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Pediatric mortality profile due to Malignant Brain Tumor in Brazil between 2012 and 2022

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ABSTRACT

OBJECTIVE

To identify the mortality profile due to malignant brain tumor in pediatric patients in Brazil from 2012 to 2022.

METHOD

Mortality and population data were collected from the *Secretaria de Vigilância em Saúde e Ambiente, e Departamento de Informática do Sistema Único de Saúde (DATASUS)* and tabulated using Excel.

RESULTS

A total of 4,370 deaths were recorded during the analyzed period, with the Southeast region reporting the highest number, 1,753 deaths. In contrast, the South and Central-West regions had the lowest numbers of total deaths, with 619 and 381, respectively. In 2012, 458 deaths were recorded, marking the highest mortality rate during the period. The sex, race, and age group with the highest mortality rates were males (2,312 deaths), the white population (2,222 deaths), and children aged 5 to 9 years (1,605 deaths). The brain, excluding the lobes and ventricles, accounted for the highest number of deaths (1,152), while the parietal lobe had the lowest number.

CONCLUSION

Overall, understanding these data helps inform public health policies and supports the implementation of new treatment technologies aimed at reducing mortality rates.

KEYWORDS

Mortality; Pediatric patients; Malignant neoplasms of the brain; Brazil.

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INTRODUCTION

Malignant neoplasms of the central nervous system account for approximately 30% of all neoplasm-related deaths in pediatric patients, with the brain region being the most affected among this population.[1] These neoplasms originate from glial cells and can be classified according to their histopathology as astrocytomas, oligoastrocytomas, oligodendrogliomas and glioblastomas.[2] They can also be classified into 4 different grades, according to their level of proliferation, so that grade I consists of non-infiltrative lesions and can be treated with surgery, while grades III and IV correspond to more aggressive tumors that present infiltrative lesions and require complementary treatments to surgery, such as chemotherapy and radiotherapy.[3]

Medulloblastomas are the most common malignant neoplasms in children and they are characterized mainly by their location in the cerebellar region and histological heterogeneity, which increases their likelihood of becoming a diffuse neoplasm. This characteristic makes treatment challenging, since high doses of radiation have a major impact on neurological development when applied on very young children.[4,5] As a result, there was a concern about the use of radiotherapy in children aged 3 years or younger in the 1980s, which led to a decrease in the necessary radiotherapy doses for this population and consequently increased treatment failures, although post-treatment complications remained.[6]

In addition, astrocytomas stand out as high incidence tumors among the population between 0 and 14 years of age, with pilocytic and pilomyxoid astrocytomas being the most common subtypes in this age group. Both are typically located in the hypothalamic region, with significant potential for diffusion, leading to a worse prognosis.[7,8] This brain location encompasses the diencephalon, since pilomyxoid astrocytomas were known as pilocytic astrocytomas of the diencephalon.[8]

Therefore, malignant brain neoplasms are divided into 10 main subtypes according to their topographic location, corresponding to the brain, excluding lobes and ventricles; frontal lobe; temporal lobe; parietal lobe; occipital lobe; cerebral ventricle; cerebellum; brain stem; brain with invasive lesion and, lastly, malignant brain neoplasm, unspecified.[2] This information is essential for understanding the cellular metabolism within the neoplastic microenvironment, since intense angiogenesis occurs in tumors larger than 1 to 2 mm in diameter, which in turn, increases the capillary network in the region. This proximity to blood vessels may indicate the occurrence of metastasis, essential information for the effectiveness of the treatment, since tumors with this characteristic are resistant to chemotherapy.[9,10] This highlights the importance of knowing the specific location of the tumor in order to relate the most appropriate treatment to the specificities of this neoplasm, which, in Brazil, varies between the combination of medication, surgery, chemotherapy, and radiotherapy.[2]

In this way, the current study aims to verify the number of deaths in pediatric patients due to malignant brain neoplasms in the predefined period above, as well as to obtain the number of deaths by age group, sex and administrative region and calculate the mortality indicators for the variables studied, in addition to defining the most recurrent neoplastic subtypes as the causes of death during this period.

