

ARTICLE

Sociodemographic and clinical factors associated with cryptorchidism in live births in Brazil: A 20-year analysis

Diego Bessa Dantas,¹ Dionata da Costa,¹ Edila Andrade,¹ Maria do Socorro Bastos,¹ Fabiana Gomes,² João Simão de Melo-Neto¹

¹*School of Physiotherapy and Occupational Therapy, Federal University of Pará (UFPA), Belém*

²*School of Medicine of São José do Rio Preto (FAMERP), São José do Rio Preto, SP, Brazil*

Abstract

Background: Cryptorchidism is a congenital disorder that causes an irregularity in the permanent or temporary descent of one or both testicles. In Brazil, there are no comprehensive studies describing the association of demographic, social, and clinical characteristics in relation to cryptorchidism.

Objectives: This study aims to verify possible associations of clinical and sociodemographic characteristics in patients with cryptorchidism.

Design and Methods: An analytical, descriptive and retrospective study was carried out based on secondary data of 5,168 live births with cryptorchidism recorded in the Live Birth Information System (SINASC), Brazil from 1999 to 2018. The socio-demographic factors analyzed were the geographic region, age, education and marital status of the mothers. The clinical factors analyzed were the duration and type of pregnancy. The place of birth was also analyzed as a secondary outcome.

Results: This research analyzed all live births during the study period, in Brazil. The chance of cryptorchidism in the neonate is more common in women who become pregnant later (≥ 30 years of age) and with a higher level of education (≥ 8 years). The risk of cryptorchidism in relation to the federation units is higher in Paraíba, Pernambuco, Sergipe, São Paulo, and Santa Catarina. Regarding the clinical characteristics, the shorter pregnancies, which characterize premature births, are a risk for the appearance of cryptorchidism in the country.

Conclusion: Thus, in this study, we found that sociodemographic and clinical factors have specific characteristics that predict cryptorchidism in newborns in Brazil.

Introduction

Cryptorchidism, also called undescended testicle, is a congenital alteration that causes an irregularity in the permanent or temporary descent of one or both testicles, with a predominance of 1.8

to 8.4% in boys born weighing more than 2500 g at birth. There is an association with a future danger of infertility in men with cryptorchidism, caused by a decrease in semen quality.¹ Cryptorchidism not only alter the handers and function of Sertoli cells and Leydig cells, but also for the germ cells.¹⁻³

It is believed that the testicular descent process occurs in two phases of the gestational period: between 8 to 15 weeks and 25 to 35 weeks of gestation, through the excretion of hormones. The congenital alteration that prevents the descent of the testicles probably occurs due to supposed interruptions in one or both phases. However, the processes that lead to these interruptions are not well defined.^{4,5} Epidemiological studies show that maternal smoking and gestational diabetes are associated with the risk of developing cryptorchidism. In addition, low birth weight and delayed intrauterine growth are the most noticeable characteristics in boys with cryptorchidism.⁵

Cryptorchidism, in most cases, is later accompanied by a reversibility of the case, that is, there is a spontaneous descent from the testicle to the scrotum. This change occurs more frequently in individuals in their first months of life and those who were born prematurely.⁶ It is estimated that, annually, 30% of premature births are affected by cryptorchidism worldwide. In addition, testicular ectopia has a higher incidence among these individuals. It is also observed that 3 to 5% of full-term newborn present cryptorchidism, being the most prevalent unilateral type, a condition in which one of the testicles is not present in the scrotal.⁷ The exposure of pregnant women to different types of pesticides can lead to adverse results in pregnancy, and thus, cryptorchidism is closely linked to environmental issues.

Currently, Brazil is first on the world ranking of pesticide consumption, of which more than half are at great risk to human health.⁸ From studies on the subject, it was deduced that women, before or during pregnancy, who have constant contact with pesticides, are at great risk of giving birth to individuals with congenital malformations. In addition, some of these pesticides can act as endocrine disruptors, which can cause problems for live births, such as cryptorchidism. Other environmental issues such as air pollution, deforestation, and exposure to heavy metals were also

Significance for public health

Better understanding which groups are exposed to a greater risk of cryptorchidism, makes these factors extremely important for the development of public policies that can favor the reduction of cases of the disease in Brazil. This research found that the occurrence of cryptorchidism is increasing in the country, and that sociodemographic characteristics, such as region where they live, level of education, marital status and maternal age, as well as clinical characteristics, such as duration and type of pregnancy, and place of occurrence, may be associated with this phenomenon.

identified as possible generators of a testicular ectopic condition.⁹ However, in Brazil, there are no comprehensive studies describing the association of demographic, social, and clinical characteristics in relation to cryptorchidism. Taking the available data into account, the investigation of these factors becomes extremely important for the development of public policies that may favor a decrease in cases of the disease in the country. Thus, this study aims to verify possible associations of the aforementioned factors.

