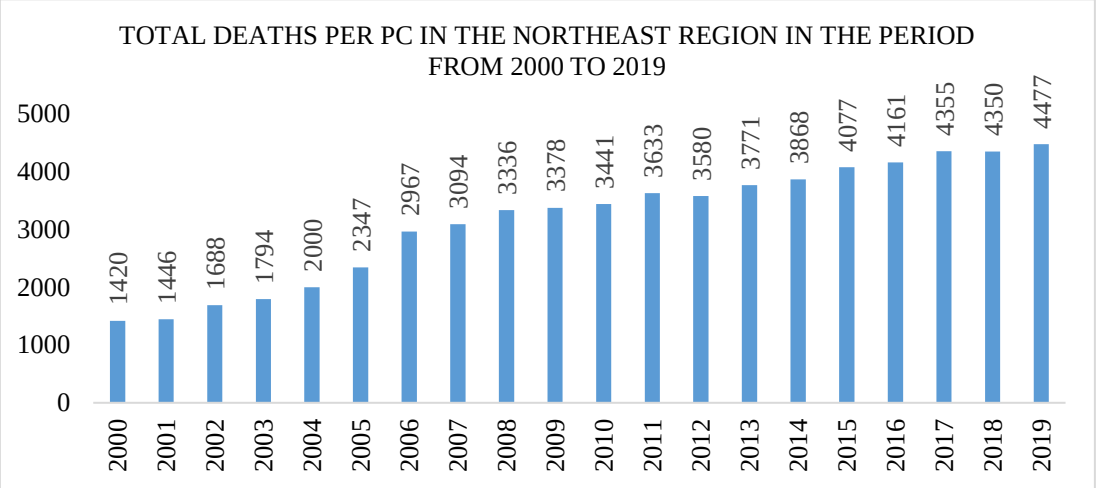
In Northeast Brazil, the total number of deaths from PC, Graph 10, a constant and growing increase in terms of deaths is observed. A higher mortality from PC was observed in the age group over 80 years old in

Northeastern Brazil. Literature reports that the Northeast has the highest percentages of deaths from PCs in Brazil. It is suggested that this is due to a lack of access to health care, lack of budget, difficulties in diagnosis and early treatment[24,25]. The data found by Vasconcelos[26] are similar to the results presented here. In addition, in this region there is strong resistance to the digital rectal exam, a study reinforces the idea about its importance in the early diagnosis of PC[27].

Graph 10: Comparison of PC mortality in the Northeast region of Brazil between 2000 and 2019



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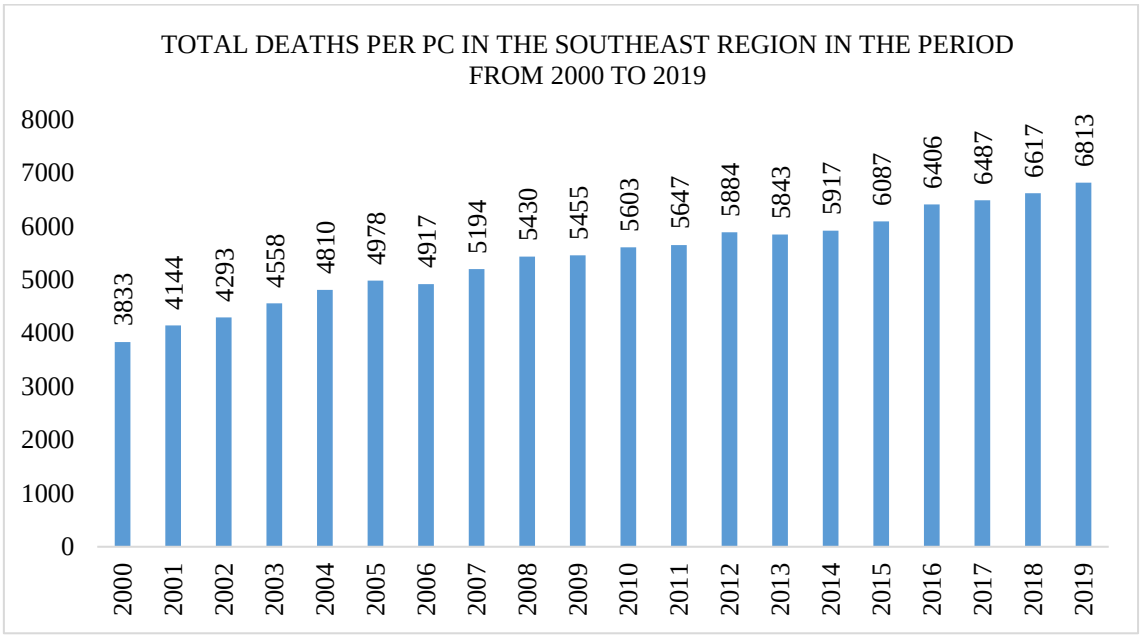
Graph 11 shows the number of deaths from PC in Southeastern Brazil. This region is the most economically developed in the country. As it has the largest population in the country, a higher number of deaths from PC is expected in the Southeast region, as observed in this result. Between 2000 and 2019, there was an increase in the number of PC around 178%. Cesar[24] observed that the mortality rate in the Southeast region is between 1.88% and 2.04%, ranking fourth (4) in comparison with the macro-regions of Brazil. This number is expected to continue to grow due to increased life expectancy and the current mode of social behavior.