Thus, this study is justified because understanding the data regarding deaths due to malignant brain neoplasms during the described period is of utmost importance for the adequacy of palliative care and support strategies for pediatric patients diagnosed with malignant brain neoplasms. Based on this analysis, this study opens up opportunities for the implementation of measures that reduce mortality in this population.

METHODS

This is a retrospective ecological study with a quantitative approach, conducted with secondary data from the *Secretaria de Vigilância em Saúde e Ambiente*. The following steps were necessary to carry out this work: i) Literature review on the subject; ii) Data collection through the systems of the *Secretaria de Vigilância em Saúde e Ambiente*, *Departamento de Informática do Sistema Único de Saúde (DATASUS)* and *Instituto Brasileiro de Geografia e Estatística (IBGE)*; iii) Processing of the collected data using Excel 2019; and iv) Analysis and description of the results found.

Data collection related to mortality was conducted through the ICD-10 Mortality Monitoring Panel, which is available in the Department of Epidemiological Analysis and Surveillance of Noncommunicable Diseases of the *Secretaria de Vigilância em Saúde e Ambiente*. The variables analyzed were the administrative region, age group, race and sex. All data were collected based on the following indicators: (C71) Malignant neoplasm of the brain; (C71.0) Malignant neoplasm of brain, excluding lobes and ventricles; (C71.1) Malignant neoplasm of frontal lobe; (C71.2) Malignant neoplasm of temporal lobe; (C71.3) Malignant neoplasm of parietal lobe; (C71.4) Malignant neoplasm of occipital lobe; (C71.5) Malignant neoplasm of cerebral ventricle; (C71.6) Malignant neoplasm of cerebellum; (C71.7) Malignant neoplasm of brain stem; (C71.8) Malignant neoplasm of overlapping sites of brain; and (C71.9) Malignant neoplasm of brain, unspecified.

Population data from 2012 to 2021 were collected from *DATASUS*, through *TabNet*. Under the "Demographic and Socioeconomic" tab, on the "Resident Population" page. The database chosen was the "Population Projection of the Federative Units by Sex, Simple Age or Age Group: 2010-2060 (2018 edition)". The demographic data for 2022 were collected from the 2022 Population Census on the *IBGE* website. The variables used for the collection were the years chosen for the study, sex and age group.

After the collection procedures were completed, the data were tabulated in the Microsoft Excel computer program. From the data obtained, the specific mortality rate for the predicted indicators was calculated, using the formula:

$$\frac{Number\,of\,Deaths\,of\,the\,Variable\,Studied}{Total\,Population\,of\,the\,Variable\,Studied} x 1.000.000$$

The analyzed data were discussed based on the scientific literature available related to the topic, with consultation of gray literature, relating to information collected from government agencies and guidelines. As this is a study that uses secondary data from the health information system, it was not necessary to submit it to the Research Ethics Committee.

RESULTS

Mortality by Region

Between 2012 and 2022, there were a total of 4,370 deaths from malignant brain neoplasms in children aged 0 and 14 years old, with the years 2012 and 2020 presenting the highest and lowest mortality rates, being 9.8 and 7.8 deaths per 1 million inhabitants, respectively (Table 1). The year 2012 also recorded the highest number of deaths, with a total of 458 deaths, of which the Southeast region accounted for 189 of these deaths.

Table 1 - Reported Deaths of Pediatric Patients Due to Malignant Brain Neoplasms in Brazil from 2012 to 2022 by Region

YEAR	REGION										TOTAL DEATHS
	CENTRAL-WEST		NORTHEAST		NORTH		SOUTHEAST		SOUTH		
	NUMBER OF DEATHS	MORTALITY RATE	NUMBER OF DEATHS	MORTALITY RATE	NUMBER OF DEATHS	MORTALITY RATE	NUMBER OF DEATHS	MORTALITY RATE	NUMBER OF DEATHS	MORTALITY RATE	
2012	44	12,4	116	8,2	35	8,6	189	10,5	74	12,3	**458**
2013	45	12,7	108	7,7	50	9,8	175	9,9	71	11,9	**449**
2014	30	8,5	123	9,0	46	9,1	178	10,1	52	8,8	**429**
2015	42	7,2	123	9,1	39	7,8	136	7,8	58	9,9	**398**
2016	23	6,5	106	8,0	43	8,6	157	9,1	54	9,3	**383**
2017	40	11,2	114	8,7	48	9,7	156	9,1	60	10,4	**418**
2018	29	8,1	106	8,1	38	7,7	152	8,8	56	9,7	**381**
2019	30	8,4	119	9,2	28	5,7	158	9,2	55	9,5	**390**
2020	41	11,4	75	5,9	39	7,9	156	9,1	34	5,9	**345**
2021	30	8,3	111	8,8	30	6,1	153	8,9	48	8,3	**372**
2022	27	7,9	88	7,6	32	7,3	143	9,4	57	10,3	**347**
TOTAL	**381**	**x = 9,3**	**1189**	**x = 8,2**	**428**	**x = 8,0**	**1753**	**x = 9,3**	**619**	**x = 9,7**	**4370**