Design and Methods

Ethics

This study analyzed secondary data available in the Department of Informatics of the National Health System (DATA-SUS).¹⁰ The data are publicized with unrestricted use and access. Ethical assessment of the research ethics committee is not required according to the terms of the National Health Council Resolution n. 510, April 7, 2016.

Type of study

An analytical, descriptive, and retrospective study was carried out, based on secondary data on live births with cryptorchidism registered in the Live Birth Information System (SINASC) of the Ministry of Health, Brazil.

Database

SINASC is a secondary database available on the Ministry of Health's DATASUS.¹⁰ Data on live births recorded from 1999 to 2018 in Brazil in the health information system were recovered. The total number of live births with cryptorchidism in the period of interest is 5,168 children.

Primary outcomes

Sociodemographic factors were geographic regions, age, educational level, and marital status of the mothers. Classification of the factors are as follows: geographic regions (North, Northeast, Midwest, South, and Southeast); age (≤ 19 , 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, ≥ 80 years); marital status (single, married, widowed and divorced); and educational level (no schooling to 12 or more years of education).

The clinical factors analyzed were the duration and the length of pregnancy. Duration of pregnancy (less than 22 weeks, 22 to 25 weeks, 28 to 31 weeks, 32 to 36 weeks, 37 to 41 weeks and 42 weeks or more) and length of pregnancy (Single, Double, Triple or more) were classified.

Secondary outcomes

The place of occurrence (hospital or home) of the childbirth was analyzed.

Statistical analysis

The data were submitted to descriptive and inferential analysis. For the description of the data, relative and absolute frequencies were used. The data were submitted to the Shapiro-Wilk test to verify the distribution of the normality of the data. The Pearson r correlation test (parametric) was used to verify the level of correlation between the rate of live births and cryptorchidism per year. To check the coefficient of determination, the square R (r^2) test was used. In addition, linear regression was applied for data analysis.

Chi-square was used to examine associations between categorical variables ($p < 0.05$). Odds ratios (ORs) with 95% confidence intervals (95% CI) were used to quantify the degree of association for the occurrence of cryptorchidism in live births in Brazil. The statistical program used for data analysis was BioEstat 5.0.

Results

A total of 5135 children with cryptorchidism and a corresponding number of mothers were studied. The distribution of the rate of live births per 100,000 inhabitants is shown in Figure 1. We observed that there was a positive correlation with an increase in the number of children with cryptorchidism in recent years.

Sociodemographic variables

Region

The association tests showed that, children born in the North, Northeast, or Midwest region of Brazil presented a low risk for cryptorchidism, while children born in the Southeast region presented a high-risk factor for cryptorchidism (Table 1).

Regarding the federation units, no state in the North region presented results considered as a risk factor for cryptorchidism, on the contrary. In the Northeast region, the states of Paraíba, Pernambuco, and Sergipe showed results considered high risk factors for cryptorchidism, while Maranhão, Rio Grande do Norte, Alagoas, and Bahia presented a low risk. In the Midwest, the states of Mato Grosso, Mato Grosso do Sul, and Goiás presented a low risk for cryptorchidism. In the Southeast region, only the state of São Paulo and Rio de Janeiro showed high and low risk factor for cryptorchidism, respectively. In the South region, the state of Paraná presented a low risk for cryptorchidism, but the state of Santa Catarina presented the greatest risk factor in the country (Table 1).

Mother's education level

The results demonstrated that mothers who had less than seven years of study, presented low risk for cryptorchidism in their neonates. However, mothers who have a high educational level, that is, eight or more years of schooling, were associated with high risk of cryptorchidism in their neonates (Table 1).