Graph 11: Comparison of PC mortality in the Southeast region of Brazil between 2000 and 2019



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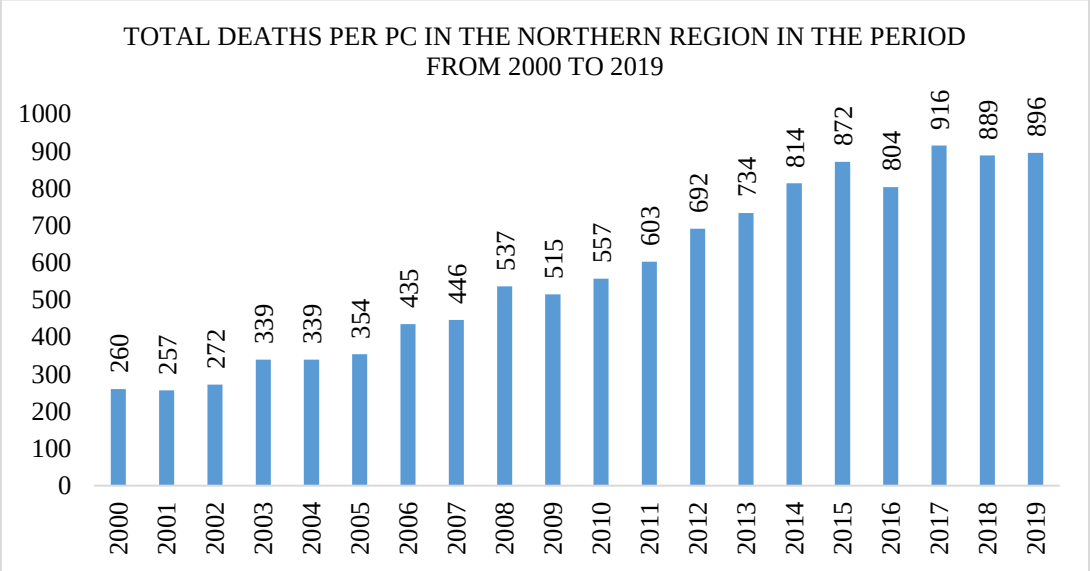
The number of deaths from PC in the northern region of the country is showed in Graph 12. According to Cesar[24], this region has the lowest mortality rate among the other regions, ranging from 1.33% to 1.82%. It is possible to notice large variations in the arrangement of data over the years reported. Between the years observed (2000 to

2019), there was an increase of 344.6% in relation to deaths from PC. It is important to mention the reliability of the data in this region.