Mortality Rate: Number of Deaths per 1,000,000 Inhabitants
x: Arithmetic Mean

Source: (Adapted from the Sistema de Informações sobre Mortalidade, 2024)

In 2012, the Southeast region had the highest number of deaths overall (Table 1), but it was the Central-West region that had the highest mortality rate, with 12.4 per 1 million inhabitants. The South came next, with a rate of 12.3 deaths per 1 million inhabitants, while the Southeast ranked third, with a coefficient of 10.5 deaths per 1 million inhabitants. Notably, the Northeast had the lowest mortality rate that year, with 8.2 deaths per 1 million inhabitants.

The year 2020 had a total of 345 deaths (Table 1), making it the period with the lowest mortality due to malignant brain neoplasms, with the highest mortality rate belonging to the Central-West region and the lowest to the Northeast and South regions, which obtained the same coefficient. Thus, the highest and lowest rates, respectively, correspond to 11.4 and 5.9 deaths per 1 million inhabitants. However, the regions with the highest and lowest number of deaths were the Southeast and South, with 156 and 34 deaths, respectively.

When analyzing all mortality rates by region within the period studied, it was observed that the South region had the highest average of these rates, leaving the Central-West and Southeast in second place, even though the Southeast region had the highest number of deaths during the period analyzed, corresponding to 1,753 deaths. The North was the region with the lowest mortality rates during 4 of the 11 years studied.

Mortality by Sex

When analyzing deaths and mortality rates from malignant brain neoplasms by sex, it was observed that males were the most affected by this tumor, with a total of 2,312 deaths in the period studied, while females had a total of 2,057 deaths in the same period (Table 2). During this period, there was 1 death in which sex was not recorded, and it was excluded from the count without affecting the calculations of mortality rates.

The years 2013 and 2020 recorded the highest and lowest male mortality rates, at 10.1 and 8.3 deaths per 1 million inhabitants, respectively. In females, the highest mortality rate was recorded in 2012, with a rate of 9.6 deaths per 1 million inhabitants, while the lowest rate occurred in 2020, with a rate of 7.3 deaths per 1 million inhabitants. For better visualization of the data, the deaths from this period are shown in Table 2.

Table 2 - Reported Deaths of Pediatric Patients Due to Malignant Brain Neoplasms in Brazil from 2012 to 2022 by Sex

YEAR	SEX				TOTAL DEATHS
	MALE		FEMALE		
	NUMBER OF DEATHS	MORTALITY RATE	NUMBER OF DEATHS	MORTALITY RATE	
2012	237	9,9	221	9,6	**458**
2013	238	10,1	211	9,3	**449**
2014	230	9,8	199	8,9	**429**
2015	215	9,3	183	8,3	**398**
2016	200	8,7	183	8,3	**383**
2017	228	10,0	190	8,7	**418**
2018	195	8,6	186	8,5	**381**
2019	202	8,9	188	8,7	**390**
2020	188	8,3	157	7,3	**345**
2021	191	8,5	181	8,4	**372**
2022	189	9,2	158	8,0	**347**
TOTAL	**2312**	**9,2**	**2057**	**8,6**	**4370**

Source: Adapted from the *Sistema de Informações sobre Mortalidade* (2024)

Although there is a higher occurrence among males in all years, it can be seen that the distribution between the two sexes is quite homogenous. The total number of male deaths during the period represents 52.9% of the total, while deaths among females account for 47.1%.