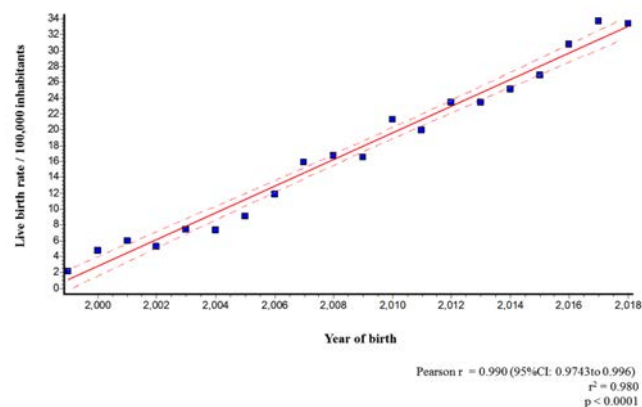


Figure 1. Distribution of the live birth rate with cryptorchidism per year.

Mother's age

In relation to maternal age, the results showed that mothers, who had delivery before the age of 24, indicated a protective factor

against cryptorchidism. Mothers who had children after 30 years of age had a greater chance of their children birthed with cryptorchidism (Table 1).

Table 1. Region, age, education level and marital status of the mothers.

	Cryptorchidism absent (n=37,977,308)	Cryptorchidism present (n=5135)	OR	95% IC	p
North	7,406,170	147	0.264	(0.224, 0.311)	0.0001
Rondônia	703,032	21	0.426	(0.277, 0.654)	<0.0001
Acre	396,418	5	0.180	(0.075, 0.433)	<0.0001
Amazonas	1,745,032	41	0.332	(0.244, 0.451)	<0.0001
Roraima	241,659	1	0.059	(0.008, 0.420)	0.0002
Pará	3,330,909	36	0.149	(0.107, 0.207)	<0.0001
Amapá	363,421	12	0.472	(0.268, 0.833)	0.0107
Tocantins	625,699	31	0.709	(0.498, 1.010)	0.0662
Northeast	21,320,374	1383	0.906	(0.852, 0.964)	0.0019
Maranhão	2,693,111	11	0.056	(0.031, 0.102)	<0.0001
Piauí	1,226,823	71	0.828	(0.655, 1.047)	0.1284
Ceará	3,284,707	228	0.996	(0.872, 1.138)	0.9866
Rio Grande do Norte	1,260,423	28	0.315	(0.217, 0.457)	<0.0001
Paraíba	1,398,953	178	1.856	(1.598, 2.156)	<0.0001
Pernambuco	3,705,930	567	2.344	(2.148, 2.558)	<0.0001
Alagoas	1,459,777	36	0.349	(0.251, 0.485)	<0.0001
Sergipe	923,425	93	1.454	(1.184, 1.785)	0.0004
Bahia	5,367,225	171	0.438	(0.376, 0.511)	<0.0001
Southeast	29,439,853	2627	1.572	(1.488, 1.660)	<0.0001
Minas Gerais	6,266,677	414	0.944	(0.853, 1.043)	0.2730
Espírito Santo	1,357,711	89	0.940	(0.762, 1.159)	0.5985
Rio de Janeiro	5,901,184	357	0.859	(0.771, 0.956)	0.0060
São Paulo	15,896,281	1767	1.905	(1.799, 2.018)	<0.0001
South	10,275,059	757	1.067	(0.988, 1.153)	0.0992
Paraná	4,153,559	145	0.486	(0.412, 0.574)	<0.0001
Santa Catarina	2,268,088	352	2.318	(2.080, 2.583)	<0.0001
Rio Grande do Sul	3,853,412	260	0.967	(0.853, 1.095)	0.6225
Midwest	5,768,464	254	0.613	(0.540, 0.695)	<0.0001
Mato Grosso do Sul	1,050,160	15	0.202	(0.122, 0.336)	<0.0001
Mato Grosso	1,261,656	34	0.382	(0.273, 0.536)	<0.0001
Goiás	2,320,427	129	0.793	(0.666, 0.944)	0.0103
Distrito Federal	1,136,221	76	0.959	(0.765, 1.203)	0.7660
Mother's age					
14 years or any less (-)	655,813	34	0.737	(0.526, 1.033)	0.0886
15 to 19 years	14,652,974	872	0.817	(0.760, 0.879)	<0.0001
20 to 24 years	21,304,161	1325	0.847	(0.796, 0.902)	<0.0001
25 to 29 years	17,564,324	1175	0.940	(0.881, 1.003)	0.0654
30 to 34 years	11,993,963	1000	1.234	(1.151, 1.322)	<0.0001
35 to 39 years	5,902,501	598	1.502	(1.379, 1.636)	<0.0001
40 to 44 years	1,494,116	153	1.474	(1.255, 1.731)	<0.0001
45 to 49 years	108,862	9	1.179	(0.613, 2.267)	0.7542
50 years or more (+)	6,368	2	4.479	(1.119, 17.919)	0.1150
Mother's education level					
None	2,110,328	42	0.219	(0.162, 0.297)	<0.0001
1 to 3 years	4,887,778	198	0.437	(0.379, 0.504)	<0.0001
4 to 7 years	15,957,621	1114	0.734	(0.687, 0.784)	<0.0001
8 to 11 years	25,796,262	2734	1.436	(1.359, 1.517)	<0.0001
12 years or more (+)	9,207,348	1019	1.319	(1.232, 1.413)	<0.0001
Mother's marital status					
Single	27,186,900	2340	0.912	(0.864, 0.964)	0.0012
Married	20,436,073	1854	1.006	(0.950, 1.065)	0.8339
Widow	136,960	13	1.050	(0.609, 1.810)	0.9713
Judicially separated	547,561	60	1.215	(0.942, 1.567)	0.1519
Consensual union	8,342,110	851	1.154	(1.073, 1.243)	0.0001