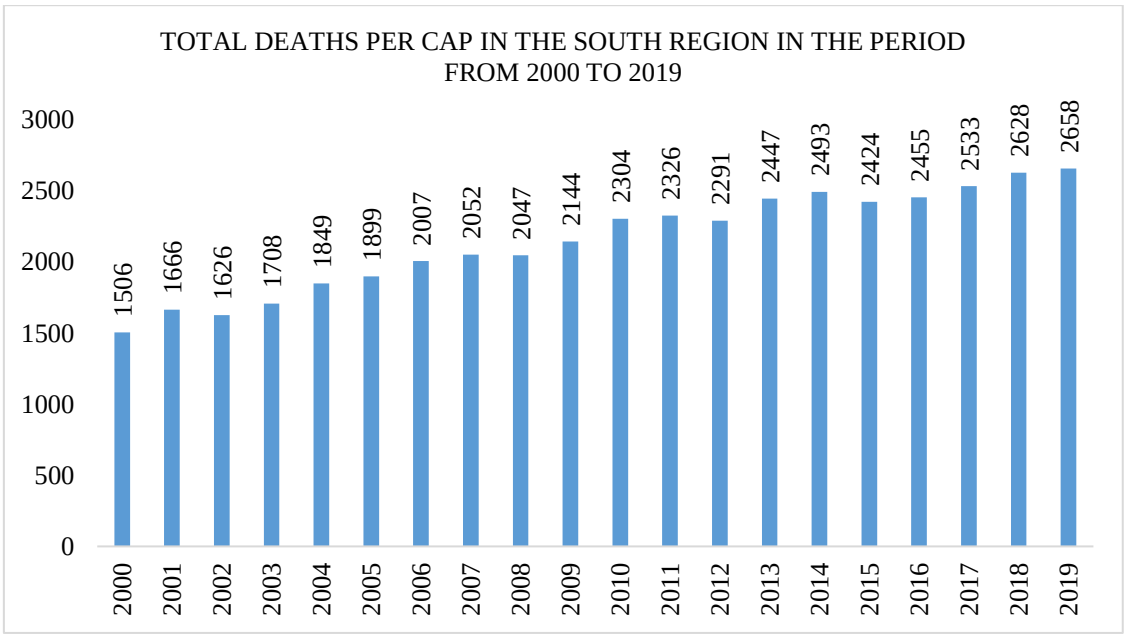
Graph 12: Comparison of PC mortality in Northern Brazil between 2000 and 2019



From: BRAZIL, 2021,adapted.

Graph 13 shows the total number of deaths from PC in the southern region of Brazil. According to Cesar[24], the South has the highest mortality rate from PCs in Brazil, ranging from 2.13% to 2.37%, this was also seen in all age groups analyzed, with emphasis on men from 80 years old. A possible explanation for this is the intensive use of pesticides in monoculture areas[20].

Graph 13: Comparison of PC mortality in southern Brazil between 2000 and 2019



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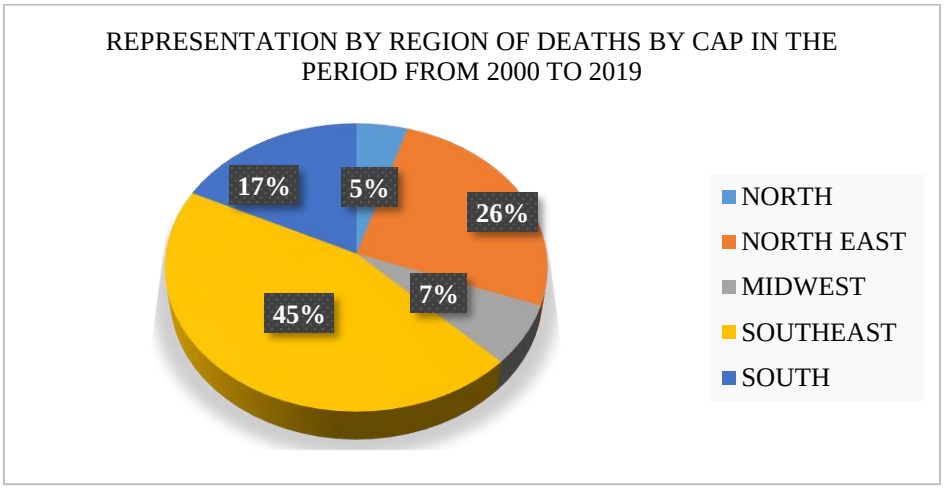
An overall representation, based on the total analysis of deaths, of the percentage of deaths from PCs between 2000 and 2019 in all regions of Brazil showed in Graph 14. The Southeast region is noteworthy, accounting for 45% of all deaths from PC throughout Brazil. The North region has the lowest percentage, 5%. Previous studies[24,28] found results similar to those analyzed in this present work. An important fact to report is that of all deaths recorded in

Brazil, between 2000 and 2019, 2% are deaths caused by prostate cancer.