Mortality by Race

Table 3 shows the number of pediatric deaths due to malignant brain neoplasms distributed throughout the period studied. It is evident that the white population accounts for the majority of deaths, with 2,222 cases recorded over the 11 years. Next, the brown population stands out, with 1,702 deaths. The black population accounts for 175 deaths, while the indigenous population records 24 deaths. The Asian population has the lowest absolute number, with 7 deaths. In addition, the Blank/Unknown category totals 240 deaths.

Table 3 - Reported Deaths of Pediatric Patients Due to Malignant Brain Neoplasms in Brazil from 2012 to 2022 by Race

YEAR	RACE						TOTAL
	WHITE	BLACK	YELLOW	MIXED-RACE	INDIGENOUS	BLANK/UNKNOWN	
2012	241	19	0	166	1	31	**458**
2013	222	21	0	164	2	40	**449**
2014	219	15	2	168	2	23	**429**
2015	221	15	0	134	2	26	**398**
2016	187	17	0	157	2	20	**383**
2017	210	8	0	176	3	21	**418**
2018	182	21	1	158	1	18	**381**
2019	200	16	1	154	2	17	**390**
2020	177	13	1	140	2	12	**345**
2021	171	19	2	158	1	21	**372**
2022	192	11	0	127	6	11	**347**
TOTAL	**2222**	**175**	**7**	**1702**	**24**	**240**	**4370**

Source: Adapted from the Sistema de Informações sobre Mortalidade (2024)

Regarding the annual distribution, 2012 was the year with the highest number of deaths recorded, totaling 458 deaths. Of these, 241 occurred in the white population and 166 in the brown population. In 2013, 449 deaths were recorded, with the majority also concentrated among the white population (222 deaths) and the mixed-race population (164 deaths). In 2014, 429 deaths were recorded, 219 among whites and 168 among mixed-race individuals. In 2015, deaths totaled 398, with 221 among whites and 134 among mixed-race individuals (Table 3).

In the following years, the trend of higher numbers of deaths in the white and mixed-race populations continued. In 2016, there were 383 deaths in total (8.8%), with 187 among whites and 157 among mixed-race individuals. In 2017, there was an increase to 418 deaths, with 210 among whites and 176 among mixed-race individuals. In 2018, deaths totaled 381, of which 182 occurred in the white population and 158 in the mixed-race population. Finally, 2022 was the year with the lowest number of deaths recorded, totaling 347 cases, 192 among white people and 127 among brown people (Table 3).

Mortality by Age Group and Topographic Location

As can be seen from Table 4, among the 4,370 deaths recorded in the period from 2012 to 2022, 1,605 of these deaths belonged to the age group between 5 and 9 years, while the age group under 1 year presented 254 deaths, this being the lowest value recorded for the period. Furthermore, category C71.0, that is, Malignant neoplasm of the brain, except lobes and ventricles, was the location of the brain with the most deaths recorded, corresponding to 1,152 deaths, while the parietal lobe (C71.3) and frontal lobe regions were the locations with the lowest deaths recorded throughout the studied period, presenting 5 and 11 deaths, respectively. In the analyzed period, there were also 1,803 deaths recorded due to unspecified malignant neoplasms of the brain (C71.9).

Table 4 - Reported Deaths of Pediatric Patients Due to Malignant Brain Neoplasms in Brazil from 2012 to 2022 by Location and Age Group

LOCATION	AGE GROUP				TOTAL
	INFANT	1-4 YEARS	5-9 YEARS	10-14 YEARS	
(C71.0) Malignant neoplasm of brain, excluding lobes and ventricles	85	308	389	370	**1152**
(C71.1) Malignant neoplasm of frontal lobe	2	4	2	6	**14**
(C71.2) Malignant neoplasm of temporal lobe	0	0	3	8	**11**
(C71.3) Malignant neoplasm of parietal lobe	0	0	3	2	**5**
(C71.4) Malignant neoplasm of occipital lobe	1	6	4	2	**13**
(C71.5) Malignant neoplasm of cerebral ventricle	16	28	19	20	**83**
(C71.6) Malignant neoplasm of cerebellum	13	171	191	163	**538**
(C71.7) Malignant neoplasm of brain stem	15	120	360	145	**640**
(C71.8) Malignant neoplasm of overlapping sites of brain	7	46	27	31	**111**
(C71.9) Malignant neoplasm of brain, unspecified	115	556	607	525	**1803**
Total	**254**	**1239**	**1605**	**1272**	**4370**