p≤0.05, Chi-square test with Yates correction. OR, odds ratio; 95% CI, confidence interval.

Mother's marital status

The mothers' marital status showed no association for the occurrence of cryptorchidism (Table 1).

Clinical variables

Type of pregnancy

The type of pregnancy showed no association (Table 2).

Gestation duration

The results on the duration of pregnancy revealed that women who had a gestation of 37 to 42 weeks or more, had a protective factor in the appearance of cryptorchidism, whereas women who had a shorter pregnancy between 28 to 36 weeks of gestation had a high-risk factor (Table 2).

Place of occurrence

The place where the birth occurred (hospital and home) was evaluated. The results demonstrated that the births at home had a low risk, but the ones that occurred in the hospital presented high risk for cryptorchidism (Table 2). Cryptorchidism not only alter the handers and function of Sertoli cells and Leydig cells, but also for the germ cells.

Discussion

Cryptorchidism may result in infertility, caused by a decrease in semen quality by altering a function of sertoli, leydig cells and germ cells.^{1,3} However, with these implications, sociodemographic and clinical factors are rarely studied in Brazil. Thus, this study investigated and identified that there are specific associations of these factors that predict cryptorchidism in newborns in Brazil.

Cryptorchidism presented increased risk in the federation units: São Paulo, Paraíba, Pernambuco, Sergipe, and Santa Catarina. Although the South region has the most prevalence, only the federation units São Paulo presented increased risk. Some factors that have been related to this increased risk, among them are pesticide use and smoking. In this context, the particularities of each site have to be considered. Regarding the use of pesticides, some federation units have a high use of pesticides for sugarcane. The federation units: São Paulo (66%), Paraíba (37%), and Pernambuco (38%) present sugarcane as the predominant agricul-

tural crop type.¹¹ Sergipe (15%) presents sugarcane as the second predominant agricultural crop type and interestingly it is the place of association with the lowest risk among all.¹¹ However, Santa Catarina differs from the other federation units; it presented the largest tobacco crops (7%) in Brazil.¹¹ In this context, the relationship between cryptorchidism and tobacco should be considered. It is public knowledge that smoking is associated with a risk in the development of cryptorchidism;⁵ despite the continuous decrease in recent years of tobacco consumption by women in Brazil, there is still a considerable percentage (11.2%). In a study¹² to evaluate the prevalence of pregestational and gestational smoking, the authors observed higher incidence of tobacco in women from the South and Southeast regions of Brazil, which reflects in the higher risk of cryptorchidism in Santa Catarina (South) and São Paulo (Southeast). In addition, we observed an increasing number of live births with cryptorchidism, and hence, the higher use of pesticides may be taken into account. Recently, Brazil was affected by an outbreak of Zika virus, which until then, was associated with microcephaly and other clinical findings, including intrauterine infections.¹³ Meanwhile, a study was published evaluating the relationship of cryptorchidism in children with microcephaly due to the Zika virus. In their findings, Rômulo *et al.*¹⁴ reported that, of the children evaluated with microcephaly, over 34% also had cryptorchidism. It was then hypothesized that cryptorchidism is an additional impairment of congenital Zika syndrome. However, since the outbreak of the Zika virus epidemic occurred in the Brazil, these findings have contributed to a high risk of cryptorchidism in the last years. The chance of cryptorchidism in the neonate is more common in women who become pregnant later and with a higher level of education. Late pregnancy has been pointed out as a risk factor for cryptorchidism, especially when it is primiparous, indicating that the presence of subfertility is directly linked to increased risk.¹⁵ In addition, women with higher levels of education have access to opportunities that directly influence their choices regarding the gestational process and their own reproductive health.¹⁶ Thus, the higher level of education may be related to choosing to have children later, as it also indicates a high probability of interruption in the gestational process in some circumstance of life.¹⁶ For instance, a study reported that, among the reasons listed for choosing the termination of pregnancy, women tend to cite the continuity of studies as a priority.¹⁶