Graph 14: Comparison of PC mortality in macro-regions of Brazil between 2000 and 2019



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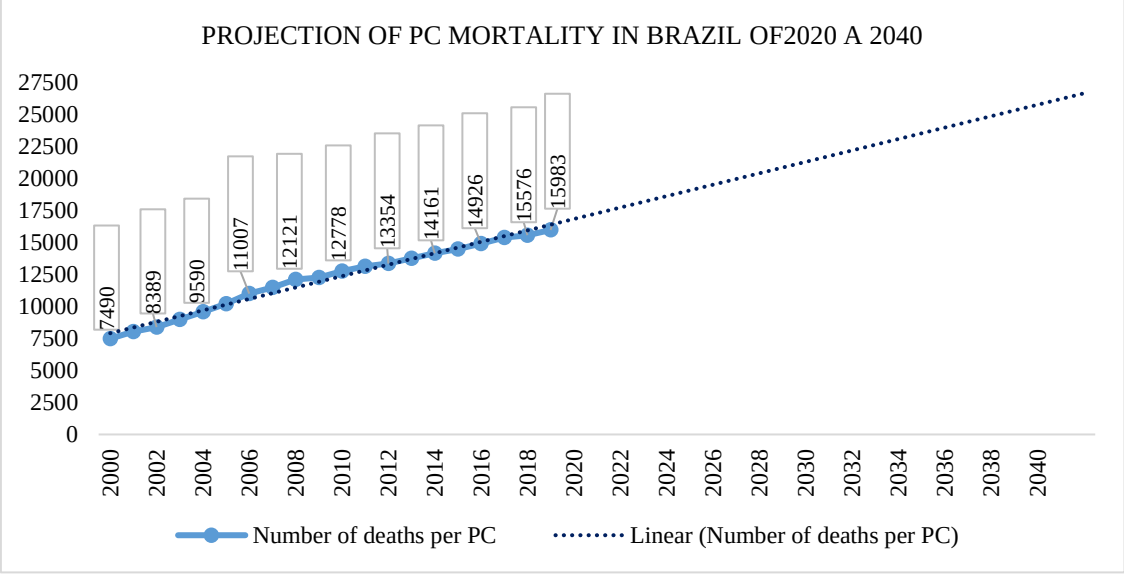
Graph 15 shows the real curve of mortality from PCs until 2020 and its projection until 2040. At the current rate, it there is an expectetion that by 2040 Brazil will have around 26,000 deaths from PC across the country. Prostate cancer is a pathology closely related to the patient's age, so much so that its incidence is higher in men over 60 years of age and its mortality much more accentuated after 80 years of age, as mentioned above. Therefore, the results presented are worrisome. Furthermore, oncology services are quite costly to public coffers, which further aggravates the problem presented. Another point to think about is that the regions of Brazil are very heterogeneous in terms of socioeconomic status; difficulties in accessing health care and tracking PCs are also common. In addition, in this work we analyzed the mortality in consequence of PC throughout the country and its respective macro-regions, over a 20-year period, and its projection until 2040.

Graph 15: Projection of PC mortality in Brazil until 2040



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The process for the restoration of organic functions in patients with prostate cancer requires the use of several drugs, which can affect other vital functions of the body. To deal with all these pharmacotherapeutic processes, clinical management and observations on pharmacological conditions, the presence of a pharmacist who is part of the health team that assists the cancer patient is essential. Thus, the pharmacist can act directly during the clinical management of the patient, contributing to the promotion of their health[29].

III. CONCLUSION

Prostate cancer (PC) is a very heterogeneous pathology that originates through changes in nucleotide sequences throughout an individual's life. In the study presented here, we found that PC is heterogeneous in the Brazilian territory in relation to its incidence and mortality, with very high numbers in some regions of the country, such as the Northeast and Southeast regions, in total discrepancy with the low indices presented by the North region. Overall, this suggests a different behavior of PC in different geographic regions.

Screening for PC through the measurement of PSA is an important tool to aid in the initial diagnosis of prostate cancer. Considering that the tracking campaigns popularly known as "Novembro Azul" are unequal in different geographic spaces in Brazil, as well as there are several budget limitations, which makes the diagnosis and notification of PC even more difficult. In a way, this represents the diverse socioeconomic inequalities that so afflict the nation.

It is expected that more investment in PC tracking campaigns, earlier detection and notification will occur. Thus, being able to guide the constituted government to better direct the public purse to the treatment units, aiming at a reduction in mortality. Another relevant fact about the treatment in question is genetic counseling, which consists of analyzing an individual's genetic set in order to search for genes that can trigger prostate cancer.

Prostatic cancer is a patology closely related to advancing age, family predisposition and lifestyle. Therefore, educational campaigns and health education are essential so that, throughout life, the individual can be informed about the disease and take care of himself, in order to minimize the risks, especially if there are already cases in the family.

As far as we know, this is the first work that aims to analyze the general incidence of prostate cancer nationwide, comparing it between regions of Brazil and states vs capitals. In order to understand the behavior of PC, its mortality profile throughout the country and its projection until 2040 were drawn, which highlighted the need for greater attention to this pathophysiological disorder.

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