Source: (Adapted from the Sistema de Informações sobre Mortalidade, 2024)

As we can see in Table 5, in relation to the mortality of children under 1 year of age, there were 254 total deaths recorded in the period analyzed. The highest mortality rate in this age group was recorded in 2012, with a coefficient of 11.0 deaths per 1 million inhabitants, corresponding to 32 deaths. In 2018, this amount decreased significantly, with the coefficient for this year being 5 deaths per 1 million inhabitants, which is equivalent to 15 deaths in the population under 1 year of age during this period.

Table 5 - Number of Deaths and Mortality Rate of Pediatric Patients Due to Malignant Brain Neoplasms Reported in Brazil from 2012 to 2022 by Age Group

YEAR	AGE GROUP								TOTAL DEATHS
	INFANT		1-4 YEARS		5-9 YEARS		10-14 YEARS		
	NUMBER OF DEATHS	MORTALITY RATE	NUMBER OF DEATHS	MORTALITY RATE	NUMBER OF DEATHS	MORTALITY RATE	NUMBER OF DEATHS	MORTALITY RATE	
2012	32	11,0	124	10,6	159	10,3	143	8,5	**458**
2013	27	9,3	143	12,3	150	9,9	129	7,8	**449**
2014	21	7,1	129	11,1	162	10,8	117	7,3	**429**
2015	24	8,0	104	8,9	150	10,1	120	7,6	**398**
2016	21	7,1	103	8,8	141	9,6	118	7,6	**383**
2017	24	8,2	137	11,6	149	10,2	108	7,0	**418**
2018	15	5,0	109	9,2	136	9,4	121	8,0	**381**
2019	29	9,8	94	7,9	162	11,1	105	7,0	**390**
2020	21	7,1	91	7,7	126	8,6	107	7,2	**345**
2021	22	7,5	109	9,3	138	9,4	103	7,0	**372**
2022	18	7,6	96	9,3	132	9,6	101	7,4	**347**
TOTAL	**254**	**x = 8,0**	**1239**	**x = 9,7**	**1605**	**x = 9,9**	**1272**	**x = 7,5**	**4370**

Mortality Rate: Number of Deaths per 1,000,000 Inhabitants
x: Arithmetic Mean

Source: Adapted from the *Sistema de Informações sobre Mortalidade* (2024)

Among pediatric patients, 1,239 were aged 1 to 4 years at the time of death. It is observed that for the age group analyzed, the year with the highest mortality rate recorded was 2013, followed by 2017, with 12.3 and 11.6 deaths per 1 million inhabitants, respectively. The lowest mortality rates for the population aged 1 to 4 years were recorded in 2020, with a rate of 7.7 deaths per 1 million inhabitants; in 2019, with 7.9 deaths; and in 2018, with 8.8 deaths due to malignant brain neoplasms (Table 5).

In the period analyzed, there were 1,605 deaths recorded in the age group of 5 to 9 years. Calculating the mortality rates per 1 million inhabitants, it was found that the highest mortality coefficient was 11.6 in 2019, followed by the mortality coefficients of 10.8, 10.3 and 10.2, recorded, respectively, in 2014, 2012 and 2017. The lowest mortality rate per 1 million inhabitants was 8.6 deaths, recorded in 2020, followed by the lowest coefficients found in 2018 and 2021, with 9.4 deaths in both years (Table 5).

Of the total deaths registered during the period studied, there were 1,272 deaths in the age group of 10 to 14 years. Among the years analyzed, 2012 was the one with the highest mortality rate, at 8.5 deaths per 1 million inhabitants in the age group of 10 to 14 years, in a sequential and decreasing manner, the years 2018 and 2013 recorded the highest rates after 2012, with 8.0 and 7.3 deaths per 1 million inhabitants, respectively. The years with the lowest rate recorded were 2017, 2019 and 2021, with all presenting a mortality rate per 1 million inhabitants equal to 7 deaths (Table 5).