Regarding the clinical characteristics, the shorter pregnancies, which characterize premature births, are a risk for the appearance of cryptorchidism. The length of pregnancy has been shown to be

Table 2. Place of occurrence, type of pregnancy and duration of pregnancy.

	Cryptorchidism absent (n=37,977,308)	Cryptorchidism present (n=5135)	OR	95%CI	p
Place of occurrence					
Hospital	70,537,053	5136	5.257	(2.909, 9.499)	<0.0001
Residence	784,305	11	0.192	(0.106, 0.348)	<0.0001
Type of pregnancy					
One	70,804,395	5058	0.997	(0.819, 1.215)	0.9776
Double	1,340,900	98	1.023	(0.838, 1.250)	0.8603
Triple and more (+)	69,789	3	0.601	(0.193, 1.865)	0.5056
Duration of pregnancy					
27 weeks or any less (-)	364,640	29	1.092	(0.758, 1.573)	0.7065
28 to 31 weeks	483,995	69	1.970	(1.553, 2.498)	<0.0001
32 to 36 weeks	4,152,476	673	2.410	(2.222, 2.613)	<0.0001
37 to 41 weeks	63,659,869	4275	0.525	(0.488, 0.566)	<0.0001
42 weeks or more (+)	1,607,141	73	0.618	(0.490, 0.778)	<0.0001

p \leq 0.05, Chi-square test with Yates correction. OR, odds ratio; 95%CI, confidence interval.

a risk factor for cryptorchidism in some studies^{4,17} and reveals that women who have had a shorter pregnancy are at greater risk of having children with undescended testicles, given the two phases of testicular descent that occur between weeks 8 and 15, and weeks 25 and 35 respectively. Corroborating the results of this study, which points out that pregnancies of 37 weeks or more had a protective factor in the appearance of cryptorchidism, in contrast, women who had a shorter pregnancy between 28 to 36 weeks of gestation had a high risk factor. Knowing the clinical and sociodemographic factors that may be associated with the appearance of cryptorchidism is essential for the development of public policies. However, in Brazil, similar to other developing countries, there are limitations in the quality of data collected. It is possible to observe a large number of unknown or unreported data that greatly impair the reliability of the analysis carried out in studies using secondary banks. Although there is a reduction in underreporting, there is still room for improvement. Another limitation is the alteration of terms and items in the collection worksheets, reducing the standardization in the collection and late release of data on the platform.¹⁸ In this study, we found that the sociodemographic and clinical factors have specific characteristics that predict cryptorchidism in newborns in Brazil. The risk of cryptorchidism in relation to the federation units is higher in Paraíba, Pernambuco, Sergipe, São Paulo, and Santa Catarina. The chance of cryptorchidism in the neonate is more common in women who become pregnant later and with a higher level of education. Regarding the clinical characteristics, the shorter pregnancies, which characterize premature births, are a risk for the appearance of cryptorchidism in the country. These findings can potentially be used to direct new guidelines and improve the guide to public health policies.

Correspondence: João Simão de Melo-Neto, School of Physiotherapy and Occupational Therapy, Federal University of Pará (UFPA), Street Augusto Corrêa 01, University City: José Silveira Neto, Guamá, 66075-110 Belém, PA, Brazil. Tel. +55.91.32018892. E-mail: jsmeloneto@ufpa.br

Contributions: The authors participated in all the stages of the study.