DISCUSSION

Based on the results obtained in this study, the Southeast region stands out as having the highest number of deaths recorded in 2012, this can be explained by its large population aged 0 to 14 years, which in the year mentioned had the highest population record of this age group among all regions in the 11 years analyzed, equivalent to 17,948,526 inhabitants.[a] Despite the high number recorded, the region did not have the highest mortality rates, considering its population density.

On the other hand, the highest mortality rates during the analyzed period belong, respectively, to the Central-West, South and Southeast regions, with most of the deaths occurring among the white population. These findings may reflect the population density of each region, since, according to the 2022 Population Census, available on the *IBGE* website, these regions are predominantly Caucasian, although the national population is predominantly brown.[11] Therefore, it is noteworthy that these regions may be more vulnerable to mortality from these neoplasms when compared to the rest of the country due to genetic factors, since, according to a study conducted by Ostrom, *et al*. (2019), the Caucasian population is the most susceptible to the development of central nervous system tumors, especially men.[12]

Based on the results found, a high mortality rate was observed in the category C71.0 (malignant neoplasm of the brain, except lobes and ventricles), which recorded 26.4% of the total deaths analyzed. These findings align with the results of Leece, *et al*. (2017), who highlighted a high incidence of pilocytic and pilomyxoid astrocytomas in patients aged 0 to 14 years.[7]

It is noteworthy that these tumors show a peak incidence in the age group of 5 to 9 years, this being the age group with the highest number of deaths found in this study.[13] Other important sites of occurrence of astrocytomas are the brainstem and cerebellum, with the latter site also being the main region of development of medulloblastomas, which is consistent with the predominance of deaths in subcategories C71.7 and C71.6, respectively, thus serving as a possible explanation for these data.[2,13]

Furthermore, the study highlights that pilocytic astrocytomas can also appear in the cerebral hemispheres, which may contribute to mortality related to tumors in the parietal and frontal lobes.[14] These regions have the lowest mortality rates when compared to other regions of the cerebrum, which may be explained by both the lower occurrence of these tumors in these regions and their greater accessibility to them, making it more feasible to perform complete resection of local tumors, such as through supraorbital craniotomy.[14,15] Tumors in the thalamic region, for example, are difficult to access and, therefore, more difficult to remove completely with surgery, which may be related to worse prognoses and higher mortality rates.[16]

Finally, it is mentioned that the most commonly used treatment for pilocytic astrocytomas in pediatric patients is complete removal of the tumor; however, even with resection, there may be recurrence, which could serve as justification for the mortality peaks observed across different pediatric age groups.[17]

[a] Available: http://tabnet.datasus.gov.br/cgi/tabcgi.exe?ibge/cnv/popsvsbr.def. Accessed on: 02/12/2024.

CONCLUSION

Based on the information presented and the results found, the highest absolute number of deaths, according to the demographic variables studied, was among male patients, aged 5 to 9 years old and from the Southeast region. Regarding the mortality rate, which represents the absolute risk of death, it is higher in males, aged between 5 and 9 years and in the Central-West region. It was also found that, accounting for 26.4% of deaths, brain neoplasms that do not involve lobes and ventricles were the most recurrent in the period, when excluding those cases whose location was not recorded.

In overview, this study points to a complex network of factors that influence the mortality rates of pediatric patients in Brazil due to malignant brain neoplasms, which permeate gender, age, region of residence and the neoplastic topography. This highlights the point that healthcare professionals come to understand the specific needs of this population and are able to adapt their care approach, achieving greater effectiveness in health interventions. Furthermore, constant epidemiological surveillance, combined with an understanding of the factors that lead to the development of neoplasms, helps guide public health policies in promoting health and providing appropriate treatments for the affected conditions, and also influences the implementation of new treatment technologies, in an attempt to globalize Brazil's health standards and reduce mortality rates.

As for the limitations of the method, it is worth noting that records from both *DATASUS* and the *Sistema de Vigilância em Saúde e Ambiente* may result in underreporting of neoplasia cases, due to the presence of the "blank/unknown" field. This field generates a lack of more specific information that may reduce understanding of the diseases studied. Furthermore, data on population counts by race/color are unavailable on *DATASUS* and on the *IBGE* website, and consequently, it was not possible to calculate mortality rates for this variable, thus representing a limitation to the study. However, the limitations of this study were mitigated, as it was possible to calculate specific mortality rates without prejudice, because the variables worked on were all recorded.

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