Conflict of interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethics approval and consent to participate: Ethical assessment of the Research Ethics Committee is not required according to the terms of the National Health Council Resolution n. 510, April 7, 2016.

Availability of data and materials: This study analyzed secondary data available in the Department of Informatics of the National Health System (DATASUS). The data are publicized with unrestricted use and access.

Patient consent for publication: Not applicable.

Received for publication: 1 July 2020.

Accepted for publication: 28 September 2020.

©Copyright: the Author(s), 2021

Licensee PAGEPress, Italy

Journal of Public Health Research 2021;10:1850

doi:10.4081/jphr.2021.1850

This work is licensed under a Creative Commons Attribution NonCommercial 4.0 License (CC BY-NC 4.0).

References

- Rodprasert W, Virtanen HE, Mäkelä J.A, Toppari J. Hypogonadism and cryptorchidism. *Front Endocrinol* 2020;10:906.
- Huff DS, Fenig DM, Canning DA, et al. Abnormal germ cell development in cryptorchidism. *Horm Res* 2001;55:11-7.
- Dong LH, Hildorf S, Clasen-Linde E, et al. Postnatal germ cell development in cryptorchid boys. *Asian J Androl* 2020;22:258-64.
- Gurney JK, McGlynn KA, Stanley J, et al. Risk factors for cryptorchidism. *Nat Rev Urol* 2017;14:534-48.
- Barthold JS, Reinhardt S, Thorup J. Genetic, Maternal, and environmental risk factors for cryptorchidism: An update. *Eur J Pediatr Surg* 2016;26:399-408.
- Virtanen HE, Toppari J. Epidemiology and pathogenesis of cryptorchidism. *Hum Reprod Update* 2008;14:49-58.
- Désiré AM, Buhendwa C, Césaire TMA, et al. Epidemiology, diagnosis and therapeutic approaches of cryptorchidism at the Panzi General Hospital, DR Congo: A 5-year retrospective study. *Ethiop J Health Sci* 2020;30:107-14.
- Cremonese C, Freire C, Meyer A, Koifman S. [Pesticide exposure and adverse pregnancy events, Southern Brazil, 1996-2000]. [Article in Portuguese]. *Cad Saude Publica* 2012;28:1263-72.
- Asmus CIRE, Camara VM, Landrigan PJ, Claudio LA. Systematic review of children's environmental health in Brazil. *Ann Global Health* 2016;82:132-48.
- Ministry of Health, Executive Secretariat. DATASUS, Health Information. Available from: <http://www2.datasus.gov.br/DATASUS/index.php?area=0205>
- Pignati WA, Lima FANS, Lara SS, et al. [Spatial distribution of pesticide use in Brazil: a strategy for Health Surveillance]. [Article in Portuguese, En]. *Cien Saude Colet* 2017;22:3281-93.
- Domingues RMSM, Figueiredo VC, Leal MDC. Prevalence of pre-gestational and gestational smoking and factors associated with smoking cessation during pregnancy, Brazil, 2011-2012. *PLoS One* 2019;14:e0217397.
- Russo F.B, Jungmann P, Beltrão-Braga P.C.B. Zika infection and the development of neurological defects. *Cell Microbiol* 2017;19. doi: 10.1111/cmi.12744/
- De Vasconcelos RAL, Ximenes RAA, Calado AA, et al. Cryptorchidism in children with Zika-related microcephaly. *Am J Trop Med Hyg* 2020;102:982-4.
- McGlynn KA, Graubard BI, Klebanoff MA, Longnecker MP. Risk factors for cryptorchidism among populations at differing risks of testicular cancer. *Int J Epidemiol* 2006;35:787-95.
- Biney AAE, Nyarko P. Is a woman's first pregnancy outcome related to her years of schooling? An assessment of women's adolescent pregnancy outcomes and subsequent educational attainment in Ghana. *Reprod Health* 2017;14:123.
- Hutson JM, Balic A, Nation T, Southwell B. Cryptorchidism. *Semin Pediatr Surg* 2010;19:215-24.
- Timoteo F, Korkes F, Baccaglioni W, Glina S. Bladder cancer trends and mortality in the Brazilian public health system. *Int Braz J Urol* 2020;46:224-33.